2024

台灣消化系聯合學術演講年會

高雄 Ko-hiông Kaohsiung

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2024 消化系聯合學術演講年會

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論文摘要

台灣消化系醫學會(第五十四屆)學術演講年會
台灣消化系內視鏡醫學會(第三十三次)學術演講年會

會長演講（台灣消化系醫學會）

New Advance of Immune Mediated Cell Therapy and Microbiome in Cancer Treatment

Deng-Chyang Wu（吳登強）

Kaohsiung Medical University Hospital
（高雄醫學大學附設中和紀念醫院）

In recent years, there has been extensive research on the relationship between the gut microbiota and cancer, and accumulating evidence reveals the role of the microbial community in defining the efficacy and toxicity of cancer treatments. Dr. Koh's research team discovered that certain bacteria in the gut microbiota, such as Bacteroides spp. and Burkholderiales spp., can translocate to other organs, promoting the activation and proliferation of T cells and enhancing systemic anti-tumor immune responses. Findings from a study at UPenn confirmed that the compositional differences of the gut microbiota, antibiotic treatments, or heterologous fecal microbiota transplantation significantly impact the Adoptive cell transfer (ACT) therapy in tumor-bearing mice. The study revealed that depleting bacteria using vancomycin induces an increase in systemic CD8α^+ DCs, which sustain tumor-specific T cells in an IL-12-dependent manner, leading to reduced tumor growth in mice. Conversely, treatment with neomycin and metronidazole showed no effect, highlighting the role of specific gut microbial communities in host responses.

Dr. Kenya Honda published a study in an international journal indicating that 11 strains of bacteria isolated from healthy human feces, when co-colonized in the gut, effectively induce IFN-γ-producing CD8 T cells in the mouse intestine and other organs without causing inflammation. This enhances the host's resistance to Listeria monocytogenes infection and augments the efficacy of immune checkpoint inhibitors in a syngeneic tumor model. The gut microbiota can be easily modulated through various strategies, including fecal microbiota transplantation (FMT), probiotics, and the use of specific antibiotics. Preclinical studies have elucidated the mechanisms by which microbiota influence cancer treatment outcomes, and clinical trials have demonstrated the potential of microbiota in modulating cancer therapies, making them a promising and widely effective biological therapeutic approach.

It is worth noting that recent research has shifted attention to bacteria-mediated synergistic cancer therapy (BMSCT), combining microbiota-based therapies with different conventional anticancer treatments such as chemotherapy, photothermal therapy, reactive oxygen and nitrogen species therapy, immunotherapy, or prodrug-activating therapy. Due to the unique characteristics of microbiota, including tumor-targeting specificity, high motility, immunogenicity, and their use as gene or drug carriers, several types of bacteria have been utilized in the treatment of solid and metastatic tumors. With the development of synthetic biology, engineered and modified microbes have been endowed with controlled expression of therapeutic proteins. Additionally, they are used for targeted drug delivery, photothermal therapy, magnetic hyperthermia, and photodynamic therapy, effectively enhancing the anti-tumor efficiency of synergistic cancer therapies.

會長演講（台灣消化系內視鏡醫學會）

The impact of environmental factors on gastrointestinal health

Chao-Hung Kuo（郭昭宏）

Kaohsiung Municipal Siaogang Hospital
（高雄市立小港醫院）

胃道道疾病是一個多因子的疾病，除了基因及生活習慣之外，環境因子更不能輕忽！環境因子的危害對微生態的影響不容忽視，民眾要重視環境因子造成的危害，不亞於基因及生活習慣的影響，才能讓腸胃道健康更全面性。

胃道道疾病發生主因有三個面向，第一是病人本身基因，包括大腸癌及胃癌都有基因性問題。基因雖不能改變，但基因也會受到外在因子的影響而被誘發或改變，例如飲食習慣若煙酒不斷、喜食刺激物，可能會誘發疾病；另外消化系統相關健康狀態是生活習慣也會影響，如果三餐不正常造成便秘、熬夜讓胃酸變多，這些都會影響到。綜括而言，影響腸胃道健康要素第一是基因，第二是生活習慣。第三要鄭重呼籲的是，民眾要重視「環境因子不能輕忽」！生活週遭中，空氣污染物的來源除了室外環境有 PM2.5、PM10、懸浮微粒、室內環境中有有機溶物、苯等污染物的存在確實會影響到腸胃健康。空氣中的苯確實會影響微生態，苯的長期暴露會影響微生態的豐富度。微生態的豐富度愈不好，人體就愈容易生病，也許是間接造成相關性。另外文獻中發現空氣中的 PM2.5 或懸浮微粒會引起胃腸潰瘍疾病，並且造成十二指腸潰瘍的程度還大於胃潰瘍。最近荷蘭也有發表幾篇相關報告，空污也許和癌症也有相關，包括肝癌及大腸癌。另外輪胎產生的「微膠粒」也有文獻報告會導致大腸癌，其可能機轉與改變微生態可能相關，其間的相互關連性，台灣本土資料未來值得再深入探討。目前也有團隊正在進行人體試驗，希望透過益生菌可中和吸附在腸胃道內的重金屬，藉由排泄排出之作用，評估對病人腸胃道健康之影響。

綜上所述，一定要重視環境因子造成對身體健康的危害，其實不亞於基因及生活習慣的影響。

特別演講（1）

未來十年的消化醫學趨勢

Ming-Shiang Wu（吳明賢）

National Taiwan University Hospital
（臺大醫院）

後疫情時代的醫療有二大趨勢，一是由疾病的醫學轉為健康的醫學，二是由治療的醫學向預防的醫學邁進。台灣的消化系醫學，過去在肝臟、胃及腸道的研究及臨床成果，一直都有很好的傳承。隨著高齡化社會的來臨，疾病的型態也由急性傳染病變成慢性病和癌症為主，一些因現代社會生活習慣所造成的肥胖和代謝性疾病，也會水漲船高。而由於基因序列分析、腸道菌培養及人工智慧等技術的進展，未來 10 年消化醫學，勢必朝向精準醫療和智慧醫療發展。透過基因研究、微生物分析等技術，更容易理解消化系疾病的發病機制和個體差異，實現精準治療和預防。同時，AI 在影像診斷、病理分析等領域的應用將提高診斷準確性和效率，隨著醫療科技的不斷創新，像是微型胃視鏡等技術，將使治療更為輕便和無創。

特別演講（1）

未來十年的內視鏡趨勢

Cheng-Tang Chiu（邱正堂）

Linkou Chang Gung Memorial Hospital
（林口長庚紀念醫院）

In the next decade, the field of gastrointestinal endoscopy is expected to witness several significant trends and advancements. Here are insights into potential developments:

- **Precision Diagnosis and Personalized Treatment:** With technological advancements, we anticipate a more precise diagnosis of diseases using gastrointestinal endoscopy. There may be developments in personalized treatments to more effectively address the unique needs of each patient.
- **Wider Application of Artificial Intelligence:** Over the next ten years, the use of artificial intelligence in gastrointestinal endoscopy is likely to become more extensive. This includes real-time image analysis, lesion detection, and treatment planning, aiming to enhance diagnostic sensitivity and treatment effectiveness.
- **Wearable Technology and Non-invasive Detection:** Novel wearable endoscopy technologies may further improve the patient experience while enabling non-invasive detection and monitoring. Such technologies are expected to enhance patient acceptance and reduce unnecessary discomfort.
- **Advancements in Minimally Invasive Surgery:** As technology progresses, endoscopic surgeries may become more minimally invasive, reducing patient pain and recovery time. This is expected to expand the application of endoscopic surgery and improve surgical outcomes.
- **Real-time Education and Training:** Innovations in education and training may include the application of virtual reality and augmented reality to enhance the skills of doctors and medical students.
- Green endoscope can progress towards a more environmentally friendly and sustainable direction, lowering the carbon footprint , and contributing to the sustainability of healthcare and related fields.

In summary, the gastrointestinal endoscopy field in the next decade will continue to focus on improving diagnostic and treatment outcomes while emphasizing patient comfort and personalized therapy. Technological innovation and interdisciplinary collaboration will be key to achieving these goals.

Details regarding diverse fields will be revealed in this lecture.

特別演講（2）

Mass Spectrometry as Emerging Tools in Clinical Laboratories

Yu-Ju Chen（陳玉如）

Institute of Chemistry, Academia Sinica
（中央研究院）

Personalized proteomics starts to impact the development of precision medicine by facilitating discovery of protein biomarkers, molecular signature of disease subtype and response to treatment of individual patients. Learning from the proteogenomics research from Taiwan Cancer Moonshot project, proteomics-informed classification demonstrated differentiation of the diverse clinical trajectories of patients within early stages of lung cancer and breast cancer. The findings have inspired our search for protein biomarkers to identify the subgroups of patients with stage I disease who are at a high risk of early recurrence and who would benefit from a more aggressive therapeutic approach or more intensive follow-up. Nevertheless, due to the inherent technical demands of protein assays – including sensitivity, robustness and operative issues –there is a need to translate the protein-based companion biomarkers into clinics. To meet the rigorous regulatory standards of clinical laboratories, I will present our experiences to focus on using thyroglobulin (Tg) as a biomarker and an immuno-multiple reaction monitoring (iMRM) MS-based assay as a model for establishing a Clinical Laboratory Improvement Amendments (CLIA) compliant laboratory. Most excitingly, I will also share our experience on the development of a nanoprobe-based mass spectrometry assay to discover a new type of biomarker based on the serum protein variants barcode. The assay offers rapid diagnosis with 20 μl serum within 1 hour for early detection of gastrointestinal cancers.

外賓演講（1）

How to deal with ESD complications

Ken Ohata

NTT Medical Center Tokyo, Japan

ESD was developed as an endoscopic treatment for early-stage gastrointestinal cancer and has become widely used, especially in Asia. The recurrence rate is lower than that of EMR, and both short- and long-term outcomes are excellent. On the other hand, ESD is a complicated procedure and is associated with a high frequency of complications.

In order to perform ESD safely, it is important to have sufficient knowledge of troubleshooting measures. In this lecture, I would like to share a lot of actual case videos, mainly focusing on bleeding and perforation, which are major ESD-related adverse event.

外賓演講（2）

Refractory *H. pylori*: balancing the benefits vs risks of achieving *H. pylori* eradication

John Kao

University of Michigan, USA

Management of *H. pylori* has evolved since its discovery in 1980s by Nobel Laureates Marshall & Warren from more simple but highly effective triple BID therapy to now more complicated quadruple QID therapy in part due to emergence of multi-antibiotic resistant *H. pylori* strains prompting the World Health Organization to list clarithromycin-resistant *H. pylori* as a high-priority organism for the development of new antibiotics. Clinically, we are seeing an increasing number of patients infected with multi-antibiotic resistant *H. pylori* and physicians are running out of treatment options while considering the risk of treatment harm which is intrinsic to getting rid of *H. pylori* colonization as well as repeated antibiotic assaults on our gut microbiome. In this lecture, we will examine the current understanding of the negative impacts of *H. pylori* treatment and strategies to assess risk and benefits of pursuing further treatment. Future research directions will also be discussed regarding the adverse events of *H. pylori* treatments.

外賓演講（3）

Pathways to brain-gut and gut-brain communication in GI disease: new insights and future directions

Nicholas J. Talley

The University of Newcastle, Australia

There is mounting evidence to support the rich interconnectedness between the gut and brain. Population-based research show strong and consistent associations between anxiety, depression, and disorders of gut-brain interactions (DGBIs), including the irritable bowel syndrome (IBS) and functional dyspepsia (FD), contradicting the hypothesis that the high prevalence of anxiety and depression in the clinic was mainly due to neurotic health seeking behaviour. Independent long term follow-up studies suggest that psychological distress can predict the new onset (incidence) of a DGBI in about 50% of cases (brain-gut predominant), while in the remainder DGBIs predict the new onset of psychological distress (gut-brain predominant). The intestinal microbiota is altered in DGBIs (microbial dysbiosis). There is evidence low-grade intestinal inflammation and immune activation is present in a subgroup with DGBIs (e.g. increased intestinal eosinophils and/or mast cells), in at least some cases induced by food antigens recognized as foreign (exposed by the interaction in the lumen of food and intestinal bacteria breaking down immune tolerance), and/or acute gastroenteritis. Brain-gut pathways include the autonomic nervous system and the hypothalamic-pituitary-adrenal axis including corticotrophin releasing factor which may act through reducing the small intestine mucus layer and increasing intestinal permeability. Gut-brain pathways include ascending pain pathways (via the vagus nerve), cytokines (e.g., tumour necrosis factor alpha) in response to bacterial translocation and inflammation, 5-hydroxytryptamine secretion by entero-endocrine cells, and psychoactive chemicals of bacterial origin which may enter the blood stream, such as gamma-aminobutyric acid, fatty acids and 5-hydroxytryptamine precursors. The gut-brain axis may prime each other respectively in early life for later problems. Psychological treatments are known to improve IBS and FD in controlled trials versus waitlist controls. In randomised, double-blind placebo-controlled trials, faecal microbial transfer, certain probiotics, and a non-absorbable antibiotic have been shown to improve DGBIs. The next wave of research is likely to involve preventative microbiological gut based treatments for primary psychological presentations, both to treat the presenting complaint (by reversing intestinal inflammation and/or dysbiosis), and inoculate against later DGBIs.

外賓演講（4）

Recent advance of endoscopy for inflammatory bowel disease

Kazuo Ohtsuka

Tokyo Medical and Dental University Hospital, Japan

Patients with inflammatory bowel disease (IBD) is continuously increasing. On the other hand, the ratio of IBD surgery is decreasing because management of IBD has been improved. Factors contributing to this are the emergence of new drugs, mainly molecular-targeted drugs, and the progress of disease monitoring.

Important target of treatment of IBD is mucosal healing (MH). However, inter- and intra- observer difference occur as for assessment of MH because of human nature. Furthermore, specialists for IBD endoscopy are not common. Applications of artificial intelligence (AI) will change this situation. The first approved AI for IBD in Japan is EndoBRAIN-UC. This evaluates ulcerative colitis (UC) activity, with 74% sensitivity, 97% specificity, and 91% accuracy for determining the histological activity, and its reproducibility was perfect. The other system is the deep neural network system based on colonoscopic images of ulcerative colitis (DNUC) that assesses mucosal healing and histological activity from endoscopic images. In addition, it is possible to predict the events such as hospitalization, surgery, steroid use, and relapse. Then we developed and applied it for video colonoscopy. In a prospective evaluation, the sensitivity of histological remission was 97.9% and the specificity was 94.6%. AI will reduce needs for biopsies, and help improve the quality of training of IBD endoscopy. AI-assisted endoscopy for IBD will be widely spread in future.

Crohn's disease forms lesions in entire gastrointestinal tract. Especially, stenosis is important complication. Half of the reasons for surgery are due to it. Endoscopic balloon dilation (EBD) is an alternative treatment for stenosis. Balloon assisted endoscopy has a good ability for reach deep part of small intestine. It has been utilized EBD for even the lesion existed in the deep part of small intestine. EBD is less invasive and can avoid resection. However, it often needs re-dilation. Ulceration at stricture site is a risk for re-stenosis. Therefore, pre-treatment before EBD is critical.

Endoscopy that is utilized for both assessment and treatment plays important roles in the management of IBD.

外賓演講（5）

Advances in Early Detection and Management of Steatotic Liver Disease

Masashi Hirooka

Department of Gastroenterology and Metabology,
Ehime University Graduate School of Medicine, Japan

Non-alcoholic fatty liver disease (NAFLD) poses a growing health concern globally, with its progressive form leading to fibrosis and potentially severe complications. Despite the acceptance of the MASLD terminology in Japan, little has changed in current practices. Early detection of fibrosis in fatty liver is crucial to prevent its progression. Guidelines emphasize using transaminase abnormalities and B-mode ultrasound for initial NAFLD (MASLD) screening. However, relying solely on B-mode ultrasound is insufficient, and emerging techniques like attenuation methods are anticipated for future adoption.

Cases with FIB-4 exceeding 1.3 recommend specialist consultation, with active use of elastography for fibrosis diagnosis. Notably, even mild or absent fibrosis in fatty liver correlates with poorer outcomes compared to healthy individuals, underscoring the need for dietary improvements. This review consolidates the current state of NAFLD (MASLD) diagnosis, highlighting the importance of evolving diagnostic methods, such as attenuation methods and elastography, for early detection of fibrosis. Additionally, it emphasizes the imperative for lifestyle modifications to enhance patient prognosis.

外賓演講（6）

Endoscopic resection and adjuvant chemoradiotherapy for esophageal SCC

Ryu Ishihara

Osaka International Cancer Institute, Japan

The presentation synthesizes the evolution of treatment protocols for esophageal cancers, focusing on endoscopic resection (ER), adjuvant chemoradiotherapy (CRT), and the implications of updated Japanese guidelines and diagnostic methodologies. The transition in treatment paradigms, particularly the expansion of ER indications and the reassessment of diagnostic tools like endoscopic ultrasound (EUS), underscores a dynamic landscape in managing esophageal squamous cell carcinoma (SCC).

Initially, the 2017 Japanese guidelines recommended ER specifically for early-stage SCC, targeting epithelial (EP) or lamina propria mucosa (LPM) cancers. A significant update in 2020 broadened these indications to include clinical mucosal (MM) and submucosal 1 (SM1) cancers, reflecting a shift towards more inclusive criteria based on the latest ESD/EMR guidelines. This evolution was partly driven by recognizing diagnostic discrepancies between clinical and pathological assessments, notably the reclassification of a substantial number of MM/SM1 cancers as EP/LPM cancers, which are more amenable to curative ER.

The role of diagnostic modalities in determining the invasion depth of superficial esophageal cancer was critically examined, with particular focus on the debated efficacy of EUS. Despite its widespread use, a multicenter study concluded that EUS did not enhance diagnostic accuracy and, in fact, contributed to an increased rate of overdiagnosis. Consequently, current guidelines now advocate for non-magnifying and magnifying endoscopy as the standard diagnostic approach, sidelining EUS due to its limitations.

Further analysis delved into the metastatic risk and efficacy of adjuvant therapies following ER. A systematic review examining the curability of ER in pMM and SM cancers unveiled a metastasis rate of 5.6% in pMM cancers without vascular invasion, highlighting the challenges in establishing a consensus recommendation due to limitations in the reviewed studies. This has spurred ongoing prospective research aimed at refining future guidelines. Additionally, data from the Japan Esophageal Society, encompassing 119 hospitals, revealed a high success rate of en bloc resection with minimal complications, predominantly employing the ESD technique.

Comparative studies, such as the multicenter JCOG 0502, evaluated the outcomes of esophagectomy versus CRT for esophageal SCC. Despite no significant difference in overall survival between the two treatments, the CRT group demonstrated a lower progression-free survival (PFS), primarily attributed to increased regional recurrences. This underscores the potential need for a broader radiation field in CRT to effectively target regional lymph nodes and mitigate the spread of metastasis.

The JCOG 0508 study further assessed the efficacy of adjuvant CRT following ESD in patients with pathological SM cancer or vascular invasion, showing favorable 3-year and 5-year survival rates. Yet, the presence of vascular invasion emerged as a significant factor in progression risk, necessitating a nuanced approach to adjuvant therapy selection. A retrospective study comparing adjuvant CRT to esophagectomy, despite methodological limitations,

indicated no significant difference in survival outcomes between the two modalities after propensity score matching, highlighting the complexity of treatment decisions in this context.

In conclusion, the evolving treatment landscape for esophageal cancer, characterized by expanded ER indications, critical evaluation of diagnostic techniques, and nuanced approaches to adjuvant therapy, reflects a deeper understanding of disease complexities. These advancements, informed by both retrospective and prospective studies, advocate for a stratified treatment strategy based on individual metastatic risk and histopathological features, aiming to optimize patient outcomes in the management of esophageal cancer. This body of work underscores the importance of continuous research and guideline updates to enhance the efficacy and precision of esophageal cancer treatments.

專題討論（1）

Emerging trend of young-onset colorectal cancer: Taiwan on the crossroad

Emerging trend of young-onset colorectal cancer: Global and Taiwan perspectives

Yu-Min Lin（林裕民）

Shin-Kong Wu Ho-Su Memorial Hospital
（新光醫院）

The rising incidence of early-onset colorectal cancer (EO-CRC) in individuals under 50 years old poses a significant global health challenge. In Western countries, there is a notable decline in CRC rates among older adults, while younger demographics are experiencing a substantial increase. This trend underscores a complex interplay of genetic, environmental, and lifestyle factors, with sedentary lifestyles, obesity, dietary changes, dysbiosis, and gaps in early screening being key contributors.

In response to this trend, Taiwan's increasing cases of EO-CRC have led to a reevaluation of screening practices, highlighting unique regional factors. Consequently, there is a need to develop public health policies that are both effective and cost-efficient, particularly in balancing the economic aspects with the benefits of early detection and proactive prevention for at-risk groups.

Effectively managing this trend involves assessing the cost-effectiveness of updated screening methods and lifestyle modification programs. A comprehensive understanding of both international and regional patterns of EO-CRC is crucial. Addressing this issue requires a collaborative approach in research, policy formulation, and healthcare implementation, prioritizing cost-efficiency.

The goal is to develop a holistic and economically sustainable strategy that encompasses prevention, early detection, treatment, patient care, and education. This approach is designed to tackle the growing incidence of EO-CRC, emphasizing the need for coordinated efforts to enhance outcomes for younger CRC patients.

專題討論（1）

Emerging trend of young-onset colorectal cancer: Taiwan on the crossroad

Should we lower the age to initiate colorectal cancer screening? : Clinical perspectives

Han-Mo Chiu（邱瀚模）

National Taiwan University Hospital
（臺大醫院）

While many developed countries with population-based screening programs in place for decades are experiencing a gradual decrease in colorectal cancer (CRC) deaths or incidence, the majority of both developing and developed countries have observed an increasing trend of young-onset CRC, particularly in the 40 to 49 age group. Cohort studies from the US indicate that those born after 1960 experienced a dramatic increase in CRC incidence upon reaching ages 40 to 49, significantly higher than older cohorts at the same age.

The American Cancer Society first lowered the recommended age to initiate CRC screening to 45 in 2018, a decision later echoed by other major professional societies. Similarly, other countries such as Canada and Australia are also considering lowering the age for screening initiation. Taiwan, where CRC has been one of the most incident cancers over the past two decades, has also seen a significant rise in CRC incidence among the 40 to 49 age group. Incidence rates in both males and females rank among the highest globally, far surpassing the threshold incidence level of 30 per 100,000, which warrants consideration for population screening.

Before implementing population screening in the younger age group, several important factors such as population size of 40 to 49 age group, cost-effectiveness of screening, manpower capacity, and funding sources must be carefully evaluated. It's crucial to recognize the pivotal roles individuals aged 40 to 49 play in society and within their families. Non-invasive tests like the fecal immunochemical test (FIT) should be the primary screening method considered in Taiwan, given its utilization in the national screening program since 2004 and demonstrated effectiveness in reducing CRC mortality.

This presentation will address the most updated evidence concerning this specific issue and whether early screening could indeed lead to additional effectiveness compared to initiating screening at age 50.

專題討論（1）

Emerging trend of young-onset colorectal cancer: Taiwan on the crossroad

Should we lower the age to initiate colorectal cancer screening? : NGO perspectives

Hwan-Ruey Liu（劉桓睿）

Taiwan Young Patient Association
（台灣年輕病友協會）

Today, we gather to advocate for a critical shift in public health policy: lowering the age to initiate colorectal cancer screening. As a representative of NGO, I bring forth compelling reasons why this change is urgently needed to combat the rising incidence of colorectal cancer among younger populations.

First and foremost, recent epidemiological data unequivocally demonstrate a concerning trend: a significant increase in the incidence of colorectal cancer among individuals under the age of 50. This shift in demographics underscores the inadequacy of current screening guidelines, which predominantly target individuals aged 50 and above. By lowering the age threshold for screening, we can effectively capture and intervene in colorectal cancer cases at an earlier, more treatable stage.

Moreover, advancing screening initiation age aligns with the principles of proactive and preventive healthcare. Colorectal cancer often develops slowly over time, with precancerous lesions gradually progressing to malignancy. By initiating screening at a younger age, we can detect and remove these precancerous polyps before they have the chance to evolve into invasive cancers. This proactive approach not only saves lives but also reduces the burden on healthcare systems by mitigating the need for costly and intensive treatments associated with advanced-stage disease.

Additionally, lowering the age for colorectal cancer screening promotes equity in healthcare access and outcomes. Individuals with lower socioeconomic status and those lacking access to healthcare bear a disproportionate burden of colorectal cancer morbidity and mortality. By expanding screening eligibility to younger age groups, we can address disparities in early detection and ensure that all individuals, regardless of their background or circumstances, have equitable access to life-saving screening services.

Furthermore, lowering the age for colorectal cancer screening can safeguard labor productivity. Colorectal cancer not only imposes a significant burden on individuals and families but also on economies due to lost productivity from illness and premature death. By detecting and treating colorectal cancer at an earlier stage, we can minimize the impact of the disease on the workforce, ensuring a healthier and more productive population.

In conclusion, lowering the age to initiate colorectal cancer screening is not merely a recommendation; it is an imperative guided by evidence, equity, and economic productivity. As NGOs committed to advancing public health, it is incumbent upon us to champion policies that prioritize prevention, early detection, and equitable access to care. Together, let us take a bold step towards a future where colorectal cancer is no longer a leading cause of morbidity and mortality, but rather a preventable and manageable disease.

專題討論（1）

Emerging trend of young-onset colorectal cancer: Taiwan on the crossroad

Economic impact of colorectal cancer screening in the young population

Ming-Fang Yen（嚴明芳）

Taipei Medical University
（臺北醫學大學）

專題討論（2）

Toward HBV treatment excellence

Before NUC treatment: Observation matter

Chao-Hung Hung（洪肇宏）

Kaohsiung Chang Gung Memorial Hospital
（高雄長庚紀念醫院）

Chronic hepatitis B virus (HBV) infection is a major global health problem progressing to liver cirrhosis, liver failure and hepatocellular carcinoma (HCC). The natural history of chronic HBV infection consists of four phases: immune tolerance, immune clearance, inactive carrier and reactivation. There is considerable agreement that patients whose disease is immune-tolerant or inactive can be safely observed without treatment. The indications for antiviral treatment for HBV are generally based mainly on the combination of three criteria: serum HBV DNA levels, serum ALT levels and severity of liver disease. Nowadays, all guidelines strongly suggest that patients with decompensated liver disease, cirrhosis and those with active disease (defined as those with elevated HBV DNA and ALT levels) should receive treatment. However, there is some grey zone where patients with elevated HBV DNA but normal or mildly elevated ALT levels (>1-<2xULN) should be managed or not. In these situations, additional evidence on disease severity either via liver biopsy or non-invasive assessment is advised to help making decision.

Currently, pegylated interferon and daily oral nucleos(t)ide analogues (NUC) are the first-line medications of choice. Moreover, now pegylated interferon has been rarely used in clinical practice because of its subcutaneous injection and significant side effects. NUCs are more convenient and effective in suppressing HBV replication, decreasing liver inflammation and fibrosis and reducing the risk of cirrhosis and HCC. However, long-term therapy is usually needed to maintain HBV suppression, but the ultimate goal of functional cure with HBsAg clearance is rarely achieved. This review will discuss the current practice and guideline for chronic HBV infection before NUC treatment.

專題討論（2）

Toward HBV treatment excellence

During NUC treatment: Fibrosis matter

Tung-Hung Su（蘇東弘）

National Taiwan University Hospital
（臺大醫院）

Oral antiviral therapy is a standard treatment for chronic hepatitis B aimed at suppressing viral replication, reducing liver inflammation, and preventing disease progression. Fibrosis is a crucial indicator of liver damage and a predictor of disease progression. Monitoring fibrosis is essential in managing chronic hepatitis B, as advanced fibrosis and cirrhosis are associated with an increased risk of liver-related complications, including liver failure and liver cancer.

During chronic hepatitis B treatment with oral antiviral therapy, fibrosis remains an important issue and should be monitored for several reasons. Liver fibrosis may be used to assess disease progression. Regular evaluation of fibrosis status through non-invasive methods such as transient elastography or serum biomarkers allows for early detection of advanced fibrosis or cirrhosis. Conversely, the progression of fibrosis despite treatment may suggest treatment failure or the presence of additional risk factors such as alcohol consumption. Knowledge of fibrosis status guides treatment decisions, including the continuation or discontinuation of antiviral therapy. Patients with significant fibrosis or cirrhosis may require more intensive monitoring to achieve optimal viral suppression and prevent disease progression. Fibrosis staging helps stratify patients based on their risk of developing liver-related complications. Patients with advanced fibrosis or cirrhosis require closer monitoring for signs of decompensation, hepatocellular carcinoma, and other complications necessitating timely intervention. Understanding the implications of fibrosis progression motivates patients to adhere to antiviral therapy and adopt lifestyle modifications aimed at reducing liver injury, such as avoiding alcohol consumption and maintaining a healthy weight.

In conclusion, during chronic hepatitis B treatment with oral antiviral therapy, fibrosis remains crucial in patient management. Monitoring fibrosis progression allows timely intervention to prevent liver-related complications and optimize treatment outcomes. Further research is needed to elucidate the mechanisms underlying fibrosis progression and identify novel therapeutic targets to halt or reverse liver fibrosis in patients with chronic hepatitis B.

專題討論（2）

Toward HBV treatment excellence

Adherence matter

Wen-Juei Jeng（鄭文睿）

Linkou Chang Gung Memorial Hospital
（林口長庚紀念醫院）

The World Health Organization defines medication adherence as the degree to which an individual's actions, such as taking medication, adhering to a prescribed diet, or making lifestyle changes, align with the recommendations provided by a healthcare professional. Poor adherence results in treatment failures, heightened healthcare expenses, and exposes patients to potentially life-threatening risks. The failure to adhere to long-term therapies has long been acknowledged as a significant issue, often compromising the efficacy of medical treatment. Regarding chronic hepatitis B treatment, where oral nucleos(t)ide analogues (Nuc) stand as the mainstay of choice, the average adherence rate by systemic review and meta-analysis was 74.6% (95% confidence interval [CI] 67.1%-82.1%), which is comparable among different economic-income settings. Adherence rates below 90% increase the risk of adverse liver events including liver cancer, hepatic decompensation, and liver-related mortality. Self-discontinuation during long-term treatment without scheduled monitoring even poses a hazard to delayed retreatment in certain high-risk patients, especially those with cirrhotic status. In this session, we'll review the factors influencing patients' adherence and the impact of maladherence in CHB patients treated with Nuc.

專題討論（2）

Toward HBV treatment excellence

After NUC treatment: Monitoring matter

Pin-Nan Cheng（鄭斌男）

National Cheng Kung University Hospital
（成功大學醫學院附設醫院）

With advent of nucleos(t)ide analogues (NUC), long-term suppression of hepatitis B virus (HBV) becomes feasible in patients with chronic hepatitis B (CHB). Although NUC exhibits excellent virus suppression and reduces liver associated complications, monitoring during NUC and off-NUC period is of important and necessary to maximize treatment efficacy and to achieve high safety.

During NUC treatment, periodic assessment of ALT and serum HBV DNA should be carried out. Achieving normalization of ALT and loss of detectable HBV DNA are the two goals of NUC treatment and are also associated with better clinical outcomes. For safety concerns, renal function should be regularly followed up in all NUC treated patients. For patients who fulfilled criteria of stopping NUC treatment, off-NUC monitoring is a critical issue. To minimize the risk of hepatic decompensation after NUC cessation, close monitoring of ALT and serum HBV DNA is required and should be implemented differently according to the use of TDF/TAF or ETV. Retreatment may be needed in CHB patients who present with HBV viremia and abnormal ALT. Finally, surveillance of hepatocellular carcinoma during NUC and off-NUC treatment in all CHB patients is mandatory.

專題討論（3）

Advances in diagnosis and treatment for gastrointestinal cancer

Esophageal and gastric cancer: immunotherapy and more

I-Chen Wu（吳宜珍）

Kaohsiung Medical University Hospital
（高雄醫學大學附設中和紀念醫院）

This presentation offers a comprehensive overview of the latest advancements in the treatment of esophageal cancer (EC), and gastric / gastroesophageal junction (G/GEJ) adenocarcinoma. The integration of immune checkpoint inhibitors (ICIs) with chemotherapy (C/T) has set a new standard in the treatment of metastatic EC, offering significant benefits, notably in patients with positive PD-L1. Key studies, including ATTRACTION-1, KEYNOTE-590, and Checkmate 648, illustrate the varied response rates and survival advantages across different therapy lines, underscoring the superiority of ICI-based regimens over chemotherapy alone. For resectable EC, adjuvant Nivolumab significantly extends median disease-free survival to 22.4 months (CheckMate 577; Hazard Ratio: 0.69) in patients have received neoadjuvant chemoradiotherapy and surgery. Further insights are anticipated from ongoing trials, such as KN-976, SKYSCRAPER-07, and KUNLUN, which are exploring the efficacy of Pembrolizumab, Atezolizumab, and Durvalumab, respectively in the neoadjuvant setting.

The treatment landscape for G/GEJ adenocarcinoma has also evolved. The Siewert classification is crucial in determining the treatment approach, differentiating between esophageal and gastric cancer treatments. HER-2 positive cases have shown favorable outcomes with trastuzumab combined with C/T. Recently, the DESTINY-Gastric01 trial has proven the antibody drug conjugate, Trastuzumab Deruxtecan (T-Dxd), achieves better objective response rates (ORR), median overall survival (OS), and median progression-free survival (PFS) compared to 2nd-line chemotherapy. Furthermore, the emergence of Claudin 18.2 as a novel target presents a promising avenue for HER2 negative patients, with both the SPOTLIGHT and GLOW trials demonstrating that Zolbetuximab with C/T significantly improves ORR, OS, and PFS over C/T alone in the 1st-line treatment. The use of ICIs in combination with C/T as a first-line treatment has shown encouraging results, especially when positive PD-L1. In conclusion, the advent of ICIs and/or other novel agents has marked a significant progression in treating EC and G/GEJ adenocarcinoma, enhancing survival outcomes and patients' quality of life.

專題討論（3）

Advances in diagnosis and treatment for gastrointestinal cancer

Integrating systemic and liver-directed therapy for hepatocellular carcinoma

Chiun Hsu（許 駿）

National Taiwan University Cancer Center
（臺大醫院癌醫中心分院）

The advancement of immune checkpoint inhibitor (ICI)- based combination regimens ushers in a new era of multi-modality management for patients with hepatocellular carcinoma (HCC). Neoadjuvant or peri-operative ICI-based therapy may help improve resectability and the opportunity of cure, as suggested by many single-arm clinical trials. Systemic therapy may also help reduce recurrence after curative therapy through adjuvant therapy or delay progression when combined with liver-directed therapy (LDT), such as trans-catheter arterial chemo-embolization.

Incorporation of these multi-modality approaches into clinical practice guidelines requires high-level evidence from clinical trials. For neoadjuvant or peri-operative systemic therapy, overall survival, which is considered a gold standard for regulatory approvals of new anticancer therapy, may be confounded by the patients' disease status and available subsequent therapies. Endpoints such as progression-free survival and objective response rate may catch efficacy signals earlier. Definition of the target population is also critical, particularly in patients with intermediate-stage HCC. Many classifications or scoring criteria have been proposed to sub-categorize this heterogeneous patient population. Design of clinical trials and interpretation of trial results should take into account the confounding effects of the patient heterogeneity. Finally, efficacy and safety of novel LDT demonstrated in highly specialized centers may not be generalizable into routine clinical practice. Randomized trials incorporating these novel LDT approaches, which may not be always feasible, may be associated with high dropout rate and failure of the randomized subjects to receive the assigned experimental treatment, producing discrepancy between intent-to-treat and per-protocol patient populations.

專題討論（3）

Advances in diagnosis and treatment for gastrointestinal cancer

Advancement in the treatment for advanced GIST and NETs

Hui-Jen Tsai（蔡慧珍）

National Health Research Institutes
（國家衛生研究院）

Gastrointestinal stromal tumors (GISTs) and neuroendocrine tumors (NETs) are rare tumors and may origin from different sites. GISTs are mainly originated from gastrointestinal tract, including stomach, small intestine, and large intestine, and a small proportion of them may origin from peritoneum or others within abdominal cavity. NETs are heterogenous tumors with different grade and of different primary sites. The most common sites of NETs include gastroentero-pancreas (GEP) and lung. Early stage of GISTs can be treated with curative surgery followed by adjuvant imatinib treatment for high risk patients and have a good prognosis. Early-stage NETs can usually be cured by surgical resection. For advanced GISTs and NETs, there has been improvement in the treatment strategies in the recent decades. However, there is still unmet medical needs for these patients. GISTs usually harbor *c-KIT* or *PDGFRA* mutations but around 10-15% of patients are *c-KIT* and *PDGFRA* wild type. Primary resistance and secondary resistance to imatinib are a big issue for advanced GIST patients. Recently, tyrosine kinase inhibitor (TKI) targeting PDGFRA has been approved and implicated into the treatment for advanced GISTs with PDGRFA exon 18 mutations. Some novel agents, such as heap shock protein 90 (HSP90) inhibitors has also been investigated for the use in GIST. Regarding, advanced NETs, many targeted therapies have been developed based on the characteristics of NETs, such as expression of somatostatin receptor, mTOR activation and hypervascularity. Somatostatin analogues (SSA), everolimus (mTOR inhibitor), and sunitinib (multi-targeted TKI) have been shown to improve the survival and quality of life of functional or advanced GEP-NET patients by phase II/III trials in the recent decades. In addition, everolimus has also been shown to improve the survival of lung NETs by phase III clinical trial. Other target agents, such as surufatinib, lenvatinib, axitinib, pazopanib, and cabozantinib have also been shown their efficacy in advanced GEP-NETs in phase II or III clinical trials. Recently, cabozantinib has been shown to prolong the PFS of GEP-NET patients failed to one line of targeted agent. Combinational treatment is also a treatment option. The efficacy of everolimus combined with SSA has also evaluated in clinical trials. Combination of targeted agent with chemotherapeutic agent may also be a treatment option. Exploration of other novel targeted agents or combinations is still ongoing not only to prolong the survival but also maintain the quality of life of advanced NET patients. In conclusion, exploration of the molecular pathogenesis is important to develop novel agents for treatment of advanced GISTs and NETs.

專題討論（3）

Advances in diagnosis and treatment for gastrointestinal cancer

Neoadjuvant chemotherapy in resectable pancreatic cancer

Yung-Yeh Su（蘇勇曄）

National Health Research Institutes
（國家衛生研究院）

Upfront resection (UR) followed by adjuvant chemotherapy remains the standard treatment for resectable pancreatic cancer. There is increasing evidence suggesting favorable outcomes toward neoadjuvant chemotherapy followed by surgery (NAC). We conducted a retrospective study consisted of 159 resectable patients including 46 patients (29%) underwent neoadjuvant chemotherapy (NAC) and 113 patients (71%) received upfront resection (UR). In NAC group, 35 of 46 patients (76%) underwent R0/R1 resection and 34 of 35 resected patients (97%) underwent adjuvant chemotherapy. On the other hand, in UR group, 100 of 113 patients (89%) underwent R0/R1 resection but only 58 of 100 resected patients (58%) received adjuvant chemotherapy. The median progression free survival (PFS) in NAC and UR were 22.0 months (95% CI, 10.2 - not estimable) and 9.2 months (95% CI, 7.4-11.2), respectively. The median overall survival (OS) in NAC and UR were 35.3 months (95% CI, 29.7- not estimable) and 21.7 months (95% CI, 18.5-27.9), respectively. In conclusion, our study demonstrates that NAC is superior to UR in resectable pancreatic cancer with better survival.

專題討論（3）

Advances in diagnosis and treatment for gastrointestinal cancer

Biliary tract cancer: biomarker-guided therapy

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Taipei Veterans General Hospital
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In recent years, precision medicine has emerged as a transformative approach in the field of oncology. This paradigm shift is particularly promising for biliary tract cancer, a group of malignancies originating in the bile ducts and gallbladder, which have historically presented significant treatment challenges. Precision medicine leverages cutting-edge technologies, such as genomics, proteomics, and targeted therapies, to tailor treatment strategies to the unique genetic and molecular profiles of individual patients. In the context of biliary tract cancer, this means identifying specific genetic mutations or alterations that drive tumor growth and selecting therapies that directly target these aberrations. This approach has the potential to enhance treatment efficacy, and ultimately improve patient outcomes. In this talk, we explore the latest advancements in precision medicine for biliary tract cancer, highlighting key biomarkers, such as IDH mutation, RET fusion, G12C mutation, FGFR2 fusion and HER2 amplification. As precision medicine continues to evolve, it offers hope for a brighter future in the treatment of biliary tract cancer, bringing us closer to personalized and more effective therapeutic options for patients facing these aggressive diseases.

專題討論（4）

Forum of Small Intestinal Disease and Inflammatory Bowel Disease: Present Status and Future Expectation

Advanced Therapy for Inflammatory Bowel Disease

Jen-Wei Chou（周仁偉）

China Medical University Hospital
（中國醫藥大學附設醫院）

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is a chronic and relapsing disease of the gastrointestinal tract. Historically, clinical response and remission have been the primary therapeutic goals for patients with IBD. Previous researches demonstrate that mucosal healing in patients with active mucosal inflammation is associated with prolonged clinical remission and longer time to relapse, as well as with reductions in hospitalizations and surgeries. Therefore, mucosal healing is an increasingly important therapeutic goal in IBD patients.

At present, the treatment of IBD depends on the severity and extent of disease. Medical treatment of IBD mainly targets mediators of inflammation to stop or suppress pro-inflammatory processes. The first generation of therapeutic agents for the treatment of IBD consists of nonspecific immunomodulatory drugs such as sulfasalazine/5-aminosalicylic acids, corticosteroids, thiopurines, and methotrexate. Increased understanding of the pathogenesis of IBD has led to the development of a second generation of therapeutic agents comprised of monoclonal antibody-based biologics.

The introduction of biological agents during the last 20 years has revolutionized in treating IBD and dramatically changes the strategy of IBD treatment. According to the mechanisms of action, biological agents can be classified into several different types, including anti-tumor necrosis factor (ant-TNF), anti-interleukins, anti-integrin molecules. However, the monoclonal antibodies have some limitations in treating IBD, including the safety, cost, and sustained efficacy. In fact, about 10-30% of IBD patients treated with anti-TNF agents are primarily non-responders, and 23-46% are secondary non-responders. Based on the above reasons, novel orally available small molecules have been developed to treat IBD such as Janus kinase inhibitors and sphingosine-1- phosphate receptor modulators.

However, the impact of these new drugs in changing the natural history of IBD is still under debate. Recent evidence seems to suggest that the extent of their efficacy might be, at least partially, depending on the timing of their introduction and on the subsequent management strategy. Therefore, the potential role for a more dynamic approach with treatments based on sequence or combination advanced therapies has been extensively studied in clinical practice. However, there are currently no curative therapies, and in most cases, lifelong treatment is required. Thus, therapeutic drug monitoring and prevention of complications are needed during these sequence or combination advanced therapies for IBD patients. In addition, more controlled data are required to evaluate the optimal timing, efficacy, and mitigation of safety concerns in these novel therapies.

專題討論（4）

Forum of Small Intestinal Disease and Inflammatory Bowel Disease: Present Status and Future Expectation

Precision Medicine in Small Intestinal Disease and Inflammatory Bowel Disease: Tailoring Treatment for Better Outcomes

Chia-Hung Tu（涂佳宏）

National Taiwan University Hospital
（臺大醫院）

Inflammatory bowel disease is characterized with great variations regarding to clinical manifestation, prediction of disease course, response to treatment, which reflects complexed disease mechanism, genetic contributions, and environmental impacts. To resolve the uncertainties, the existing clinical guidelines of disease management categorize and separate patients into different groups or scenarios and fit them into multiple 'standards of treatment'. However, this approach is limited by uncertain and suboptimal selection between ever-expanding treatment options, ceiling of therapeutic effects, and risk of over- and under-treatment. Much of the limitations can be rooted to the probability theory as fundamentals of medical experiments and clinical trials, which leaves the outcomes of low-probability unsolved and leads to conclusions that often deviate from real-world experiences.

An alternative approach is aspired by the development of precision medicine, in which clinical intervention is individualized by patient profiles, especially genetic background and predictive factors beforehand. This can be achieved by techniques of whole-genome profiling, multi-factor prediction of treatment outcome instead of single-predictor calculation, real-world big data instead of hypothesis-driven randomized controlled trials, and the application of artificial intelligence. In the presentation, I will list some of the many notable progresses in the field of IBD management, as the latest examples that the mainstream of medical practice has begun shifting from evidence-based medicine toward personalized medicine.

專題討論（4）

Forum of Small Intestinal Disease and Inflammatory Bowel Disease: Present Status and Future Expectation

Update on the Application of Capsule Endoscopy and Deep Enteroscopy

Chen-Shuan Chung（鍾承軒）

Far Eastern Memorial Hospital
（亞東紀念醫院）

Small bowel had been considered as the “dark continent of gastrointestinal tract” previously. The diagnosis and management of small bowel diseases are always challenging before the introduction of capsule endoscopy (CE) and deep enteroscopy. Device-assisted enteroscopy (DAE) and CE are continuously evolving with the development of new design to facilitate more complex diagnostic and therapeutic enteroscopic interventions for small bowel disorders. Each enteroscopic approach, including radiological, endoscopic and surgical methods complement each other in clinical practicing. Future randomized controlled trials will be needed to assess their ultimate benefits in different scenarios in terms of personalized medicine care. Herein, I will give a review of the update knowledge in the application of CE and DAE.

專題討論（4）

Forum of Small Intestinal Disease and Inflammatory Bowel Disease: Present Status and Future Expectation

Recent Advance in Diagnosis and Treatment of Small-Bowel Tumor

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Changhua Christian Hospital
（彰化基督教醫院）

Recent advances in the diagnosis and treatment of small-bowel tumors have significantly improved patient outcomes. Diagnostic techniques such as capsule endoscopy, double-balloon enteroscopy, and computed tomography enterography enable earlier detection, crucial for effective treatment planning. In this talk, we will provide an updated information regarding the diagnosis and management of small-bowel tumors.

專題討論（5）

Advanced therapeutic endoscopy: ARMS/ARMA debate

1. The pre-treatment evaluation of anti-reflux mucosal intervention (ARMS/ARMA)
A: HRM and PH monitor are necessary

Yen-Po Wang（王彥博）

Taipei Veterans General Hospital
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The current mainstay treatment for gastroesophageal reflux disease (GERD) is medical treatment involving antisecretory therapy, including proton pump inhibitors (PPIs) and histamine type 2 receptor antagonists. For chronic GERD patients, esp. In patients with hiatal hernias, laparoscopic fundoplication can also be considered for management. Anti-reflux mucosal intervention is a newly developed endoscopic treatment that can reduce gastroesophageal junction opening by scarring formation . According to the recently published Lyon Consensus 2.0, esophageal testing is suggested for all patients prior to invasive GERD management. Ambulatory reflux monitoring off antisecretory therapy can be used to diagnose unproven GERD. Catheter-based pH impedance monitoring on antisecretory therapy can further determine the cause of persistent symptoms. High-resolution manometry can be used to exclude the achalasia spectrum in PPI nonresponders and provide supportive evidence of GERD, such as hiatal hernia and esophageal hypomotility. Currently, there are no good predictors of the response to anti-reflux mucosal intervention. Esophageal functional testing may provide useful information for management guidance in the future and therefore should be performed in pretreatment evaluation of anti-reflux mucosal intervention.

專題討論（5）

Advanced therapeutic endoscopy: ARMS/ARMA debate

1. The pre-treatment evaluation of anti-reflux mucosal intervention (ARMS/ARMA)
B: Endoscopy and symptom-based

Jiunn-Wei Wang（王俊偉）

Kaohsiung Medical University Hospital
（高雄醫學大學附設中和紀念醫院）

In the context of anti-reflux interventions, thorough pre-treatment evaluation is critical for optimal patient outcomes. Endoscopy serves as a cornerstone in this assessment, allowing direct visualization of the esophageal mucosa, identification of anatomical abnormalities, and assessment of mucosal integrity. It provides valuable insights into the severity of reflux-related damage, aiding in treatment planning.

Complementing endoscopy, symptom-based evaluation plays a pivotal role. By closely examining patient-reported symptoms such as heartburn, regurgitation, and chest pain, healthcare providers gain a comprehensive understanding of the subjective experience of reflux. Symptom assessment guides the selection of interventions tailored to the individual patient's needs and helps monitor treatment effectiveness.

Highlighting the crucial role of a holistic approach, the integration of endoscopic findings with patient-reported symptoms takes center stage in evaluating anti-reflux mucosal intervention prior to treatment. Such a comprehensive assessment not only enhances diagnostic precision but also informs a more personalized and effective treatment strategy for individuals seeking relief from gastroesophageal reflux-related symptoms.

專題討論（5）

Advanced therapeutic endoscopy: ARMS/ARMA debate

2. The best anti-reflux mucosal intervention: ARMA vs. ARMS
A: Prefer ARMA

Chien-Chuan Chen（陳建全）

National Taiwan University Hospital
（臺大醫院）

The incidence of gastroesophageal reflux disease (GERD) is increasing. GERD not only affects the patient's quality of life, but also increases the risk of development of Barrett's esophagus and esophageal adenocarcinoma.

Proton pump inhibitors (PPIs) have been the mainstay of medical management of GERD. However, about 20% to 30% of patients with erosive reflux disease and 40% of patients with non-erosive reflux disease do not respond to PPIs. Moreover, no significant improvement is observed in symptoms with doubling the dose of PPIs. The potential adverse effects of long term PPIs use are also a matter of concern. These adverse effects include *Clostridium difficile* infection, bone fracture, hypomagnesemia, higher incidence of chronic kidney disease in susceptible populations and community-acquired pneumonia.

Anti-reflux surgery (ARS: open or laparoscopic fundoplication) has been the mainstay of treatment for patients not responsive to PPIs and documented reflux on pH-impedance analysis. However, a quarter of patients restart PPIs on long-term follow-up. Moreover, a requirement of re-intervention exists in about 15% and 30% patients after laparoscopic or conventional fundoplication, respectively. Other adverse events known to occur with ARS include dysphagia, gas bloating, and inability to belch. Patients with refractory GERD may not agree to ARS due to its invasive nature and possible adverse events as mentioned above. In a randomized controlled trial comparing ARS with PPIs, the remission rates are similar in both arms at 5-year follow-up. However, adverse events, including gas bloating, dysphagia and flatulence were significantly higher in the ARS arm.

There is an unmet need for minimal invasive treatment modalities for patients who do not respond to PPIs and are unwilling for ARS. Minimally invasive endoscopic options for GERD have been in place for more than a decade now. Some of these have not stood the test of time either due to inefficacy, non-durable response, or safety issues. These include implantation of injection devices (Enteryx [Boston Scienntific Corp, Natick, MA, USA], Gatekeeper [Medtronic, Minneapolis, MN, USA], Plexiglas microspheres [Artes Medical, San Diego, CA, USA], NDO Plicator [NDO Surgical, Mansfield, MA, USA]). The currently available endoscopic anti-reflux modalities (EARMs) include radiofrequency ablation (RFA), transoral incisionless fundoplication (TIF), medigus ultrasonic surgical endostapler (MUSE), and anti-relux mucosectomy/ mucosal ablation (ARMS/ ARMA).

In this lecture, these novel procedures will be presented and discussed.

專題討論（5）

Advanced therapeutic endoscopy: ARMS/ARMA debate

2. The best anti-reflux mucosal intervention: ARMA vs. ARMS
B: Prefer ARMS

Chu-Kuang Chou（周莒光）

Chiayi Christian Hospital
（嘉義基督教醫院）

Gastroesophageal reflux disease (GERD) is a digestive disorder that causes heartburn and acid reflux symptoms. Proton pump inhibitors (PPIs) are the primary treatment for GERD. However, some patients require long-term use of PPIs, and up to 40% do not respond entirely to these medications.

While surgical fundoplication is an effective treatment option for GERD, it is invasive and may not be an acceptable choice for all patients. On the other hand, anti-reflux mucosectomy (ARMS) is an endoscopic approach that shows significant promise in managing GERD. ARMS involves the removal of the gastric cardiac mucosa, which reduces the opening of the gastroesophageal junction through the healing process of the resulting scar.

This section examines the benefits and drawbacks of ARMS over other anti-reflux management strategies, ARMA, and explores potential advancements based on this approach.

專題討論（5）

Advanced therapeutic endoscopy: ARMS/ARMA debate

3. The most appropriate management for refractory GERD in patients with bariatric sleeve surgery
A: ARMS/ARMA

Kuan-Chih Chen（陳冠至）

Far Eastern Memorial Hospital
（亞東紀念醫院）

Gastroesophageal reflux disease (GERD) is a common and complex complication, especially among individuals who have undergone sleeve gastrectomy surgery. It presents significant challenges for both patients and healthcare providers.

Sleeve gastrectomy (SG), a surgical procedure designed to aid weight loss, involves the removal of a portion of the stomach. While effective for weight reduction, this surgery can increase the likelihood of developing GERD symptoms.

The exact reasons behind the heightened risk of GERD in SG patients are not yet fully understood. However, there are several potential factors that contribute to this association. One possibility is that the reduction in stomach size and capacity leads to increased pressure within the remaining stomach, causing stomach acid to flow back into the esophagus. Besides, changes in the anatomy following the surgery, such as alterations in the position of the lower esophageal sphincter, could also contribute to the development of GERD symptoms.

Effectively managing GERD in patients who have undergone SG poses a challenge. Lifestyle modifications, including dietary adjustments, avoiding trigger foods, and maintaining a healthy weight, are often recommended. Physicians might also prescribe medications like proton pump inhibitors to decrease stomach acid production. For patients with body-mass index > 35 and medically refractory GERD should be considered for either Roux-en-Y gastric bypass or fundoplication

For those patients who refuse further surgery, antireflux mucosectomy (ARMS) and antireflux mucosal ablation (ARMA) could be considered. In this debate, we will investigate the effectiveness and safety of ARMS and ARMS for refractory GERD after bariatric surgery, especially SG.

專題討論（5）

Advanced therapeutic endoscopy: ARMS/ARMA debate

3. The most appropriate management for refractory GERD in patients with bariatric sleeve surgery
B: Others

Ming-Wun Wong（翁銘彣）

Hualien Tzu Chi Hospital
（花蓮慈濟醫院）

Gastroesophageal Reflux Disease (GERD) exhibits a strong correlation with obesity. Notably, weight reduction, particularly when achieved through bariatric surgery, has been demonstrated to significantly alleviate GERD symptoms. However, the type of bariatric surgery plays a critical role in these outcomes. Specifically, sleeve gastrectomy (SG) poses a significant risk for the onset of new reflux symptoms, with the incidence of de novo reflux demonstrating a direct correlation with the length of the follow-up period, ranging between 8% and 30%.

GERD is the primary contributor to diminished quality of life following bariatric surgery, potentially leading to decreased physical activity and heightened mental and emotional distress, culminating in reduced social interaction. Due to these severe potential repercussions, GERD remains the predominant reason for revisional surgery post-SG. Refractory GERD, characterized by the persistence of GERD symptoms despite comprehensive medical treatment, is particularly challenging.

Our presentation aims to synthesize current literature and explore management strategies for refractory GERD beyond ARMS (Anti-Reflux Mucosectomy) and ARMA (Anti-Reflux Mucosal Ablation) in patients who have undergone SG.

專題討論（6）

Cutting- edge advance and perspective of Microbiota

Gut microbiota: a new path to treat obesity

Jyh-Ming Liou（劉志銘）

National Taiwan University Hospital
（臺大醫院）

Obesity stands as a significant risk factor for cardiovascular disease, metabolic disorders, chronic hepatitis, and various cancers, making it a global health concern. Despite its widespread impact, shedding excess weight proves challenging and sustaining weight loss even more so. The intricacy lies in the regulation of energy intake, expenditure, and subsequently, body weight. These processes are governed by intricate hormonal, neural, and metabolic mechanisms influenced by numerous environmental factors and internal responses. Recent research suggests that, alongside lifestyle factors, host genetic factors and gut microbiota may contribute to obesity development. Animal studies reveal the pivotal role of gut microbiota in the onset of obesity in mice. The microorganisms within the gut microbiota directly impact food digestion, absorption, and metabolism. Additionally, they exert a range of protective, structural, and metabolic effects on both the intestinal environment and peripheral tissues. This influence extends to body weight modulation through the regulation of metabolism, appetite, bile acid metabolism, as well as the hormonal and immune systems. The opportunities, limitations and challenges of using gut microbiota-related approaches as a means to achieve and maintain a healthy body weight will be discussed.

專題討論（6）

Cutting- edge advance and perspective of Microbiota

Gut Microbiota may Modulate the Clinical Course of Chronic Hepatitis B

Yen-Hsuan Ni（倪衍玄）

National Taiwan University Hospital
（臺大醫院）

HBeAg seroconversion (HBe-SC) and repetitive ALT flare-ups in chronic hepatitis B (CHB) patients may increase their risk of severe complications. HBe-SC is mainly due to an attack of the host immune cells against the viral antigen-expressed hepatocytes, but the details remain elusive, especially why and how the host immune responses are provoked. We hypothesized gut microbiota trigger the immune reactions to lead to HBe-SC through gut-liver axis. Patients with CHB in different disease phases were recruited. A variety of HBV-hydrodynamic injection (HDI) mouse models were established. Multi-platform metabolomics assays were performed to explore the gut microbiota and their metabolites in the event of HBe-SC. *Ruminococcus gnavus* was found to be the most abundant in patients with immune-tolerance (IT) and poor response to antiviral treatments. *Akkemansia muciniphila* was highly enriched in patients who underwent HBe-SC in an immune-active (IA) state. Their cause-effect relationship was proven by HBV-HDI mouse models in BALB/c, C57BL/6J, C3H/HeN and germ-free mice. Patients of IT phase demonstrated a higher level of cholesterol to bile acids (BAs) metabolism than those of IA phase. Outgrowth of *R. gnavus* prolonged HBV persistence via increasing BAs metabolism in mouse models. R. gnavus encoded bile salt hydrolase to deconjugate the primary BAs and control the total pool of BAs. *A. muciniphila* counteracted *R. gnavus* through *A. muciniphia's* secretome metabolites, which comprised of small molecules structurally similar to apigenin, lovastatin, ribavirin etc., and their cholesterol-lowering, antibacterial and antiviral properties may finally lead to HBV elimination. In conclusion, *R. gnavus* and *A. muciniphila* play opposite roles in HBe-SC and the bacterial metabolites of *A. muciniphila* highlight the targets of future anti-HBV therapy.

專題討論（6）

Cutting- edge advance and perspective of Microbiota

Gut butyrate-producers confer post-infarction cardiac protection

Patrick C. H. Hsieh（謝清河）

Institute of Biomedical Sciences, Academia Sinica
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Embark on a journey that uncovers the intricate interplay between our gut microbiota and the remarkable process of heart repair. This presentation delves into the captivating realm where gut microbes wield profound influence over the recovery following a heart attack. Explore how these microscopic inhabitants orchestrate a symphony of effects on immune cell composition and essential short-chain fatty acids, intricately weaving into the tapestry of post-infarction cardiac healing.

Navigate through the world of specialized gut bacteria, with a spotlight on the remarkable butyrate-producers, whose presence has been linked to a heightened capacity for cardiac protection post-heart attack. Venture into both human and animal studies that shed light on the enrichment of these beneficial bacteria in the aftermath of myocardial infarction. Delve deeper to understand how the introduction of these microbes ignites the production of beta-hydroxybutyrate, a powerful ketone associated with enhanced cardiac function in the wake of heart injury.

This multidimensional exploration uncovers the nexus between microbial metabolites, immune dynamics, and the intricacies of heart repair. As we decipher these mechanisms, novel avenues emerge for potential therapeutic interventions that could reshape the landscape of post-infarction outcomes. These studies not only highlight the captivating connection between our gut and heart but also emphasize the promising potential of harnessing this relationship to usher in a new direction of cardiovascular health enhancement.

專題討論（6）

Cutting- edge advance and perspective of Microbiota

慢性腎臟病病人的腸道菌與代謝體對系統併發症的影響
The effect gut microbiota and metabolites on systemic complications in patients with kidney disease

Yi-Ting Lin（林憶婷）

Kaohsiung Medical University
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Chronic Kidney Disease (CKD) is characterized by a progressive decline in renal function over time. Recent years have witnessed an escalating interest in the role of the gut microbiota in the pathogenesis of CKD. Research indicates a distinct alteration in the gut microbiome composition of CKD patients compared to healthy individuals, a phenomenon termed dysbiosis. This dysbiosis exacerbates systemic inflammation, oxidative stress, and the generation of uremic toxins, thereby accelerating CKD progression. The urea levels associated with CKD increase precipitate changes in the gut microbiome, leading to enhanced production of microbiome-derived toxins. Moreover, modifications in the gut microbiota coupled with compromised intestinal barrier integrity in individuals with CKD or End-Stage Kidney Disease (ESKD) are linked to endotoxemia and the accumulation of gut-derived toxins such as indole metabolites (indoxyl sulfate, indole-3 acetic acid) and phenol metabolites (p-cresyl sulfate, phenyl sulfate). Notably, indoxyl sulfate, a prominent protein-bound uremic toxin, is known to accumulate in CKD patients, contributing to cardiorenal syndrome and brain damage through its cardiovascular, kidney, and neurology toxicity. This toxin is associated with an elevated risk of cardiovascular morbidity and target organ damage. Furthermore, p-cresyl sulfate, another significant uremic toxin originating from gut microbiota, is associated with cardiovascular complications in CKD patients. These microbiota-derived metabolites have been implicated in systemic complications, including cardiovascular disease, cognitive impairment, and mineral bone disorders. However, a comprehensive understanding of the intricate interplay between the gut microbiome, CKD, and additional contributory factors remains elusive, necessitating further research. This knowledge is crucial for developing novel therapeutic strategies targeting the gut microbiome to ameliorate outcomes in CKD patients.

專題討論（7）

Obesity: Endoscopic sleeve gastroplasty (ESG) vs laparoscopic sleeve gastrectomy (LSG) debate

Introduction of ESG

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Obesity is a chronic relapsing progressive disease process which requires a range of medical interventions to advance treatment and prevention of obesity-related comorbidities. Step-up approaches of obesity management include lifestyle and dietary modification, anti-obesity medications, endoscopic bariatric and metabolic therapies (EBMT) as well as bariatric surgeries. Endoscopic sleeve gastroplasty (ESG) is one of the promising EBMT. According to the literature, ESG is non-inferior to or with lower short- and mid-term weight loss than laparoscopic sleeve gastroplasty, but fewer devastating adverse events and lower incidence of post-procedural gastroesophageal reflux diseases. Combination of ESG with lifestyle, dietary modification and anti-obesity medication, such as glucagon-like peptide-1, improves efficacy on weight control. However, long-term data and randomized controlled trials in comparison with other bariatric procedures are warranted. Herein, I will give a review of the current evidence on the clinical application of ESG in obesity management.

專題討論（7）

Obesity: Endoscopic sleeve gastroplasty (ESG) vs laparoscopic sleeve gastrectomy (LSG) debate

ESG procedure and complication trouble shooting

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Endoscopic sleeve gastroplasty (ESG) has emerged as a promising weight loss intervention validated through clinical trials. Overall, it presents low risks and can be performed on an outpatient basis. However, mastering the procedural techniques may pose challenges, requiring dedicated learning. Additionally, awareness and management of potential complications are essential skills to acquire. This presentation aims to delve into these aspects, shedding light on the complexities of ESG as an effective tool in combating obesity.

專題討論（7）

Obesity: Endoscopic sleeve gastroplasty (ESG) vs laparoscopic sleeve gastrectomy (LSG) debate

Introduction of LSG

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Obesity is increasing and became a global disease. Various of medical diseases are closely associated with obesity. Bariatric surgery is one of the most effective treatment for morbid obesity. One of the important mechanism for bariatric procedure is restriction of intake. Many restrictive procedures, such as vertical banded gastroplasty and adjustable gastric banding has been prescribed. The long term outcome are not significant In past two decades, sleeve gastrectomy(SG) has increasely been use and became the most popular bariatric surgery in Taiwan, also worldwide. SG was original a stage procedure of duodenal switch for super obese patients. However, it became a stand-along bariatric procedure with a good weight loss outcome as well as improvement of co-morbidity. Compare to Roux-en Y gastric byass, surgical technique of SG is relative simple. In this section, we will make a brief review the development history of SG, surgical safety, long term weight loss outcome and co-morbidity resolution.

專題討論（7）

Obesity: Endoscopic sleeve gastroplasty (ESG) vs laparoscopic sleeve gastrectomy (LSG) debate

LSG procedure and complication trouble shooting

Sheng-Shih Chen（陳盛世）

Kaohsiung Veterans General Hospital
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專題討論（8）

Last mile in DAA era: chance and challenge

Path toward HCV elimination: Reprogramming in WHO guidance and current status in Taiwan

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In the 2016 World Health Assembly, WHO called for elimination of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection by 2030. Our government has organized lots of efforts in HCV control since 2016, and tends to elimination HCV by 2025.

In 2023, WHO published “Guidance for country validation of viral hepatitis elimination and path to elimination” to describe all program targets and impact targets in details. This validation should be in country level using status in 2015 as baseline. Can Taiwan meet all targets in the guidance by 2025?

There were one program target (% of awareness) and one impact target (% of mortality decrease) might be barriers. Based on new definitions, we try to re-calculate these two targets. Annual incidence of HCV viremia in high risk patients <2% might hard to meeting. Unlimited reimburse of DAA treatment course should be one of resolution. We have given suggestion to the National Health Insurance.

In the lecture, I will present Taiwan’s current national status in approaching targets of WHO guidance.

專題討論（8）

Last mile in DAA era: chance and challenge

HCV consortium in Taiwan: Accumulation real world evidence for HCV care

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Real-world data is the most critical step to valid the evidence from successful clinical trials. In the fiend of hepatitis C virus (HCV) treatment in Taiwan, two large consortiums have been established. The first one is a precipitating investigator-initialed interferon-based cohort, Taiwanese Chronic Hepatitis C Cohort (T-COACH), which comprised more than 17,000 chronic hepatitis C (CHC) patients from 22 sites. There are 8 publications of the T-COACH consortium. The study results encompassed the predictors of hepatocellular carcinoma (HCC) and the benefit of HCV eradication in reducing liver and non-liver related outcomes. With the innovation and application of directly-acting antivirals (DAAs) in Taiwan, TASL HCV Registry (TACR), which is a prospective, observational, nationwide DAA-treated CHC cohort is organized and supervised by the Taiwan Association for the Study of the Liver (TASL). As of December 2023, The TACR comprises 43,756 patients recruited from 21 tertiary hospitals, 27community hospitals and 5 primary care clinics. The patient number represented nearly one-third of the DAA treated patients in Taiwan. TACR consortium has explicitly addressed the treatment efficacy of novel DAAs including sofosbuvir/ledipasvir with or without ribavirin, sofosbuvir/velpatasvir, and glecaprevir/pibrentasvir in Taiwanese CHC patients. Meanwhile, the short-term outcome including platelet count recovery, glycemic control and renal function improvement have been proven in TACR cohort. Studies regarding long-term liver and non-liver related outcome in TACR are ongoing to unveil the real-world benefits of HCV eradication by DAAs in Taiwanese CHC patients.

專題討論（8）

Last mile in DAA era: chance and challenge

Risk and characteristics of post post-SVR HCC

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Hepatitis C virus (HCV) infection is the lead cause of hepatocellular carcinoma (HCC) in the world. In patients without antiviral treatment, the natural history indicates that about cirrhosis is the key determinant for HCC, with an estimated risk of 1%-4% per year. Most patients with HCC present with cirrhosis, and therefore, various surrogate makers for invasive liver biopsy, including AST/ALT ratio, APRI index, FIB-4 index, FibroTest and liver stiffness measurements (LSMs) can predict HCC development. Furthermore, risk factors that fasten the carcinogenesis and hepatic fibrosis, such as hepatitis B virus (HBV)/human immunodeficiency virus (HIV) coinfection, male sex, alcohol exposure may increase the risk of HCC development. However, a subset of patients develops HCC without evidence of cirrhosis or advanced hepatic fibrosis. HCV viral genotype 3, which promotes the derangement of hepatic lipogenesis, is proposed to enhance HCC development. Further, the transforming potential of NS3 protein and core protein has been described.

In contrast to interferon (IFN), which only eradicate HCV in a limited proportion of patients, the introduction of direct-acting antivirals (DAAs) further advances the viral cure in almost all patients with HCV. Although the overall risk of HCC development significantly decreases following treatment-induced sustained virologic response (SVR), there are still risks of HCC development after viral cure. Currently, the potential risks of HCC after HCV cure include lack of hepatic fibrosis regression, concomitant presence of metabolic-dysfunction associated fatty liver disease (MAFLD), presence of diabetes mellitus (DM), continuous alcohol consumption, or poor suppression of HBV or HIV viremia. The pathogenesis of HCC after HCV cure remains elusive. In additional to the aforementioned risk factors, the genetic and epigenetic modifications in hepatocyte may play a central role in the HCC carcinogenesis in the absence of virus.

In the era of DAA, the development of HCC remains a significant concern especially among those with advanced hepatic fibrosis. A number of factors including DM, underlying MAFLD and alcohol consumption have been associated with progression to HCC after HCV cure. Promising HCC predictive models are being developed but most require validation and standardization. The pathogenesis of HCC after HCV cure remains poorly understood. The understanding of the molecular mechanisms leading to HCC could facilitate the identification of novel biomarkers for early HCC detection.

專題討論（8）

Last mile in DAA era: chance and challenge

Interaction between HCV and MAFLD/MASLD: viewpoints before and after SVR

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Fatty liver disease or steatotic liver disease (SLD) is now the major cause of chronic liver disease, and also leading to the main etiology for liver-related outcomes. Chronic hepatitis C (CHC) remain the main cause of liver cirrhosis and hepatocellular carcinoma globally. In 2020, metabolic dysfunction-associated fatty liver disease (MAFLD) has been proposed as a new definition for patients with fatty liver disease. The diagnosis of MAFLD was initially based on the detection of liver steatosis, either by histology, noninvasive biomarkers, or imaging modalities. The major intent of this steatosis-centered new nomenclature was to shift towards a diagnosis of inclusion based on the presence of metabolic dysfunction and hepatic steatosis. The new algorithm was formulated regardless of alcohol consumption or other concomitant liver diseases. Recently, the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) have achieved a new nomenclature of SLD for it. The new nomenclature is based on an affirmative and non-stigmatizing approach. SLD was chosen as an overarching term to encompass the various aetiologies of steatosis. NAFLD was renamed MASLD, encompassing patients who have hepatic steatosis and have at least one cardiometabolic risk factor. All the above-mentioned efforts for the precise definition of the metabolic liver disease imply not only the clinical importance but also the heterogenicity of the complex metabolic disease.

The prevalence of combined SLD and CHC was reported between 30 to 70% and the major risk factors included metabolic syndrome, obesity, type 2 diabetes, and dyslipidemia. SLD increased risk of disease progression on CHC. SLD did not impact the efficacy of current CHC direct acting antiviral therapy. However, SLD may exacerbate after SVR, mainly subsequent to the changes of lipid profile and BMI. Therefore, the long-term cardiometabolic outcome needs further elucidation. In conclusion, patients of chronic viral hepatitis need to screen SLD and consider a more aggressive control of SLD given the poor outcomes if combining SLD. The interplay between NAFLD and other common liver diseases such as viral hepatitis infections and alcoholic liver disease awaits investigation and exploration.

專題討論（9）

Precision Medicine of GI oncology

An Innovative Revisit of Circulating Tumor Cells in GI Oncology

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During past four decades cancer remains the number one cause of death in Taiwan. In the age of genomic-informed precision cancer medicine, there is a keen need to translate this paradigm into GI oncology and facilitates therapeutics development for better treatment outcome. Circulating tumor cells (CTC) are fugitive malignant cells found in the peripheral circulation in patients with solid tumors. These cells are enriched with cancer initiating cells and may contribute to prognostic and predictive information in disease management. In this short presentation, a brief overview of technology development and clinical validation of CTC in pancreatic cancer and in colorectal cancer in our laboratory will be provided. Moreover, the utility and potential of such technology will be highlighted in representative clinical cases. Comprehensive, real-time cancer characterization with liquid biopsy for genophenotyping in GI oncology is now feasible. Prospective studies are needed to uncover its clinical implications.

專題討論（9）

Precision Medicine of GI oncology

The Association of Microbiome and GI oncology

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Gastrointestinal cancer exerts a significant impact on healthcare systems worldwide. Among the array of factors influencing oncogenesis, certain microorganisms like *Helicobacter pylori*, hepatitis B and C viruses have been identified as playing pivotal roles. Moreover, disparities in microbiota composition have been observed between healthy individuals and those afflicted by cancer, hinting at potential implications. Research indicates that specific microorganisms and their byproducts may either foster or impede tumorigenesis through various mechanisms. Emerging studies suggest that the intricate makeup of the microbial community serves as a critical factor, potentially serving as biomarkers and predictors of treatment responses in cancer therapy. This discourse will delve into the latest discoveries concerning the intricate relationship between the gut microbiome and GI cancer, shedding light on prospective diagnostic and therapeutic applications.

專題討論（9）

Precision Medicine of GI oncology

The Perspective of Proton / Particle Therapy for GI oncology

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In the rapidly evolving domain of gastrointestinal (GI) oncology, precision medicine stands at the forefront, transforming treatment paradigms through the integration of proton and particle therapy. This approach marks a pivotal shift towards targeted therapeutic interventions, offering significant advantages in minimizing the adverse side effects traditionally associated with conventional treatments. The presentation, drawing upon the pioneering efforts at Taipei Medical University Hospital and reflecting global advancements, underscores the exceptional precision and reduced toxicity that characterize these innovative therapies.

Central to the presentation is an in-depth analysis of the clinical effectiveness and fundamental principles of proton therapy, highlighting its superior dose distribution capabilities in contrast to traditional radiotherapy methods. Proton therapy distinguishesitself by its ability to deliver concentrated doses of radiation directly to the tumor while significantly reducing exposure to surrounding healthy tissues. This advantage is due to the unique physical properties of protons, which enable a steep dose drop-off beyond the tumor, effectively eliminating the "exit dose" phenomenon commonly associated with photon-based radiotherapy. The importance of this attribute in reducing treatment-associated morbidity and enhancing the management of GI cancers over the long term is emphasized.

Furthermore, the GI oncology treatment landscape is witnessing a significant transformation, with a notable increase in the application of proton and particle therapy specifically in the treatment of liver, pancreatic, and rectal cancers. This development represents a major advancement, underscoring the critical role of precision therapies in tackling cancers that present substantial treatment challenges. The discussion will elaborate on the strategic importance of the therapies' dose precision and tissue-sparing benefits, which are crucial for enhancing treatment efficacy and improving patient outcomes for these cancers.

In summary, this presentation provides insights into the current and potential future applications of proton and particle therapy in GI oncology. By initiating a dialogue on the technological advancements and collaborative efforts required to optimize these therapies, it aims to highlight their role in advancing precision medicine within GI oncology, thereby paving the way for more effective and patient-centric cancer care.

專題討論（9）

Precision Medicine of GI oncology

New Advance of Immunotherapy for GI oncology

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In recent years, immunotherapy has emerged as a groundbreaking approach in the field of oncology, transforming the landscape of cancer treatment. This lecture aims to provide a comprehensive overview of the latest developments and breakthroughs in harnessing the immune system to combat gastrointestinal (GI) cancers.

The presentation will delve into the diverse array of immunotherapeutic strategies tailored specifically for GI malignancies, exploring the intricacies of immune checkpoint inhibitors. By dissecting the molecular and cellular mechanisms underpinning these advancements, we will gain insights into how immunotherapy is reshaping the treatment paradigm for esophageal, colorectal, gastric, pancreatic, and hepatobiliary cancers.

Additionally, the lecture will address the challenges and opportunities associated with combining immunotherapy with other modalities such as chemotherapy, radiation therapy, and targeted therapies.

Immunotherapies in resectable gastrointestinal cancers, especially in neoadjuvant or adjuvant settings, offer a potential paradigm shift. Clinical trials demonstrate improved disease-free survival with adjuvant PD-1 therapy in esophageal cancer. Neoadjuvant approaches, especially in dMMR rectal cancer, showcase the potential for non-operative, immunoablative strategies.

Biomarkers like microsatellite instability-high (MSI-H), tumor mutational burden (TMB), and PD-L1 expression have been explored to predict treatment responses. However, challenges persist in biomarker identification.

In conclusion, while the benefits of PD-1/PD-L1 blockade are restricted to specific patient subsets, ongoing research in new target development, predictive biomarkers, and combination therapies promises to refine immunotherapeutic strategies for gastrointestinal cancers in the future.

專題討論（10）

Recent advances and challenges in IBD treatment

How to choose advanced therapy: Learning from head-to-head trials

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Past and present head-to-head trials have improved our knowledge about drug positioning, risk stratification, treatment strategies. With the development of new biologics, a number of head-to-head studies are ongoing; their results might dramatically change our clinical practice in the near future.

The perspective of IBD trial also changed over time, facing the evolution of treatment goals and the increasing need for personalized therapy. The evolving goals for treatment in IBD, such as treat-to-target and tight control based on therapeutic monitoring and early intervention, have highlighted the increasing need for head-to-head performance trials to determine whether these strategies are cost-effective in reducing disease progression(reducing corticosteroid use, disability, bowel damage, hospitalizations, and surgeries), and to clarify the positioning of medical therapies, and strategies in the therapeutic algorithms.

專題討論（10）

Recent advances and challenges in IBD treatment

The role of combination therapy in difficult-to-treat IBD: where have we been?

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The definition of difficult to treat IBD from IOIBD has three domain, including 1. Treatment failure: the failure of advanced therapies , including biologics and oral small molecules, with at least two different MOA (mechanisms of action) and postoperative recurrence of Crohn's disease, two surgeries in adults and one in children; 2. Disease phenotype: chronic pouchitis refractory to antibiotic treatment, complex perianal disease; 3. Patient domain: Patient's coexisting psychosocial issues that impair adequate clinical management. This definition could serve as the standardization of clinical trials enrolment of patients with difficult-to-treat IBD and further data collection, comparison, and study for treatment policy for difficult to treat IBD.

We still has the therapeutic ceiling in IBD treatment, with overall clinical remission rates are at best 50%. The combination therapies, such as dual targeted therapy with two different mechanisms of actions of biologics and/or small molecules, has been explored in rheumatological and dermatological disease. The combination biological DMARDs showed no additional disease control in rheumatic disease, but increased the adverse events. But some of the biologics were not approved in IBD treatment, the results were not adequately extrapolating to IBD care. Several retrospective studies showed promising results in refractory IBD and IBD with EIMs. Dual targets therapy are under investigation prospectively and may has potential beneficial in some difficult cases.

The indications for dual target therapy are recommended to uncontrolled luminal activity and IBD with uncontrolled EIMs. The first RCT of dual targeted therapy was natalizumab plus infliximab in CD patients. The result showed no statistically significant in clinical remission through 32 weeks, compared to infliximab alone. The natalizumab was not worldwidely used due to potential risk of progressive multifocal leukoencephlopathy. In recent two prospective trials, EXPLORER Trial in CD and VEGA Trial in UC showed promising results for comibination therapy without increase adverse events . Several retrospective case series and systemic meta-analysis showed adequate clinical response/remission rates with acceptable adverse events. According to current studies, routine use of dual target therapy still had insufficient evidence in refractory IBD and EIMs.

Uncontrolled luminal activity and IBD with co-existing EIMs are suggested indication for dual targeted therapy, but further prospective RCT studies are warranted for better evaluate the benefit-to-risk ratio.

專題討論（10）

Recent advances and challenges in IBD treatment

The role of advanced therapy on complex peri-anal Crohn's disease

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Treating perianal Crohn's disease continues to present significant challenges and can profoundly diminish the quality of life for those affected. Advanced therapy plays a crucial role in the management of complex perianal Crohn's disease. Anti-tumor necrosis factor (anti-TNF) therapies, including infliximab and adalimumab, are the preferred medical therapy for this condition. Infliximab has demonstrated efficacy in improving fistula closure rates in randomized controlled trials.

In patients who do not respond to anti-TNF therapy, vedolizumab and ustekinumab may be considered. Combination therapy with immunosuppressives and anti-TNF agents may be beneficial in achieving optimal outcomes in patients at high risk of disease progression.

In addition to medical therapy, surgical interventions may be required. A multidisciplinary approach involving gastroenterologists, colorectal surgeons, endoscopists, and radiologists is often necessary for optimal management.

Emerging therapies such as local injection of mesenchymal stem cell therapy are also being explored for their potential benefits in treating perianal Crohn's disease.

In conclusion, managing complex perianal Crohn's disease often requires a combination of advanced medical and surgical therapies, with the choice of treatment tailored to the individual patient's disease characteristics and response to therapy.

專題討論（10）

Recent advances and challenges in IBD treatment

Is it the time for treatment de-escalation in IBD?

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Inflammatory Bowel Disease (IBD), encompassing Crohn's Disease (CD) and Ulcerative Colitis (UC), has traditionally been managed with escalating therapeutic strategies aimed at inducing and maintaining remission. However, the evolving understanding of IBD pathogenesis, coupled with advancements in diagnostic methodologies and therapeutic options, raises the question of the appropriateness and timing of treatment de-escalation in the management of IBD. This abstract explores the current landscape of IBD treatment, emphasizing the potential benefits and challenges associated with de-escalating therapy. Recent studies suggest that a significant proportion of IBD patients in sustained clinical remission might be over-treated, leading to unnecessary exposure to the risks associated with long-term use of immunosuppressants and biologics, including infections and malignancies. The concept of treatment de-escalation, which involves reducing the intensity or discontinuing certain medications, is gaining traction as a strategy to minimize these risks while maintaining disease control.

This speech critically examines the evidence supporting treatment de-escalation in IBD, including factors predictive of successful de-escalation, such as biomarkers of inflammation, mucosal healing, and patient-specific characteristics. It also addresses the psychological impact on patients, the economic benefits, and the potential for personalized medicine approaches in guiding de-escalation decisions. Despite the promising prospects of treatment de-escalation, several challenges remain, including the lack of standardized criteria for initiating de-escalation, the risk of disease relapse, and the need for close monitoring and patient education. The review concludes with recommendations for future research directions, emphasizing the need for well-designed, prospective studies to establish evidence-based guidelines for treatment de-escalation in IBD.

In summary, the question of whether it is time for treatment de-escalation in IBD is complex and necessitates a nuanced approach. While the potential benefits are significant, careful patient selection, ongoing monitoring, and further research are essential to safely and effectively implement this strategy in clinical practice.

專題討論（11）

Endoscopic management of complicated and difficult pancreaticobiliary diseases

Endoscopic ultrasound-guided biliary drainage for biliary obstruction

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ERCP trans-papillary stenting across strictures has become the standard treatment for benign or malignant biliary obstruction. Recent randomized clinical trial (Paik 2018) showed that EUS-guided biliary drainage (EUS-BD)procedures are comparable to ERCP for the primary palliation of unresectable malignant distal biliary obstruction in terms of technical and clinical success. Besides EUS-BD has lower rates of overall adverse events (6.3% vs 19.7%, $P = 0.03$), without post-procedure pancreatitis and higher rate of stent patency with a less re-intervention rate.

A recent meta-analyses (Park 2019) indicated that as the primary palliative treatment of MDBO, EUS-BD has similar technical and clinical success rates with a comparable safety profile. However EUS-BD posed a risk of bile peritonitis, while ERCP presented a risk of pancreatitis. Endosonographer must be familiar with procedures to reduce the risk of bile peritonitis by utilizing dedicated devices

The basic steps of EUS drainage treatment are puncture, guidewire placement, fistula dilation, and stent placement. Participants must be familiar with the process and prepare the necessary instruments and medical materials in advance.

EUS-BD may be a good, safe, and promising treatment modality as salvage procedure after failed ERCP or for the first-line palliation of unresectable malignant distal biliary obstruction.

專題討論（11）

Endoscopic management of complicated and difficult pancreaticobiliary diseases

Exploring innovative endoscopic solutions for pancreatic disorders

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Endoscopic interventions have revolutionized the management of pancreatic diseases, offering less invasive alternatives to traditional surgical approaches. This review explores recent advancements in endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS)-guided procedures, focusing on pseudocyst drainage, pancreatic duct drainage, walled-off necrosis (WON) management, and the EUS rendezvous technique.

ERCP remains a cornerstone in the diagnosis and treatment of pancreaticobiliary diseases. With technological enhancements, such as high-definition imaging and therapeutic accessories, ERCP has become increasingly precise and effective. It allows for the removal of pancreatic duct stones, stent placement in strictures, and dilation of strictures to alleviate obstruction.

EUS-guided pseudocyst drainage has emerged as a minimally invasive alternative to surgical drainage for symptomatic pancreatic pseudocysts. By accessing the pseudocyst through the stomach or duodenum under EUS guidance, endoscopists can safely create a fistula and drain the fluid, often placing stents to maintain patency and facilitate drainage.

Similarly, EUS-guided pancreatic duct drainage offers a less invasive approach for managing pancreatic duct strictures or obstructions. Utilizing EUS to access the pancreatic duct, endoscopists can perform various interventions, including dilation of strictures, stone extraction, and stent placement, thus improving pancreatic duct drainage and relieving symptoms.

The endoscopic management of pancreatic walled-off necrosis (WON) presents a significant advancement in the treatment of necrotizing pancreatitis. EUS-guided drainage and debridement allow for direct access to necrotic collections, facilitating drainage and necrosectomy under real-time imaging guidance, often in conjunction with transluminal stent placement to maintain patency.

The EUS rendezvous technique combines the advantages of EUS and ERCP, particularly in cases where conventional ERCP fails due to anatomical challenges or failed cannulation. In this approach, EUS is used to identify the pancreatic duct and create a fistula, allowing for subsequent ERCP-guided interventions or stent placement.

The advancements in endoscopic management provide patients with pancreatic diseases minimally invasive options, lessening reliance on surgery and its risks. Yet, ongoing research is crucial to refine techniques, standardize protocols, and evaluate long-term outcomes, ensuring continued progress in pancreatic disease management.

專題討論（11）

Endoscopic management of complicated and difficult pancreaticobiliary diseases

Recent advances in cholangiopancreatoscopy

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Difficult biliary and pancreatic stones, including large and/or impacted bile duct and pancreatic duct stones, cystic duct stones, and intrahepatic duct stones cannot usually be treated by conventional endoscopic retrograde cholangiopancreatography (ERCP). Recently, cholangiopancreatoscopy-assisted lithotripsy using electrohydraulic lithotripsy (EHL) or laser lithotripsy (LL) provides an alternative modality for ductal clearance. Indeterminate biliary stricture is defined as a diagnosis cannot be made after basic laboratory work-up, abdominal imaging and ERCP with biliary sampling. Indeterminate biliary stricture is still a complicated challenge in diagnosis, requiring a multidisciplinary approach. Per-oral cholangioscopy (POC)-targeted biopsies, potential to overcome the problems associated with inadequate tissue sampling and increase the diagnostic sensitivity of bile duct tumors. Combined POC-targeted biopsies with frozen section histopathology provides an immediate and efficient diagnosis and allows an early surgery for patients with bile duct tumors.

專題討論（11）

Endoscopic management of complicated and difficult pancreaticobiliary diseases

ERCP treatment in biliary complications after right liver transplantation

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Bile leak and anastomotic strictures (AS) are well-known and common complications of right liver living donor liver transplantation (LDLT) and right split liver transplantation. The morbidity associated with biliary complications is high, impairing the quality of life because of frequent hospitalizations and also has an impact on mortality.

Regardless the type of grafts and biliary reconstruction, the overall incidence of biliary complications in recipients ranges from 7.4% to 39%, leaks occur in 5.1%-23.4%, and strictures occur in 6.5%-21.5%. Endoscopic therapy is the first-line of treatment. The endoscopist should make all effort the review the operative record the understand the type of anastomosis. In a post-transplant setting, an undiagnosed sepsis, non-resolving ascites, or localized collection must prompt an aggressive evaluation and ERCP to detect and bridge the leakage site. Although ERCP approach is usually less invasive than other treatments, ERCP complications such as acute pancreatitis may be an associated morbidity. The scope position for bile duct cannulation may be more difficult to achieve selective bile duct cannulation. Endoscopic management of AS can be achieved effectively by serial ERC procedures with balloon dilation and placement of multiple stents across the strictures. AS after living LDLT are classified single, folk, trident and multiple depending on their location and morphology. AS are defined as segmental or focal narrowing around a biliary anastomosis. Non-AS are defined as one or more focal areas of narrowing of the bile ducts proximal to the biliary anastomosis. The strictures are longer, often at multiple sites. They can create technical challenges to effective endoscopic treatment.

ERCP treatment for AS after LDLT is sometimes difficult due to small-size, multiple and complex anastomoses and rotation for twisting of the AS caused by anastomotic fibrosis. PTCD followed by combined ERC treatment can also be an effective rescue if initial ERC failure. The success rate for endoscopic treatment is about 80% in our hospital. The more effective treatment modalities are needed. Placing a newly designed SEMS combined with plastic stent placement to complete bile duct drainage, dilate the stricture and drainage can be a promising future treatment.

專題討論（12）

Optimizing IBS management: current status and updates

Management of IBS: new disease, new therapies

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The irritable bowel syndrome (IBS) is diagnosed based on the Rome IV symptom criteria although current guidelines recommend a few additional non-invasive investigations even in the absence of alarm symptoms. Despite convincing evidence IBS symptoms are diet-driven and often postprandial, a relationship to eating or meals is not an IBS diagnostic criterion in Rome IV. Emerging data suggest the Rome IV criteria are most suitable for identifying more severe IBS and least useful for sub-diagnostic Rome III IBS criteria positive patients who will still likely benefit from IBS treatment. The four IBS subtypes in Rome IV are unstable if evaluated over time, calling into question the concept of subgroups based only on stool form; data-driven alternatives based on latent class analysis have been proposed. IBS overlaps more than expected by chance with several disorders (including functional dyspepsia, gastroesophageal reflux and asthma), suggesting the possibility of a similar common underlying pathogenesis. Few IBS biomarkers have been identified, which may suggest the syndrome as currently defined is too heterogeneous to be objectively characterized. In clinical practice, although guidelines recommend a positive diagnosis, the extent to which clinicians seek an underlying cause of IBS-like symptoms is variable. A number of organic diseases are IBS mimics that are important to not overlook, albeit uncommon (e.g. ovarian cancer, young onset colon cancer, alpha-gal syndrome, sucrase-isomaltase deficiency). Treatment of IBS is symptom-based and FDA approved drugs only modestly improve constipation or diarrhea-predominant IBS over placebo; mixed IBS and bloating remain orphan syndromes. No drug cures IBS but rifaximin (and fecal transplant) may temporarily relieve symptoms after cessation of therapy implicating the microbiome. Emerging treatment options based on new pathophysiologic insights include exclusion diets and anti-histamines.

專題討論（12）

Optimizing IBS management: current status and updates

Epidemiology and clinical characteristics of IBS in Taiwan

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Irritable bowel syndrome (IBS) is a relapsing functional bowel disorder defined by symptom-based criteria, including recurrent abdominal pain, change of bowel habits (constipation and diarrhea alternatively), and symptomatic relief after bowel movement. Physicians should pay attention to alarming clinical features and exclude organic diseases before reaching the diagnosis of IBS. It is important to carefully review the stool patterns to determine the predominant bowel symptoms and IBS subtypes (IBS with constipation, IBS with diarrhea, or mixed IBS) so appropriate treatment could be initiated. The chronic and relapsing nature of the disease has a high impact on patient's quality of life, resulting in frequent hospital visits and consumption of medical resources. The exact pathophysiology of IBS is complex and remains elusive. Previous studies suggested IBS to bemultifactorial, including alterations in gut microbiota, immune dysfunction, brain-gut interactions, visceral hypersensitivity, bowel dysmotility, and psychosocial comorbidities. Management of IBS includes regular exercise, diet control (low FODMAP diet), probiotics, medical treatments (antidiarrheals, serotonin agents, antispasmodics for IBS-D; fiber supplements, laxative agents, and prosecretory agents for IBS-C).

The prevalence of IBS has been reported to be high in Taiwan, 22.1% and 17.5% as defined by the Rome II and I criteria, respectively, according to the 2003 survey of a population receiving physical check-ups at a medical center. However, the prevalence of IBS based on a later nation-wide survey in Taiwan during 2005-2008 was 4.4% using the Rome III criteria. The difference may be explained by the stricter criteria of Rome III criteria on the frequency of abdominal symptoms. Recently, we conducted a study to investigate the updated prevalence and clinical characteristics of IBS in the Taiwanese population and found a 6% and 1.2% prevalence of IBS according to the Rome III and IV criteria, respectively. Compared with the control group, the IBS group had higher psychosocial stress and insomnia symptoms. The severity of psychiatric and insomnia symptoms was positively correlated with the frequency of abdominal pain. Our study suggests the pivotal role of psychiatric stress and sleep disturbance on the rising prevalence of IBS, and multidisciplinary intervention with psychiatric consultation is necessary for IBS patient care.

專題討論（12）

Optimizing IBS management: current status and updates

Update on current IBS guidelines and consensus

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Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal pain or discomfort and altered bowel habits in the absence of detectable structural abnormalities. After the announcement of the Rome IV criteria in 2016, updates of international and nationwide guidelines became available worldwide, reflecting new research findings and responses to changes in the criteria. In addition to symptoms used for diagnosis, IBS patients can have other symptoms, including dyspepsia, bloating and diet-related symptoms, which may be related to overlapping functional gastrointestinal diseases. A positive diagnostic strategy based on symptoms is favored to avoid unnecessary investigation. Laboratory tests and colonoscopy may be performed in elderly patients or patients with warning signs. Anorectal physiology tests can be considered in patients with symptoms suggestive of a pelvic floor disorder and/or refractory constipation not responsive to standard medical therapy. Diet therapy, such as a low-fermentable oligo-, di-, or monosaccharide and polyol (FODMAP) diet, can be used to improve global symptoms. Soluble fibers are also useful in the management of global IBS symptoms. In medical therapy for IBS, there is a great difference between Asian and Western countries, as the amount of available medication differs between Eastern and Western countries. Antispasmodics are suggested as first-line therapies for abdominal pain and global symptoms in Eastern countries; however, most effective medications are not available in the United States. Polyethylene glycol can be used to relieve global symptoms in IBS-constipation patients. Novel agents, including chloride channel activators, guanylate cyclase activators, sodium-hydrogen exchange inhibitors, and 5-HT4 agonists, are suggested for use in IBS-related constipation patients, while 5-HT3 antagonists and mixed opioid agonists/antagonists are suggested for use in IBS-related diarrhea patients. The nonabsorbable antibiotic rifaximin is suggested for treating IBS-related diarrhea patients. Tri-cyclic acid can be used to improve global symptoms, while other antidepressants, such as serotonin reuptake inhibitors, are not universally suggested. Psychotherapies are effective in the management of IBS patients and can be considered for referral patients. Further studies focusing on the predictors of treatment responses and novel treatment development can help improve patient management.

專題討論（12）

Optimizing IBS management: current status and updates

How to manage conditions overlap with IBS?

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Irritable Bowel Syndrome (IBS) is identified as a chronic, symptom-based functional gastrointestinal disorder, characterized in accordance with the Rome IV criteria by a duration exceeding six months of recurrent or chronic abdominal pain, which is either related to defecation or associated with alterations in stool frequency or form. IBS manifests a wide spectrum of gastrointestinal symptoms, which frequently exhibit an overlap with other functional GI disorders and conditions. This symptomatic overlap commonly occurs and adversely affects the outcomes of therapeutic interventions, presenting a notable challenge in clinical management due to the absence of comprehensive guidelines. In this presentation, we aim to synthesize the current literature, with a particular emphasis on exploring the management strategies employed when conditions such as gastroesophageal reflux disease, functional dyspepsia, or inflammatory bowel disease present concomitantly with IBS.

專題討論（13）

Recent Advances in the Treatment of *H. pylori* Infection

Update on the first-line treatment of *H. pylori* infection

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Introduction

Marshall and Warren discovered *Helicobacter pylori* (*H. pylori*) from patients with gastritis and peptic ulcer disease in 1983.[1] In 1994, the World Health Organization classified *H. pylori* infection as a Group I carcinogen for gastric cancer. Currently, *H. pylori* infection remains one of the most common chronic bacterial infections affecting humans, and is an important cause of peptic ulcer disease and gastric cancer. It also plays a role in uninvestigated and functional dyspepsia, ulcer development in patients taking low-dose aspirin or non-steroidal anti-inflammatory medication, unexplained iron deficiency anemia, and idiopathic thrombocytopenic purpura.[2] The main reasons for eradication failure for *H. pylori* infection include antibiotic resistance, poor compliance and rapid metabolism of proton pump inhibitor (PPI). Antibiotic resistance has been identified as the main reason for the eradication failure of *H. pylori* infection. While choosing a treatment regimen, antibiotic resistance of *H. pylori* should be incorporated into the decision-making process.

First line therapy

The eradication rate of clarithromycin-based triple therapy consisting of a PPI, clarithromycin, and amoxicillin or metronidazole for 7 days has fallen below 80% due to emerging antibiotic resistance worldwide.[3] Clarithromycin resistance rates have now reached to 30% in Italy and Japan, 40% in Turkey, and 50% in China and 15% in Sweden.[4] In Taiwan, clarithromycin resistance of *H. pylori* ranges from 10% to 14%.[5, 6], and 7-day standard triple therapy only achieves an eradication of 73%-82%.[7, 8] Several effective first-line eradication regimens including concomitant therapy, sequential therapy, hybrid therapy, quadruple therapy, and levofloxacin triple therapy have been developed to improve the eradication rate (Table 1). [9]

In North America, 14-day clarithromycin triple therapy is still recommended by the ACG guideline in regions with clarithromycin resistance rate <15% and in patients with no previous history of macrolide exposure for any reason.[10] However Liou *et al* reported the eradication rate of 14-day triple therapy was only 85.7% by ITT analysis in northern Taiwan.[5] In the Maastricht V/Florence Consensus Report, bismuth quadruple or non-bismuth quadruple, concomitant (PPI, amoxicillin, clarithromycin and a nitroimidazole) therapies are recommended in areas with high clarithromycin resistance (>15%).[11] In areas of high dual clarithromycin and metronidazole resistance, bismuth quadruple therapy (BQT) is the recommended first-line treatment.[11] In the Taiwan *H. pylori* Consensus Report, a 14-d clarithromycin-based therapy (hybrid, sequential, concomitant, or triple therapy) is the treatment of choice in areas with low clarithromycin resistance (≤15%). A 10-to14-day BQT is a suitable alternative first-line therapy.[9] In areas with high clarithromycin resistance (>15%), a 10-to14-day bismuth quadruple therapy is a recommended treatment, and a 14-day hybrid or concomitant therapy

is an alternative first-line therapy (Figure 1).[9]

Sequential therapy is more complex and requires changing antibiotic drugs during the treatment course, which can be confusing for patients. Concomitant therapy therefore is easier to meet patients' adherence compared to sequential therapy and tolerability is similar to standard triple therapy. The recommended treatment duration of non-bismuth quadruple therapy (concomitant) in the Maastricht V/Florence Consensus Report is 14 days, unless 10-day therapies are proven effective locally.[11] Studies from Taiwan reported that 7-day and 10-day concomitant therapy can achieve an eradication rate > 90%.[7, 12] The eradication rate of hybrid therapy (or reverse hybrid therapy) ranges from 92% to 97%.[6, 13, 14] Good results of hybrid therapy have also been reported in Spain and Iran, but unsatisfactory results have been described from Korea.[11]

H. pylori infection can be eradicated by elevating intragastric pH using an acid suppressant in combination with at least 2 antibiotics. *H . pylori* enters the growth phase from a stationary phase at intragastric pH above 5, at which point it becomes susceptible to antibiotics.[15] Although conventional PPIs have been used to suppress gastric acid secretion, recent eradication rates have decreased due to increases in antibiotic-resistant *H . pylori* strains. Increasing the dosage of PPIs and changing antibiotics have been attempted to increase the eradication rate. In addition, the development of P-CABs that can strongly suppress acid secretion has been an attractive option for increasing the eradication rate. A randomized, double-blind study was conducted to prove the non-inferiority of 20 mg vonoprazan compared to 30 mg lansoprazole for the first-line triple therapy for *H . pylori* eradication with 750 mg amoxicillin and 200 mg or 400 mg clarithromycin.[16] All drugs were administered orally twice daily for 7 days. The eradication rate with vonoprazan was 92.6% compared to 75.9% with lansoprazole in first line therapy.[16] first-linetripleVPZ-containingtherapies (VPZ/AMX/CLR) therefore show superior efficacy in Japanese individuals in terms of *H. pylori* eradication compared to PPI-containing therapies in many clinical studies.[17] VPZ-containing triple therapy shows high effects in terms of *H.pylori* eradication compared to PPI-containing therapy, especially in patients infected with CLR-resistant strains who received VPZ/AMX/CLR as first-line therapy Importantly, however, eficacy is similar between VPZ-containing and PPI-containing eradication therapy in patients infected with CLR-sensitive strains who received VPZ/AMX/CLR as first-line therapy and patients who received VPZ/AMX/MNZ as second-line therapy.[17] However, the clinical studies almost product from Japan.

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專題討論（13）

Recent Advances in the Treatment of *H. pylori* Infection

Update on the second-line treatment of *H. pylori* infection

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The Maastricht VI/Florence Consensus Report recommends various options, including bismuth quadruple therapy, fluoroquinolone-containing regimens, and high-dose proton pump inhibitor (PPI)-amoxicillin dual therapy. However, the efficacy of levofloxacin-amoxicillin triple therapy is compromised by the increasing prevalence of levofloxacin-resistant strains, necessitating novel approaches.

Recent advancements include the development of a tetracycline-levofloxacin quadruple therapy, which, in randomized controlled trials, demonstrated a significantly higher per-protocol eradication rate (98%) compared to levofloxacin-amoxicillin triple treatment (69%). Other promising alternatives encompass high-dose dual PPI-amoxicillin therapy and levofloxacin-based sequential quadruple therapy, both yielding eradication rates above 85%. Moreover, a meta-analysis underscores the superiority of vonoprazan-based regimens over PPI-based ones in second-line *H. pylori* eradication.

In conclusion, this update highlights the suboptimal efficacy of conventional therapies and recommends evolving strategies like tetracycline-levofloxacin quadruple therapy, amoxicillin-levofloxacin quadruple therapy, levofloxacin-based sequential quadruple therapy, or vonoprazan-based regimens for more effective second-line treatment of *H. pylori* infection in response to evolving resistance patterns.

專題討論（13）

Recent Advances in the Treatment of *H. pylori* Infection

Application of bacterial culture and genetic testing in the treatment of *H. pylori* infection

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Recent findings suggest that eradicating *Helicobacter pylori (H. pylori)* decreases the likelihood of gastric cancer in infected individuals. Treatment for *H. pylori* involves using a potent acid suppressant in combination with antibiotics and/or bismuth. However, the notable increase in resistance to essential antibiotics for *H. pylori* eradication necessitates conducting antibiotic susceptibility testing, continuous resistance monitoring, and judicious antibiotic use. Studies have demonstrated the superiority of therapy guided by culture-based susceptibility testing over empirical therapy as a first-line treatment for *H. pylori* infection. Nevertheless, the time-consuming and inconvenient nature of culture-based susceptibility testing limits its widespread use in clinical practice. Notably, clarithromycin resistance in *H. pylori* is associated with point mutations in 23S ribosomal RNA (23S rRNA), while levofloxacin resistance is correlated with point mutations in gyrA. Recent trials have indicated that molecular testing-guided therapy is comparable to susceptibility testing-guided therapy in first-line treatment and non-inferior in third-line treatment for *H. pylori* infection. These findings support the adoption of molecular testing-guided therapy as an effective strategy for *H. pylori* eradication.

專題討論（15）

Steatotic Liver Disease

The new definition and nomenclature of steatotic liver diseases

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The principal limitations of the terms NAFLD and NASH are the reliance on exclusionary confounder terms and the use of potentially stigmatising language. The American and European liver associations have endorsed new nomenclature of steatotic liver disease (SLD) and definition of metabolic dysfunction-associated steatotic liver disease (MASLD).

The SLD umbrella allows classification of patients under the key categories of MASLD, alcohol-associated liver disease and a new entity termed MetALD, which represents MASLD with increased alcohol intake. The diagnosis of MASLD requires the demonstration of hepatic steatosis and at least one metabolic risk factor, whereas MASLD can co-exist with other liver diseases such as chronic viral hepatitis. Despite the change in definition, over 95% of patients previously known as having NAFLD fulfil diagnostic criteria for MASLD. It is conceivable that future clinical trials and biomarker studies will continue to exclude concomitant liver diseases. As most patients with MASLD are seen at primary care and non-hepatology settings, communication with other stakeholders is essential to ensure disease awareness and smooth adoption of the changes. The term steatohepatitis was felt to be an important pathophysiological concept that should be retained. The name chosen to replace NAFLD was metabolic dysfunction-associated steatotic liver disease (MASLD). There was consensus to change the definition to include the presence of at least 1 of 5 cardiometabolic risk factors. Those with no metabolic parameters and no known cause were deemed to have cryptogenic steatotic liver disease. A new category, outside pure metabolic dysfunction-associated steatotic liver disease, termed metabolic and alcohol related/associated liver disease (MetALD), was selected to describe those with metabolic dysfunction-associated steatotic liver disease, who consume greater amounts of alcohol per week (140-350 g/wk and 210-420 g/wk for females and males, respectively).

The highlight the utility of the new consensus nomenclature to address deficiencies present with the old nomenclature, and identify areas that require research to further refine classifications of SLD.

專題討論（15）

Steatotic Liver Disease

Pathological perspectives of steatotic liver diseases

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Steatotic liver disease is due to fatty change of liver. In the past, most common steatotic liver disease was caused by alcoholism. But in recent 20-30 years, steatotic liver disease has become a very common cause of liver test elevation, paralleling the worldwide 'epidemic' of obesity in adults and not caused by alcoholism. Thus, Nonalcoholic fatty liver disease (NAFLD) was used commonly. Recently, Metabolic-associated fatty liver disease (MAFLD) has been used to replaced NAFLD, since steatotic liver disease is often associated with systemic metabolic diseases. In 2023, a new name for steatotic liver disease was used by AASLD as metabolic dysfunction-associated steatotic liver disease (MASLD). No matter the changes of the name, pathology features are all the same, i.e. fatty change, inflammation and fibrosis. Steatohepatitis mainly includes alcoholic steatohepatitis (ASH) and non-alcoholic steatohepatitis (NASH). The histology of ASH and NASH could be quite similar to each other. The classic histologic features of steatohepatitis include fatty changes, lobular inflammation and hepatocyte injury. The inflammation and hepatocyte injury would cause pericentral, perisinusoidal and pericellular fibrosis. Hepatocytes usually have ballooning change, which would cause compression of the sinusoid and reversible portal hypertension. The inflammatory cell infiltrate, located primarily in the sinusoids and around the necrotic hepatocytes, consists of mononuclear cells and polymorphonuclear cells. All of the pathology features can been seen in both ASH and NASH. Thus, clinical history is most important for the differential diagnosis. The gold standard for a diagnosis of NASH and separating it from simple fatty liver is a liver biopsy. The clinic-pathological correlations will be discussed.

專題討論（15）

Steatotic Liver Disease

Prognosis and diagnosis of steatotic liver diseases

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Steatotic liver disease (SLD) is now the major cause of chronic liver disease, and also leading to the main etiology for liver-related outcomes. NAFLD per se is associated with extrahepatic manifestations such as chronic kidney disease, cardiovascular disease and sleep apnea. In 2020, metabolic dysfunction-associated fatty liver disease (MAFLD) has been proposed as a new definition for patients with fatty liver disease. The diagnosis of MAFLD was initially based on the detection of liver steatosis, either by histology, noninvasive biomarkers, or imaging modalities. Recently, the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) have achieved a new nomenclature of SLD for it. The new nomenclature is based on an affirmative and non-stigmatizing approach. SLD was chosen as an overarching term to encompass the various aetiologies of steatosis. NAFLD was renamed MASLD, encompassing patients who have hepatic steatosis and have at least one cardiometabolic risk factor. All the above-mentioned efforts for the precise definition of the metabolic liver disease imply not only the clinical importance but also the heterogenicity of the complex metabolic disease.

Non-alcoholic steatohepatitis, an extreme form of NAFLD had higher overall mortality compared with controls, and most deaths were due to cardiovascular events. NASH was defined by histopathologic evidence as an extreme form of NAFLD. NASH has been a histologically defined disease, characterized by hepatic steatosis, ballooning, and lobular inflammation with variable fibrosis. NASH is also a potentially progressive liver disease that can lead to cirrhosis, hepatocellular carcinoma, liver transplantation, and death. It's commonly associated with related metabolic diseases, leading to cardiovascular events as its leading cause of death. The metabolic disorders include abdominal obesity, hypertension, dyslipidemia and insulin resistance (IR) and further increase the risk of cardiovascular disease (CVD), T2DM and chronic kidney disease. The scenario of a higher overall mortality due to CVD as compared with controls has made it a critical global issue.

專題討論（15）

Steatotic Liver Disease

Recent advances in the treatment of steatotic liver diseases

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While no drugs are approved for steatotic liver disease (SLD), treatments of metabolic conditions closely associated with SLD may potentially reverse insulin resistance, thereby ameliorating steatohepatitis and preventing fibrosis. Although lifestyle modification and weight loss are recommended as first-line interventions and effectively reduced steatosis, inflammation, and fibrosis, they are often unsuccessful. Therefore, pharmacological therapy may address the gap in inhibiting SLD progression. The use of approved anti-diabetic drugs has been investigated in NASH, including biguanides, glucagon-like peptide-1 receptor agonists (GLP-1RA), dipeptidyl peptidase-4 inhibitors (DPP-4i), sodium-dependent glucose cotransporter-2 inhibitors (SGLT-2i), and PPAR agonists. Novel agents for SLD are being evaluated in different phases of clinical development, and their mechanism of action include participation in de novo hepatic lipogenesis, mitochondrial fatty acid oxidation, inflammation, cell injury, collagen deposition, and fibrinolysis.

專題討論（16）

Stem cells: The state-of-The-Art

Cancer stem cell and gastric organoids

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The gastric cancer- and normal-organoids from the cancerous parts and iPS cells were established several years ago. Gastric cancer (GC) organoids are frequently used to examine the tumorigenic ability of human GC. GC organoids can be used in the identification of novel antioxidant drugs to prevent the progression of GC. GC organoids were used to examine cell proliferation and death as well as cancer development. Owing to the remarkable degree to which they recreate the cellular diversity observed in the human stomachs, they have attracted significant interest as a novel model system for precision medicine. However, many questions remain regarding the extent to which these cultures recapitulate gastro-development and mechanism of cancer progression infected by *Helicobacter pylori (H.p.)*.

The novel antioxidant drugs PEA and CA inhibited the development and invasive activity of human GC, which were evaluated using GC organoids. By contrast, SFN increased tumorigenesis. Moreover, ROS production was also inhibited by treatment with PEA and CA but not SFN. Nrf2 plays a key role in the differential effects of these antioxidant drugs on cancer invasion. PEA and CA can potentially be new antitumorigenic therapeutics for GC.

We also conclude that HDGF and TNFα are independent signals for development of *H. pylori*-infected gastric cancer. The signaling of growth factors in 3-D organoid culture systems is different from those in two-dimensional cancer cells.

專題討論（16）

Stem cells: The state-of-The-Art

iPSC 在藥物開發與細胞治療的應用
Harnessing the Power of Human iPSCs: Innovations in Drug Development and Cardiac Regeneration

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In this invited talk, I will explore groundbreaking research in the field of induced pluripotent stem cells (iPSCs) and their transformative applications in drug development and cell therapy. Drawing insights from two significant papers from our group, the first study establishes a revolutionary population-based hiPSC drug screening platform for toxicity assessment. By identifying 13 HLA-homozygous "super donors" from a diverse pool of a thousand healthy individuals, we created representative hiPSCs that can effectively mirror a substantial portion of the global population. These hiPSC-derived cardiomyocytes and neurons were employed in a high-throughput toxicity screen, demonstrating the platform's feasibility and potential for studying inter-population differences in drug toxicity and adverse reactions, offering innovative solutions for drug discovery. (Huang et al. *Cell Reports*, 2022)

The second paper delves into the combined treatment of hiPSC-derived cardiomyocytes (CMs) and endothelial cells (ECs) for regenerating the infarcted heart. Addressing critical challenges in cell transplantation therapy, this study reveals that hiPSC-ECs enhance the maturity and function of hiPSC-CMs both in vitro and in vivo. Co-transplantation of these cells in mouse models and non-human primates demonstrates a synergistic effect, significantly improving vascularization, promoting CM maturity, and enhancing cardiac function post-myocardial infarction. These findings showcase a promising strategy for clinical translation, emphasizing the potential of iPSCs in overcoming hurdles related to cell survival, vascularization, and arrhythmogenesis in cardiac regeneration. (Cheng YC et al. *Circulation*, 2023)

Join me in exploring the cutting-edge applications of iPSCs that are reshaping the landscape of drug development and offering novel therapeutic avenues for cardiovascular diseases.

專題討論（16）

Stem cells: The state-of-The-Art

Stem cell and its derivatives in disease treatment

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Stem cells and their derivatives are advanced therapies used for the treatment of diseases, particularly among the elderly population and for addressing unmet medical needs. The effectiveness of these therapies in disease treatment is significantly influenced by their administration routes and the tissue biodistribution.

Mesenchymal stem cells (MSCs) are the primary allogeneic stem cell products utilized in current cell and gene therapy. Currently, there are more than 1200 ongoing clinical trials involving MSCs, along with 8 trials concentrating on the MSC secretome and 17 trials focusing on MSC exosomes. These trials aim to tackle a variety of diseases, notably age-related neurodegeneration, bone defects, infertility, and virus-associated lung diseases.

During this presentation, I will discuss the potential biodistribution and disease treatment capabilities of both stem cells and their extracellular vesicles (EVs). The significance of administering these cells or their derivatives through appropriate routes and ensuring their effective distribution within the body's tissues will be emphasized to achieve therapeutic efficacy in disease treatment.

專題討論（16）

Stem cells: The state-of-The-Art

iPSC 於臨床疾病研究之機會與挑戰

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Since their discovery in 2007, human induced pluripotent stem cells (iPSCs) have offered vast opportunities for research and therapy development. Advances in iPSC technology have enabled their use in disease modeling, preclinical studies, and potentially in cell-based therapies. Our team successfully differentiated iPSCs from patients with autosomal dominant polycystic kidney disease (ADPKD) into cardiomyocytes, confirming key protein expression. Using electrophysiological techniques, we observed abnormalities in calcium cycling and drug responses consistent with previous findings in animal models. Notably, the similarity between the behavior of these iPSC-derived cardiomyocytes and the clinical phenotypes of ADPKD patients highlights their potential as an *in vitro* disease model. As we explore the possibilities of iPSC research, we must address challenges such as differentiation efficiency and genetic stability to fully realize their research and therapeutic promise. By elucidating iPSC-derived disease models, we aim to advance personalized approaches for ADPKD and other unmet needs in the future.

專題討論（17）
醫療糾紛及醫預法議題

漫談醫療糾紛及醫預法

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過去一年間，我已經提供超過 30 件醫療糾方當事人法律諮詢。法律諮詢中病方最想知道的是醫療事件經過的真相，通常醫療人員都不會將醫療事故的細節告訴病人或家屬，只能透過全部病歷交叉比對及影像紀錄來還原醫療事故的經過。法律諮詢中醫方最想知道的是醫療事故發生後要怎麼善後及免責，這是人性可以理解，但也就是因此雙方對於醫療糾紛的處理立場不同，有礙於溝通及調解。2024 年 1 月開始施行醫療事故預防及爭議處理法，藉由強制調解優先原則制度納入法規強制施行，並結合多元醫療爭議評析管道，使病人方更能夠清楚了解醫療事故之經過，對於減少醫療糾紛進入法律訴訟途徑應該會有幫助。本次演講主要分享我過去接觸醫療糾紛法律諮詢、調解及訴訟之經驗，以及簡述今年醫療事故預防及爭議處理法新制度。

In the past year, I have provided legal consultations to over 30 parties involved in medical disputes. In these consultations, patients are most interested in knowing the truth behind the medical incidents. Typically, medical personnel do not disclose the details of medical accidents to patients or their families. Therefore, the only way to reconstruct the sequence of events is through a comprehensive review of all medical records and imaging records.

On the other hand, healthcare providers are most interested in knowing how to handle the aftermath and avoid liability after a medical accident. While this is understandable, it also leads to different perspectives on the handling of medical disputes, which hinders communication and mediation.

Starting in January 2024, the Medical Accident Prevention and Dispute Resolution Act will be implemented. This Act incorporates a mandatory mediation priority principle into the regulations and integrates multiple channels for analyzing medical disputes. This will enable patients to have a clearer understanding of the course of medical accidents, and it should help reduce the number of medical disputes that enter the legal process. In this presentation, I will mainly share my experience in providing legal consultations, mediation, and litigation services for medical disputes, as well as briefly describe the new system introduced by the Medical Accident Prevention and Dispute Resolution Act this year.

消化系基層醫療論壇

小鎮醫師的彩色人生：醫療救人百年，藝術千秋事業

Chiu-Cheong Ling（林紹昌）

Taitung Luke's Clinic
（台東路加診所）

"Time and tide wait for no man". We all have a life seems to pass away in a hurry.

As a doctor I am always busy at my work. I started my own clinic 27 years ago.

After settling down my work at clinic, I began to think what will I leave behind on the day I passed away . Then I notice the verse "Medical treatment saves lives for a hundred years and art is a career for a thousand years."So I started to learn oil painting. At first, I have tuition class with an art teacher . Since I got more interested in it, I further my study and took classes at National Taitung University and gained my Master of Art in 2011. The topic of my thesis is " The Study and Creation of oil Paintings on Medical services."Through 21 pieces of oil paintings I recounted " the white tower" stories on different medical aspects.On dreaming of having a beautiful hotel to hang my lovely art works, I started building my own hotel. The hotel ,I named it Joy Hotel, had grand opening on 2019.

消化系基層醫療論壇

消化系內科診所執行靜脈鎮靜內視鏡檢查之臨床實務分享 -- 由消化系醫師自己執行時

Yen-Gen Chang（張延亙）

永安診所

Intravenous sedation has been widely utilized for endoscopic examination, and primarily conducted by anesthesiologists in hospitals. However, it may be carried out by gastroenterologists in Primary Clinics due to limited resources. Because of the better examination experience, intravenous sedative endoscope became more popular in the primary gastroenterology Clinics.

Intravenous sedation significantly improves patient comfort during examinations, reducing anxiety and fear and facilitating smoother procedures. However, medication selection must be customized based on individual patient health and desired anesthesia level. Typically, Benzodiazepine (Midazolam), Opioids (Fentanyl), and Propofol are combined for sedation, either separately or together. Fentanyl, a Class III controlled substance, is subject to strict regulations, while Propofol, with its shorter action duration and potent sedation capabilities, requires cautious administration.

The decision to employ an anesthesiologist for intravenous sedation varies on different clinics. In smaller clinics with lower examination volumes, outsourcing may not be cost-effective or feasible to recruit. In such cases, administering intravenous sedation by the gastroenterologist becomes necessary. Thus, establishing a medication protocol and closely monitoring patients' physiological responses is crucial. Dosage should begin at the lowest level and incrementally adjusted to optimal levels. Significant differences in sedative dosage requirements exist due to racial and individual variations, necessitating practitioners to accumulate experience. Presently, regulations do not mandate intravenous sedation for endoscopic examinations, prompting gastroenterologist to assess associated risks independently.

消化系基層醫療論壇

消化系內科診所執行靜脈鎮靜內視鏡檢查之臨床實務分享 -- 由麻醉科醫師執行時

Hsih-Hsi Wang（王世晞）

宜康診所

消化系基層醫療論壇

基層消化系專科醫師健保申報論壇

Tun-Jen Hsiao（蕭敦仁）

敦仁診所

一般演講

主題：上消化道疾病（一）

①

胃上噯氣和日間酸性逆流事件的增加有關，但和逆流症狀的嚴重程度或食道過度警覺無關

SUPRAGASTRIC BELCHING IS ASSOCIATED WITH A HIGHER NUMBER OF UPRIGHT ACID REFLUX EPISODES, BUT NOT WITH REFLUX SYMPTOM SEVERITY OR ESOPHAGEAL HYPERVIGILANCE

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Background: Supragastric belching (SGB), considered a behavioral disorder, might play a role in causing symptoms of gastroesophageal reflux disease (GERD) along with esophageal hypervigilance and anxiety, as measured by the esophageal hypervigilance and anxiety scale (EHAS).
Aims: This study assessed the prevalence of SGB and its interaction with reflux patterns and EHAS in patients exhibiting typical reflux symptoms.
Methods: Patients exhibiting typical reflux symptoms with negative endoscopy underwent 24-hour impedance-pH monitoring. Phenotyping, reflux burden, and SGB were evaluated, and over 13 SGBs in 24 hours were considered excessive. Validated GERD questionnaire (GERDQ) and EHAS scores were recorded.
Results: Of the 160 patients (mean age, 45.2; 66.3% female), 34 had non-erosive reflux disease (NERD), 58 had reflux hypersensitivity (RH), and 68 had functional heartburn (FH). NERD patients had higher BMI and more reflux episodes than those with RH and FH. No significant differences in age, sex, GERDQ scores, EHAS, or excessive SGB prevalence were found among GERD phenotypes. In the study population, 21 patients (22.5%) had excessive SGB. These patients exhibited more upright reflux acid episodes, with no significant differences in terms of age, sex, BMI, GERDQ scores, EHAS, number of upright weak and nonacid reflux episodes, or number of all types of supine reflux episodes compared to those without excessive SGB.
Conclusions: Excessive SGB prevalence among patients with typical reflux symptoms and negative endoscopy was about 22.5% and was similar across phenotypes. Those with excessive SGB tended to have more acid reflux episodes when upright, but their overall symptom severity and EHAS scores were similar to patients without excessive SGB.

②

辨別喉咽逆流患者發生咽喉酸逆流之獨立風險因子

IDENTIFYING INDEPENDENT RISK FACTORS OF PHARYNGEAL ACID REFLUX EPISODES IN PATIENTS WITH LARYNGOPHARYNGEAL REFLUX

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Background: Pharyngeal acid reflux (PAR) assessed through 24-hour hypopharyngeal multichannel intraluminal impedance-pH (HMII-pH) technique (Chen YY et al., J Neurogastroenterol Motil 2023) holds potential for predicting the response to proton pump inhibitors (PPI) therapy in patients exhibiting suspected laryngopharyngeal reflux (LPR) symptoms, particularly when combined with excessive distal esophageal acid exposure time.
Aims: This study compares clinical and physiological features between LPR patients with PAR episode(s) and health controls.
Methods: In this case-control study, we examined 21 consecutive LPR patients with PAR episode(s) and 24 health controls. All subjects underwent high-resolution impedance manometry (HRIM) (MMS catheter) and 24-hour ambulatory HMII-pH (Diversatek healthcare) while off PPI. A PAR episode was defined as a retrograde 50 % drop in baseline impedance starting from the more distal esophageal channel Z6 to the more proximal pharyngeal channel Z1, in concurrent association with retrograde esophagopharyngeal pH drops. Demographic data, clinical symptoms, endoscopic findings, and automated HRIM metrics over the upper esophageal sphincter, esophageal body peristalsis, and lower esophageal sphincter were compared between the groups.
Results: LPR patients with PAR episode(s) exhibited a significantly lower proximal contractile integral value (PCI, 171 vs. 380.5 mmHg·s·cm, $P < 0.0001$), a higher percentage of Bernstein test positivity (40 vs. 4 %, $P = 0.006$), and a higher BMI value (25.4 vs. 22.1 kg/m2, $P = 0.0006$) and were older in age (57 vs. 38 years old, $P = 0.0002$), compared to health controls. No other significant physiological characteristics differences were observed between the two groups, including the length and resting pressures of both upper and lower esophageal

sphincters, upper esophageal sphincter integrated relaxation pressure at 0.2s / 0.8s, esophageal contractile segment impedance (CSI) at 3cm / 5cm / 7cm, percentage of ineffective motility (IEM), integrated relaxation pressure (IRP) of lower esophageal sphincter, distal contractile integral (DCI), esophagogastric junction morphology, and esophagogastric junction contractile integral (EGJCI). In multivariate logistic regression analysis, LPR patients with PAR episode(s) were independently associated with a higher BMI [adjusted odds ratio (aOR) = 9.04, 95% confidence interval (CI): 1.43–56.92, P = 0.019] and a lower PCI value (aOR = 0.99, 95% CI: 0.98–1.00, P = 0.044).

Conclusions: Having a higher BMI and a lower PCI value may be independently associated with PAR episode(s) in patients with LPR patients. Our data supports the hypothesis of abnormal proximal esophageal motility in LPR patients with PAR episode(s).

③

國際驗證的 COUGH REFLUX 評分系統在咽喉逆流症狀患者的實際應用：氫離子幫浦抑制劑療效的真實世界評估

PRACTICAL APPLICATION OF THE INTERNATIONAL VALIDATED COUGH REFLUX SCORE FOR PATIENTS WITH LARYNGOPHARYNGEAL REFLUX SYMPTOMS: REAL-WORLD ASSESSMENT IN PPI RESPONSE

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Background: The COuGH RefluX score incorporates parameters such as Cough, Overweight/obesity, Globus, Hiatal Hernia, Regurgitation, and male seX. With thresholds set between 2.5 and 5.0, this validated tool distinctively predicts the likelihood of gastroesophageal reflux disease (GERD) in patients exhibiting laryngeal symptoms.

Aims: This study aimed to evaluate the practical relevance of this score, focusing on its ability to predict reflux pathology as well as the response to proton pump inhibitor (PPI) in the real-world setting.

Methods: Consecutive patients with laryngeal symptoms lasting more than three months were prospectively enrolled and characterized using the Reflux Symptom Index (RSI) questionnaire. Eligible patients with negative endoscopy underwent 24-hour impedance-pH monitoring off acid suppression for acid exposure time (AET) and mean nocturnal baseline impedance (MNBI). Proven GERD was defined as an AET of ≥ 6% according to the Lyon Consensus 2.0. A PPI response was confirmed with a 50% or more reduction in RSI. Based on the definition of COuGH RefluX scores, patients were categorized: scores ≤ 2.5 indicated unlikely GERD, scores from 3.0 to 4.5 were inconclusive GERD, and scores ≥ 5 pointed to likely GERD.

Results: Of the 175 participants with an average age of 48.4 years, 102 were classified as unlikely to have GERD, 58 as inconclusive, and 15 as likely to have GERD. There was a progressive increase in the male percentage and BMI, and hiatal hernia prevalence from the unlikely to the likely GERD groups (P < 0.05). In addition, patients with unlikely GERD had a lower prevalence of hiatal hernia and proven GERD compared to those with inconclusive and likely GERD (P < 0.05). For MNBI, patients with unlikely GERD had lower values than both the inconclusive and the

likely GERD groups (P<0.001). However, similar symptom severity, as measured by RSI, and AET were observed across the groups (P > 0.05). The PPI response showed a progressive increase from the unlikely to the likely GERD groups (PPI response rates: 12.7%, 44.8%, 73.3%; P < 0.001). In the univariate logistic regression analysis, both COuGH RefluX score groups, AET, and the number of reflux episodes were correlated with PPI response (P < 0.05). However, multivariate logistic regression analysis revealed that COuGH RefluX score groups and MNBI were independently correlated with PPI response (compared to COuGH RefluX scores ≤ 2.5: scores 3-4.5, OR = 4.190, P = 0.001; scores ≥ 5, OR = 15.772, P < 0.001; MNBI, OR = 0.409, P = 0.002).

Conclusions: Our study discloses the pragmatic significance of the COuGH RefluX score as well as esophageal mucosal integrity in the real-world setting. This tool has value in guiding both diagnostic and therapeutic managements, ensuring the cautious utilization of PPIs and targeted testing among patients with laryngeal symptoms but negative endoscopy.

④

以黏膜電阻抗預測正常內視鏡下胃食道逆流患者對氫離子幫浦抑制劑之反應

MUCOSAL IMPEDANCE AS A PREDICTOR OF PROTON-PUMP INHIBITOR RESPONSE IN GERD PATIENTS WITH NORMAL ENDOSCOPY

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Background: While acid suppression with proton pump inhibitors (PPIs) is commonly used to manage reflux-like symptoms, satisfaction with symptom control is reported in less than half of patients. Mucosal impedance (MI) serves as a tool for the real-time evaluation of esophageal mucosal integrity during endoscopy, and a low MI value indicates the chronic consequences of acid reflux. MI technology has not previously been utilized to predict the response to PPIs in patients with gastroesophageal reflux disease (GERD).

Aims: This study aimed to investigate the hypothesis that MI can predict the response to PPIs in GERD patients with normal endoscopy.

Methods: Consecutive patients with typical symptoms of GERD and non-erosive esophagitis, undergoing high-resolution manometry and 24-hour pH-impedance monitoring of acid suppressive therapies, were enrolled in this prospective study. The MI measurement was performed during the endoscopy examination using the balloon-based MI catheter with 20 sensors spanning the esophagus. GERD MI pattern was defined by low MI values (<3700Ω) in the distal esophagus and normal values proximally along the esophageal axis. Validated questionnaires, including the GERD questionnaire (GERDQ) and global symptom severity (GSS) score, were utilized to assess patient-reported outcomes. The primary outcome was response to PPI once daily defined as symptom improvement of GERDQ score at 8 weeks compared with baseline.

Results: We enrolled 48 eligible patients [median age (Q1, Q3): 46.5 (35.8, 56) years, female 63%], with 16 patients exhibiting a GERD MI pattern and 32 patients displaying a non-GERD MI pattern. In comparison to the non-GERD MI pattern group (Table), those with a GERD MI pattern had a higher body mass index (p=0.024), increased total acid exposure time (AET) (p<0.001), elevated total acid reflux events (p=0.003), a higher DeMeester score

(p<0.001), stronger symptom-reflux association (p<0.001), and a lower MNBI value (p=0.002). After 8 weeks of PPI therapy, both groups showed a reduction in GERDQ and GSS scores compared to baseline (all, p<0.001); however, the GERD MI pattern group demonstrated a more significant improvement in GERDQ score compared to the non-GERD MI pattern group [median(Q1, Q3): -5(-7, -4) vs. -3(-5, 0), p=0.027]. Concerning optimal symptom relief, only a limited number of patients in the non-GERD MI group achieved a >50% reduction in GERDQ scores after PPI treatment compared to the GERD MI group (15% vs. 50%, p=0.016).

Conclusions: MI measurement during index endoscopy accurately distinguishes GERD and non-GERD in patients with reflux-like symptoms, eliminating the need for ambulatory pH monitoring. Our study indicates that MI may serve as an important tool to provide a more efficient and cost-effective method for predicting the response to PPIs in patients with GERD despite normal endoscopy.

⑤

新型 AFS 系統胃食道交界完整性評估在胃食道逆流症患者的臨床和生理學意義

THE CLINICAL AND PHYSIOLOGICAL SIGNIFICANCE OF ESOPHAGOGASTRIC JUNCTION INTEGRITY AS CLASSIFIED BY THE NOVEL AFS SYSTEM IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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Background: In patients with gastroesophageal reflux disease (GERD), the esophagogastric junction (EGJ) plays a key role in preventing acid reflux, acting as an important anti-reflux barrier. Recently, the American Foregut Society (AFS) introduced a revised endoscopic classification of the EGJ. This encompasses evaluations of the axial hiatal hernia length, hiatal aperture diameter, and the presence or absence of the flap valve.

Aims: The aim of this study was to evaluate the clinical and physiological implications of this novel classification in GERD.

Methods: A prospective cohort of patients, who presented with GERD symptoms persisting for over three months, were sequentially enrolled and had their EGJ integrity assessed according to the AFS classification via endoscopy. The AFS classification ranges from grade I, denoting intact EGJ integrity, to grades II through IV, which signify progressive degrees of EGJ disruption. Eligible patients, without evidence of erosive esophagitis, underwent high-resolution manometry (HRM) and 24-hour impedance-pH monitoring in the absence of acid suppression. Metrics such as the lower esophageal sphincter (LES) resting pressure, EGJ contractile integral (EGJ-CI), acid exposure time (AET), mean nocturnal baseline impedance (MNBI), and reflux characteristics were recorded and compared across the different AFS classifications.

Results: Among the 110 participants, averaging an age of 48.4 years and with 64.5% being female, the AFS classification for EGJ revealed 52 at grade I, 40 at grade II, 14 at grade III, and 4 at grade IV. Patients with AFS grades III and IV exhibited diminished LES resting pressure and EGJ-CI, increased AET, a higher frequency of reflux incidents with notably acidic episodes, and an elevated DeMeester score compared to those with AFS grade I (P < 0.05). According to the Lyon Consensus 2.0, a gradational

increase in the prevalence of non-erosive reflux disease (NERD) was observed across AFS grades, with patients in grades III and IV exhibiting a higher prevalence than those in grade II, who in turn showed a higher prevalence than those in grade I (NERD prevalence: AFS grades III and IV: 38.9%, grade II: 17.5%, grade I: 5.8%, P = 0.011). Conversely, no discernible differences in other clinical and physiological parameters were observed among the groups.
Conclusions: Our research confirms the effectiveness of the AFS classification in identifying the pathophysiological features of GERD related to the state of the EGJ. Specifically, AFS grades III and IV indicate a compromised anti-reflux barrier and are associated with more severe acid reflux, even in patients without apparent esophagitis upon endoscopic examination.

主題：C 型肝炎（一）

⑥

煙氯奎寧降低 C 型肝炎患者罹患肝細胞癌之風險：回溯性研究。
HYDROXYCHLOROQUINE REDUCED THE RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HEPATITIS C VIRUS INFECTION: A RETROSPECTIVE COHORT STUDY

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Background: Chronic hepatitis C virus (HCV) infection is one of the leading causes of hepatocellular carcinoma (HCC) worldwide. Hydroxychloroquine (HCQ) is a medication primarily used to treat malaria and autoimmune diseases such as rheumatoid arthritis and lupus. However, recent studies have suggested that it may also have anti-cancer properties based on autophagy and non-autophagy-related mechanisms.
Aims: This study aims to investigate the association between Hydroxychloroquine use and the risk of hepatocellular carcinoma in patients with chronic hepatitis C virus infection
Methods: Patients with HCV infection were enrolled from Taiwan's National Health Insurance Research Database and examined for the period from January 1, 2006, to December 31, 2016. We used the Kaplan-Meier method and Cox proportional hazards regression to evaluate the association between HCQ use and HCC risk
Results: We included patients with HCV infection (n=139,263) and individual matching with 1:10. There were 1,037 cases of HCC in the HCV cohort during a follow-up period. Among the 1,598 patients using HCQ (defined as≥ 28 cumulative defined daily doses [cDDDs]), 62 had HCC. Among the 15,980 patients not using HCQ (□ 28cDDDs), 975 were diagnosed with HCC. Patients with HCV who used HCQ exhibited significantly lower risk of HCC relative to patients who did not use HCQ, with their adjusted hazard ratio(aHR) being 0.68 (95% CI, 0.51~0.92). Furthermore, a dose-response relationship between HCQ use and HCC risk was no observed. Additionally, the use of concurrent medications, such as H1-antihistamine (aHR;0.74 [CI 0.59~0.93]), nonsteroidal anti-inflammation drugs (aHR; 0.60 [0.48~0.76]) and statin (aHR;0.38 [0.32~0.46]), was associated with a lower HCC risk.

Conclusions: HCQ use may reduce the risk for HCC among patients with HCV infection. This finding provides important insights into the potential benefits of HCQ using in preventing HCC in patients with chronic HCV infection. Further studies are needed to confirm these findings and explore the underlying mechanisms.

⑦

直接抗病毒藥物治療對慢性 C 型肝炎患者脂質代謝、肝臟脂肪變性和纖維化的影響：單一醫學中心的經驗

THE IMPACT OF DIRECT-ACTING ANTIVIRAL TREATMENT ON LIPID METABOLISM, HEPATIC STEATOSIS AND FIBROSIS IN CHRONIC HEPATITIS C PATIENTS: A SINGLE MEDICAL CENTER EXPERIENCE

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Background: Hepatitis C virus (HCV) infection causes chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). Chronic HCV infections are causally linked with metabolic comorbidities such as insulin resistance, hepatic steatosis, and dyslipidemia. However, the clinical impact of HCV eradication achieved by direct-acting antivirals (DAAs) on steatosis, liver fibrosis and lipid homeostasis is still controversial.

Aims: The study aimed to investigate whether antiviral therapy of HCV with DAAs alters lipid parameters, liver fibrosis and severity of steatosis. We evaluated patients before and after the treatment.

Methods: We retrospectively analyzed 100 patients with HCV infection who were treated with DAAs and reached sustained virological response at 12 weeks after the end of treatment at Changhua christian hospital. A total of 100 patients were included in the study. Of these, 57 patients were treated with glecaprevir/pibrentasvir, and 43 patients were treated with sofosbuvir/velpatasvir. Total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG), the levels hepatic steatosis and liver stiffness were measured at the onset of treatment and 12 weeks after the end of treatment. The degree of liver fibrosis was assessed using serum biomarkers, such as AST-to-platelet ratio index (APRI) and fibrosis-4 (FIB-4) index. We used the Canon Aplio i800 ultrasound system and FibroScan to assess steatosis and liver stiffness.

Results: A total of 100 patients achieved a sustained virological response at 12 weeks after the end of treatment (SVR12). The mean age was 58.6 ± 13.1 years and 50 patients (50%) were male. TC and LDL levels were significantly increased in the 12 weeks after the end of treatment. After treatment, the mean APRI was decreased from 1.185 ± 2.488 to 0.351 ± 0.225 (P = 0.001), and the

mean FIB-4 was decreased from 2.776 ± 3.729 to 2.024 ± 1.424 (P = 0.021). APRI and FIB-4 were significantly correlated before and after treatment. Controlled attenuation parameter (CAP) using Fibroscan was significantly increased and liver stiffness measure (LSM) using Fibroscan was significantly decreased.

Conclusions: Patients with hepatitis C virus treated with DAAs showed increased TC and LDL cholesterol levels at 12 weeks after the end of treatment. Patients' severity of hepatic steatosis was increased and liver stiffness was improved after the treatment with DAAs. Further research including larger number of patients is needed to compare the efficacy of each evaluating method.

⑧

第 2 型糖尿病患者其慢性腎臟病程度與 C 型肝炎感染相關

CHRONIC KIDNEY DISEASE IS ASSOCIATED WITH HEPATITIS C INFECTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Hepatitis C virus (HCV) infection can induce insulin resistance, and patients with Type 2 diabetes mellitus (T2DM) have a higher prevalence of HCV infection. HCV can induce renal insufficiency, but the association between HCV and severity of chronic kidney disease (CKD) in T2DM remained unclear.

Aims: We aimed to evaluate the efficacy and outcomes of the in-hospital referral program and the association between HCV and severity of CKD in patients with diabetes.

Methods: From March 2022 to May 2023, 4402 T2DM patients in Taipei Veterans General Hospital were prospectively enrolled into the in-hospital referral program for HBsAg and anti-HCV antibody screening. The clinical features of patients with HBV and HCV infection were compared. Factors associated with anti-HCV (+) were analyzed.

Results: Among 4402 T2DM patients, the prevalence of HBsAg-positive and anti-HCV-positive were 8.0% and 2.4%, respectively. Anti-HCV-positive patients had older age and worse renal function, while HBsAg-positive patients had higher ALT level. The prevalence of anti-HCV (+) were 1.8%, 2.3%, 2.6%, 3.5%, and 7.8% in CKD stage 1, 2, 3, 4, and 5, respectively (p = 0.014). Independent factors associated with anti-HCV (+) were age > 65 y/o, CKD stages, and urine albumin-creatinine ratio > 300. For patients with T2DM more than 10 years, the proportion of CKD stage 1 were 26.5%, 9.5%, and 0% in patients with HCV RNA undetectable, after anti-viral treatment (interferon or DAAs) > 3 years, and after anti-viral treatment ≤ 3 years, respectively (p = 0.038).

Conclusions: The prevalence of anti-HCV antibody seropositivity increases with the severity of CKD in patients with T2DM. Patients who achieve virological response earlier have a higher proportion of maintaining in early-stage CKD.

⑨

治療後 FIB-4 與 FIB-4 動態變化是慢性 C 型肝炎患者發生肝細胞癌之預測因子：來自全國 C 型肝炎登記計劃的大型隊列研究 (TACR)

POST-TREATMENT FIB-4 AND DYNAMIC CHANGES IN FIB-4 AS PREDICTORS OF HEPATOCELLULAR CARCINOMA IN CHRONIC HEPATITIS C PATIENTS: A LARGE COHORT STUDY FROM THE NATIONWIDE HCV REGISTRY PROGRAM (TACR)

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Background: Currently, noninvasive liver fibrosis indices, like FIB-4, are used to assess liver fibrosis and predict complications, including hepatocellular carcinoma (HCC). The performance of FIB-4 at different time points (before or after treatment) and its changes during antiviral treatment in HCC risk prediction remains to be elucidated.

Aims: The purpose of this study was to investigate the impact of FIB-4 values and its dynamic changes on HCC development in patients with chronic hepatitis C who received direct-acting antivirals (DAAs).

Methods: A total of 9,679 patients who had completed DAA treatment and achieved sustained virologic response (SVR) were enrolled from the Taiwan Nationwide Real-World HCV Registry Program (TACR) and analyzed for the risk of HCC. FIB-4 was measured at baseline and at SVR. Cox regression analysis was used to identify predictors for HCC.

Results: In this cohort, a total of 138 patients (1.43%) developed HCC; 26.5% of patients had cirrhosis, and 18.1% had diabetes. The median FIB-4 value in the HCC subgroup were higher than that in the non-HCC subgroup (FIB-4 at baseline: 5.61 vs. 2.98, $P < 0.001$). After antiviral treatment, FIB-4 values in both subgroups, with and without HCC, declined. However, the median FIB-4 value in the HCC subgroup remained higher than that in the non-HCC subgroup (FIB-4 at SVR: 4.01 vs. 2.27, $P < 0.001$). The median ΔFIB-4 value in the HCC subgroup was significantly larger compared to that in the non-HCC subgroup (ΔFIB-4: -1.60 vs. -0.67, $P < 0.001$). The area under the receiver operating characteristic curves (AUROCs) of FIB-4 at baseline and SVR in predicting HCC were similar (AUROC: 0.80 and 0.79, respectively; DeLong test, $P = 0.338$). In a multivariable Cox regression analysis, diabetes mellitus (DM), alpha-fetoprotein (AFP), and FIB-4 were independent predictors in both model-1 (baseline) and model-2 (SVR). Notably, a change in FIB-4 (ΔFIB-4) with a cutoff value of -0.9086 was a significant predictor only in model-2 (SVR). In model-2 (SVR), DM (hazard ratio (HR): 1.53, 95% confidence interval (CI): 1.04-2.26, $P = 0.033$), FIB-4 at SVR (≥3.25 vs. <3.25) (HR: 2.40, 95% CI: 1.63-3.53, $P < 0.001$), ΔFIB-4 (<-0.9086 vs. ≥-0.9086) (HR: 1.85, 95% CI: 1.25-2.74, $P = 0.002$), and AFP at SVR (≥20 vs. <20 ng/mL) (HR: 16.40, 95% CI: 9.16-29.36, $P < 0.001$) were significant predictors for HCC. Patients with FIB-4 at SVR ≥3.25 and ΔFIB-4 <-0.9086 had the highest cumulative HCC incidence rates of 1.45%, 4.87%, and 10.67% at 1, 2, and 3 years, respectively. Conversely, patients with FIB-4 at SVR <3.25 and ΔFIB-4 ≥-0.9086 had the lowest cumulative HCC incidence rates of 0.22%, 0.98%, and 1.72% at 1, 2, and 3 years, respectively.

Conclusions: Our study indicates the potential of using post-treatment FIB-4 and its dynamic changes as predictive tools for HCC in patients with CHC receiving DAAs.

主題：B 型肝炎

⑩

針對之前 HCV 抗病毒治療失敗使用 VOSEVI 挽救治療的病例系列報告
A REPORT OF CASE SERIES OF VOSEVI RESCUE THERAPY FOR PRIOR HCV ANTIVIRAL TREATMENT FAILURE

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Background: Direct antiviral agents (DAA) are effective treatment for hepatitis C with overall SVR12 rate 98.3% according to the Taiwan HCV Registry (TACR) data. Vosevi (sofosbuvir, velpatasvir, and voxilaprevir) has been reimbursed by Taiwan national health insurance since September 2021. This case series reported the result of nine cases receiving Vosevi treatment for prior HCV antiviral treatment failure.
Aims: This study aims to evaluate a case series receiving Vosevi treatment for failed DAA treatment.
Methods: From September 2021 to November 2023, nine cases received Vosevi treatment. The treatment duration is 12 weeks. Risk factors for treatment failure were evaluated.
Results: Total 9 cases (age from 47 to 69 years-old) received Vosevi treatment. Seven of them were male. Among them, HCV was successfully eradicated in seven cases but failed in two cases. Both failed cases were persons who injected drugs (PWID).
Conclusions: Among our case series of rescue Vosevi treatment for failed DAA treatment, PWID is the main risk factor for rescue treatment failure.

⑪

慢性 B 型肝炎病人停止韋立德或惠立妥治療其慢性 B 型肝炎病毒復發率的比較
COMPARISON OF HBV RELAPSE RATES IN PATIENTS WHO DISCONTINUE TENOFOVIR ALAFENAMIDE VERSUS TENOFOVIR DISOPROXIL FUMARATE

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Background: The incidence and relapse pattern in CHB patients stopping tenofovir alafenamide (TAF) monotherapy are unknown.
Aims: To compare HBV relapse rate in HBeAg-negative CHB patients without cirrhosis who discontinued TAF versus tenofovir disoproxil fumarate (TDF).
Methods: A total of 379 HBeAg-negative patients without cirrhosis who received TDF (n=259) or TAF (n=120) therapy previously and had post-treatment follow-up for at least 6 months were included in this study. The propensity score-matching method (PSM) was used by creating a ratio of 1:1 to 1:2 between the off-TAF group versus the off-TDF group to adjust associated factors.
Results: The cumulative incidences of virological relapse at 13, 26 and 52 weeks in the TDF versus TAF groups were 30.5% vs. 50.3%, 50.6% vs. 72.7%, and 65.6% vs. 82.6%, respectively, and clinical relapse rates were 13.5% vs. 33.2%, 30.2% vs. 52%, and 39.2% vs. 61.6%, respectively. Patients in the off-TAF group had significantly higher rates of virological relapse (P<0.001) and clinical relapse (P<0.001) than those in the off-TDF group. Multivariate analysis showed that TAF was an independent factor for virological relapse (HR: 1.428, 95%CI: 1.103-1.848, P=0.007) and clinical relapse (HR: 1.954, 95%CI: 1.424-12.681, P<0.001) after adjusting for other factors. After PSM, patients in the off-TAF group had significantly higher rates of virological relapse (P<0.001) and clinical relapse (P<0.001) than those in the off-TDF group. However, the off-TDF group had a higher rate of ALT>800 IU/mL upon clinical relapse than off-TAF group (33.9% vs. 13.5%, p=0.003).
Conclusions: The off-TAF group had significantly higher HBV relapse rates than the off-TDF group in HBeAg-negative patients without cirrhosis

⑫

E 抗原陰性慢性 B 型肝炎病人停止貝樂克或惠立妥治療 B 型肝炎基因型 C 比基因型 B 有較高的表面抗原消失率
HBV GENOTYPE C IS ASSOCIATED HIGHER HBSAG LOSS RATE THAN HBV GENOTYPE B AFTER CESSATION OF ENTECAVIR OR TENOFOVIR THERAPY IN HBEAG-NEGATIVE PATIENTS

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Background: Comparison of hepatitis B surface antigen (HBsAg) loss rate between HBV genotype B and genotype C after cessation of nucleos(t)ide analogues remain unclear.
Aims: To compare the rate of HBsAg loss between patients with genotype B versus genotype C infection after cessation of entecavir or tenofovir disoproxil fumarate (TDF) therapy.
Methods: We performed a retrospective study of 668 HBeAg-negative and 294 HBeAg-positive patients without cirrhosis who had stopped entecavir or TDF treatment for at least 12 months. All patients fulfilled the stopping criteria proposed by the APASL 2012 guidelines.
Results: Significantly higher proportions of patients with HBV genotype B infection had virologic and clinical relapse than patients with HBV genotype C infection, among all and propensity sore (PS) matched HBeAg-negative patients. The Cox regression analysis revealed that the TDF group, old age, HBV genotype B, patients with NA experience, higher HBV DNA at baseline, and higher HBsAg levels at EOT were independent predictors of virological and clinical relapse. In contrast, HBV genotype was not an independent factor of virological or clinical relapse in all and PS matched HBeAg-positive patients. Patients with HBV genotype C had a higher HBsAg loss than those with HBV genotype B among all and PS matched HBeAg-negative patients (p=0.001). The Cox regression analysis showed HBV genotype was an independent factor of HBsAg loss after adjusting for other factors. In contrast, HBV genotype was not an independent factor of HBsAg loss in all and PS matched HBeAg-positive patients. The cumulative rates of HBsAg loss at 6 years were 60.5% versus 44.8% (p=0.008) in HBeAg-negative patients with combination of genotype C versus B and HBsAg at EOT ≤ 100 IU/mL.
Conclusions: HBeAg-negative patients with HBV genotype C infection have lower rates of HBV relapse and higher HBsAg loss than patients with HBV genotype B infection, after cessation of entecavir or TDF therapy.

⑬

HBV 核心抗原在 CD8+ T 細胞失能及衰竭中的致病角色
THE PATHOGENIC ROLE OF HBV CORE ANTIGEN IN CD8+ T-CELL DYSFUNCTION AND EXHAUSTION

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Background: Hepatitis B virus (HBV) infection is a global health concern, particularly impacting Asian populations. Host immunity plays a pivotal role in determining the course of HBV infection, with T cell-mediated immunopathologic responses influenced by persistent exposure to HBV antigens and inflammatory stimuli being critical factors in the progression of chronic hepatitis B (CHB).
Aims: To investigate and characterize the immunopathologic responses of CD8+ T cells to the HBV core antigen in chronic HBV infection.
Methods: Blood samples were collected from 10 chronic hepatitis B (CHB) patients and eight healthy control (HC) donors recruited from the Tri-Service General Hospital in Taipei, Taiwan. Utilizing bioinformatics analysis, our investigation focused on delineating the immunopathologic profile of CD8 T cells during chronic HBV infection. A paired comparative analysis was conducted between HBV- and cytomegalovirus (CMV)-specific CD8 T cells using viral antigen overlapping peptides and pMHC-tetramers.
Results: According to the bioinformatic study, the Canonical Pathway of "T-cell exhaustion signaling pathway in chronic infection" indicated that CD8 T cells were first activated via T-cell receptor (TCR) signaling; however, the resultant upregulated expression of multiple inhibitory receptors, including Tim-3, CTLA-4 and, PD-1, leads to T-cell exhaustion. In line with our study, we found that CD8 T cells from CHB patients were more activated; however, these cells showed an upregulation in the inhibitory receptor PD-1, in comparison with healthy subjects. Moreover, we also confirmed that HBVcore-specific T cells were much weaker in anti-viral cytokine response and expressed significant PD-1 upregulation than paired CMV-specific subset and bulk CD8 T cells.
Conclusions: Our research reveals the immunopathologic responses of CD8 T cells towards HBV core protein, and provides clinical application value for hepatitis management by evaluating peripheral HBVcore-specific CD8 T cells.

⑭

慢性 B 型肝炎病人接受肝臟移植後之病毒相關血清學變化及免疫逃脫突變 - 南臺灣一醫學中心之觀察性世代研究
THE VIROLOGICAL PROFILES AND IMMUNE-ESCAPE MUTATIONS IN CHRONIC HEPATITIS B PATIENTS FOLLOWING LIVER TRANSPLANTATION – AN OBSERVATION COHORT STUDY

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Background: Liver transplantation is lifesaving for chronic hepatitis B (CHB) patients with end-stage liver disease or hepatocellular carcinoma. However, recurrence of hepatitis B virus (HBV) infection after transplantation brings disastrous consequences. Despite the use of pre-emptive post-transplantation hepatitis B immunoglobulin (HBIG) and nucleos(t)ides analogs (NUCs), there is emerging evidence suggesting under-estimated hepatitis B viral activity in CHB patients who received liver transplantation.
Aims: This study aims to illustrate the features of post-transplantation hepatitis B related virological profiles in patients with recurrent hepatitis B infection after liver transplantation.
Methods: During March 2001 to July 2021, CHB patients who received liver transplantation in National Cheng Kung University Hospital were enrolled. Cross-sectional blood tests were performed in 2022 among these patients. Clinical characteristics of recipients and donors, post-transplantation virological changes and immune-escape mutations were recorded and analyzed.
Results: Ninety-six CHB patients received liver transplantation underwent cross-sectional blood test in 2022, in which eighty-four patients received hepatitis B surface antigen (HBsAg) negative liver grafts and twelves patients received HBsAg positive liver grafts. Among those eighty-four CHB patients receiving negative HBsAg grafts, forty-one (48.8%) had either positive HBsAg, or positive hepatitis B core-related antigen (HBcrAg), or detectable HBV DNA, or detectable HBV RNA, while thirty-three (39.3%) had positive HBsAg and/or detectable HBV DNA. Those with detectable HBV DNA at the time of transplantation (or predicted to have detectable HBV DNA if the HBV DNA level at the time of transplantation was not available, which was defined as having detectable HBV DNA at baseline before initiation of anti-viral therapy with anti-viral therapy duration less than or equal to 24 weeks before transplantation) were significantly at risk of serological recurrence of HBV infection, defined as positive HBsAg and/or HBcrAg (odds ratio: 2.587, 95% confidence interval: 1.055-6.348, p = 0.038). Drug resistant mutations, escape mutations, and N-glycosylation sites at surface protein was illustrated in three CHB patients receiving liver transplantation and having virological breakthrough after lamivudine treatment.
Conclusions: HBV recurrence may be more common than expected by testing of HBcrAg in addition to HBsAg and HBV DNA. Immune-escape mutations were observed in patients experiencing post-transplantation virological breakthrough after lamivudine treatment. Therefore, the strategies of pre-emptive anti-HBV treatment and surveillance may need individualized modifications.

⑮

慢性 B 型肝炎合併脂肪肝病患者之全因及各別原因死亡風險
ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY IN CHRONIC HEPATITIS B PATIENTS WITH CONCURRENT STEATOTIC LIVER DISEASE

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Background: Steatotic liver disease (SLD), including metabolic dysfunction-associated steatotic liver disease (MASLD), is prevalent in the chronic hepatitis B (CHB) population. However, the impact of SLD subtypes on all-cause and cause-specific mortality among these patients remains unknown.

Aims: This study aimed to investigate the impacts of excessive alcohol intake, pre-existing and new-onset metabolic dysfunctions on the risks of all-cause and cause-specific mortality in CHB patients with concurrent SLD.

Methods: CHB patients with concurrent SLD were consecutively recruited at the National Taiwan University Hospital. MASLD, alcohol-associated liver disease (ALD), and cryptogenic SLD were defined by the newly-proposed criteria. Cumulative incidences of all-cause and cause-specific mortality were compared after accounting for competing risks.

Results: From 2006 to 2021, 8,773 CHB patients with SLD were included. At baseline, CHB patients with concurrent MASLD (n = 6,562) or ALD (n = 55) were older, had a lower proportion of HBeAg positivity and lower levels of HBV DNA than cryptogenic SLD patients (n = 2,156). After a median follow-up of 9.1 years, ALD (adjusted HR [aHR]: 11.80, 95% CI: 5.89 – 23.60, $p < 0.001$) and MASLD patients (aHR: 1.79, 95% CI: 1.24 – 2.58, $p = 0.002$) had higher all-cause mortality risks than those with cryptogenic SLD after adjustment for clinical and viral factors. Furthermore, cumulative metabolic dysfunctions, defined by the cardiometabolic criteria of MASLD, increased the risks of all-cause, liver-related, non-liver cancer, and cardiovascular mortality with a dose-dependent effect (all $p < 0.05$), contributing to the higher risks in MASLD than cryptogenic SLD patients. During the follow-up period, new-onset diabetes mellitus (aHR: 2.26, 95% CI: 1.71 – 2.98) and new-onset hypertension (aHR: 2.03, 95% CI: 1.50 – 2.75) further increased the risk of all-cause mortality (both $p < 0.001$).

Conclusions: Among CHB patients with hepatic steatosis, concurrent ALD and MASLD increase the risk of death, and cumulative systemic metabolic dysfunctions dose-dependently increase all-cause and various cause-specific mortality. Refraining from alcohol intake and managing these metabolic risk factors are crucial for better survival in CHB patients.

主題：膽胰疾病（一）

⑯

經皮穿肝膽囊細針引流在急性膽囊炎的治療成效一個系列病例報告
CLINICAL IMPLICATIONS OF PERCUTANEOUS TRANSHEPATIC GALLBLADDER ASPIRATION IN ACUTE CHOLECYSTITIS -- A CASE SERIES

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Background: Early or emergent laparoscopic cholecystectomy is considered the gold standard for treating acute cholecystitis. However, factors such as the patient's overall condition, cholecystitis severity, anesthetic risk, and surgical resource availability sometimes make early surgery impractical in routine clinical settings. In such cases, Percutaneous Transhepatic Gallbladder Drainage (PTGBD) is advised as a temporary bridging treatment. The Tokyo Guidelines 2018 recommend gallbladder decompression via PTGBD for acute cholecystitis classified as Grade 2 or 3. As an alternative, Percutaneous Transhepatic Gallbladder Aspiration (PTGBA) offers a simpler approach to gallbladder decompression. It offers effective gallbladder decompression without leaving a catheter inside the patient, thereby simplifying post-procedure care compared to PTGBD. However, there is conflicting evidence regarding the efficacy and complications associated with PTGBA and PTGBD. Some studies suggest comparable outcomes between the two methods in terms of complications and therapeutic effectiveness, while others indicate PTGBA may be less effective than PTGBD.

Aims: To address this discrepancy, we conducted a retrospective analysis evaluating the therapeutic impact of PTGBA in cholecystitis, using the grading criteria from the Tokyo Guidelines 2018. Our aim was to determine if PTGBA is universally effective for all patients with acute cholecystitis.

Methods: Between January 1, 2019, and December 13, 2020, we retrospectively enrolled patients with acute cholecystitis admitted through our emergency room. Patients ineligible for early or emergent cholecystectomy underwent gallbladder decompression via PTGBA as their initial treatment. In cases where PTGBA was unsuccessful or ineffective, a second PTGBA or PTGBD was performed as a subsequent procedure. The technical success rate was determined by the complete decompression of the gallbladder, as observed through real-time echography. Clinical success was defined by the ability to resume oral intake without fever, abdominal pain, or septic symptoms. We recorded the technical and clinical success rates of PTGBA, as well as the duration until normal oral intake could be resumed.

Results: A total of 34 patients were included in our review. The overall technical success rate for PTGBA was 94.11% (32 out of 34 patients), with two cases of Grade I cholecystitis failing to achieve complete gallbladder decompression. No procedure-related complications were reported in all cases. The overall clinical success rate for PTGBA was 100% (9/9 patients) in Grade I cholecystitis, 95.45% (21/22 patients) in Grade 2 cholecystitis, and 33% (1/3 patients) in Grade 3 cholecystitis. The average time taken to resume normal oral intake was 65.11 ± 46.439 hours (mean, SD) for Grade I cholecystitis, and 79.23 ± 48.181 hours for patients with Grade II and Grade III cholecystitis.

Conclusions: In patients with severe cholecystitis requiring gallbladder decompression, PTGBA showed high technical and clinical success rates in Grade I and II cases. However, for those with Grade III cholecystitis, a technically successful PTGBA did not consistently ensure clinical success. Although PTGBA is a straightforward procedure that effectively decompresses the gallbladder and lessens nursing and patient care burdens, careful patient selection remains crucial.

⑰

經內視鏡超音波導引膽囊穿刺引流術配合帶有電燒增強輸送系統的管腔金屬支架治療急性膽囊炎：一項台灣多中心回顧性研究
ENDOSCOPIC ULTRASOUND-GUIDED GALLBLADDER DRAINAGE WITH ELECTROCAUTERY-ENHANCED LUMEN-APPOSING METAL STENTS FOR ACUTE CHOLECYSTITIS : A MULTICENTER RETROSPECTIVE STUDY IN TAIWAN

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Background: Surgical cholecystectomy remains the cornerstone for acute cholecystitis (AC). Nevertheless, a notable portion of patients are surgically-unfit owing to comorbidities and restricted functional capacity. Endoscopic ultrasound-guided gallbladder drainage with a lumen-apposing metal stent (EUS-GBD-LAMS) serves as an alternative therapeutic choice for high-risk surgical patients with AC.

Aims: This study aimed to assess the effectiveness and safety of EUS-GBD-LAMS.

Methods: Consecutive patients with AC who underwent EUS-GBD-LAMS with electrocautery-enhanced tip, HotAxios, were enrolled retrospectively from four tertiary centers in Taiwan from 2020/03 ~ 2023/09. Clinical and endoscopic data, including technical and clinical success rates, adverse events and survivals were analyzed.

Results: In total, 19 patients (7 females, 12 males) with mean (±SD) age of 77.8 (±16.1) year-old were enrolled. The mean score of Charlson Comorbidity Index, Tokyo severity score and ASA classification were 7.5 (±2.6), 2.4 (±0.6) and 2.7 (±0.7), respectively. The mean time from presentation of AC to EUS-GBD-LAMS was 12.6 (±17.1) days. Eleven (57.9%) patients were naïve from previous treatment while eight (42.1%) patients had percutaneous external drainage before EUS-GBD-LAMS. Technical and clinical success rate was 89.5% and 89.5%, respectively. The mean procedure time was 31.9 (±19.9) minutes. EUS-GBD-LAMS was performed through transgastric and transduodenal route in four (21.1%) and fifteen (78.9%) patients. The indwelling time of LAMS was 52.5 (±31.8) days and eight (42.1%) patients had spontaneous stone clearance before removal of LAMS while others needed a mean of 2 (±1.05) peroral cholecystoscopy sessions for stone clearance. Five (26.3%) patients experienced nine adverse events, including two (10.5%) with stent mal-deployment, one (5.3%) with carbon-pneumoperitoneum, two (10.5%) with stent occlusion due to food impaction, and three (15.8%) with recurrent cholecystitis before LAMS removal.

Conclusions: EUS-GBD-LAMS is an efficient and safe therapeutic option for surgically-unfit patients with AC. Long-term follow-up data are warranted to evaluate the durability of this minimally-invasive endoscopic treatment.

⑱

良性肝腸吻合部狹窄經內視鏡治療的成效：單一醫學中心研究
THE OUTCOMES OF ENDOSCOPIC TREATMENT OF BENIGN HEPATOJEJUNAL ANASTOMOTIC STRICTURE IN SURGICAL-ALTERED ANATOMY: A SINGLE CENTER STUDY

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Background: Benign hepatojejunal anastomotic stricture (HJAS) can manifest postoperatively, causing symptoms like pain, jaundice, or cholangitis in patients with various types of bowel reconstruction. Endoscopic retrograde cholangiopancreatography (ERCP) emerges as a valuable intervention for stricture management in surgical-altered anatomy (SAA), offering advantages in treating multiple sites despite its technical intricacies. However, ERCP in these cases may encounter challenges such as lengthy limbs, adhesions, difficult cannulation, or suboptimal scope positioning. This study explores alternative treatments for HJAS, encompassing balloon dilation, multiple stentings, self-expandable metal stents (SEMS), and combined methods. Assessment of technical and clinical success rates, along with the patency period of the anastomosis, is essential.

Aims: To investigate the results of endoscopic treatment for benign hepatojejunal anastomotic stricture in surgically altered anatomy.

Methods: Retrospectively, interventional endoscopic retrograde cholangiopancreatography (ERCP) was conducted for benign hepatojejunal anastomotic stricture (HJAS) in surgically altered anatomy (SAA) at the National Cheng Kung University Hospital from March 2015 to August 2023. All patients underwent ERCP using an end-viewing endoscope equipped with a transparent hood (gastroscope, colonoscope, enteroscope) under the guidance of physicians. A single balloon overtube was selectively employed for patients with Roux-en-Y reconstruction or extended afferent limbs of gastrojejunostomy, as needed. The choice of endoscopic treatment modalities was determined based on clinical requirements. Electronic medical records were meticulously reviewed, encompassing patient characteristics, surgical techniques, interventional endoscopy details, clinical outcomes, and complications analysis.

Results: Out of 170 patients with surgically altered anatomy who underwent ERCP, this study enrolled 47 individuals diagnosed with benign hepatojejunal anastomotic stricture (HJAS) – 27 men and 20 women, with a mean age of 63.1 ± 10.4 years. Hepaticojejunostomy was established through 15 Roux-en-Y reconstructions (31.9%) and 32 pancreatoduodenectomies (68.1%), including 6 Whipple operations and 26 PPPD. The primary indication for endoscopy was predominantly cholangitis (44.7%, n=21).

The technical success rate was 93.6%, with a clinical success rate of 91.5%. Notably, three patients failed to reach the target due to a lengthy afferent loop, and repeat endoscopy was foregone based on patient preference. One such patient underwent simple balloon dilation via PTBD using the antegrade method. Among those achieving the target, one patient encountered difficulties in direct biliary cannulation due to hepatojejunal obliteration, necessitating the use of the rendezvous method for HJAS treatment. For successfully treated HJAS cases, one patient failed to achieve clinical success due to rapid stent migration and ineffective balloon dilation.

In terms of benign HJAS treatment, recurrent biliary obstruction occurred in 5.9% (n=1) in the metal stent group and 14.3% (n=4) in the balloon dilation group, with or without plastic stents placement (p=0.37). The estimated stent patency period revealed no significant differences.

Conclusions: Interventional ERCP for benign HJAS in patients with SAA is clinically feasible, with acceptable clinical success rates and complications. Treatment with SEMS was effective, though outcomes with balloon dilation ± plastic stents were also satisfactory. Future research should explore longer-term follow-up and consider factors influencing treatment choice.

⑲

膽胰管鏡輔助下碎石術治療困難胰管結石：一醫學中心的經驗
CHOLANGIOPANCREATOSCOPY-ASSISTED LITHOTRIPSY FOR DIFFICULT PANCREATIC DUCT STONES: EXPERIENCE OF A MEDICAL CENTER

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Background: Difficult pancreatic duct stones, including large and/or impacted pancreatic duct stones, cannot usually be treated by conventional endoscopic retrograde cholangiopancreatography (ERCP). Recently, cholangiopancreatoscopy-assisted lithotripsy using electrohydraulic lithotripsy (EHL) or laser lithotripsy (LL) provides an alternative modality for ductal clearance.
Aims: We aimed to evaluate the clinical outcomes of cholangiopancreatoscopy-assisted lithotripsy in patients with difficult pancreatic duct stones.
Methods: From July, 2018 to December, 2023, a total of 12 (10 male and 2 female) consecutive patients, 51 (38-71) years old, with large and/or impacted pancreatic duct stones undergoing single-operator cholangiopancreatoscopy-assisted lithotripsy using EHL and/or LL in a medical center were retrospectively analyzed. Stone size, lithotripsy procedure, ductal clearance, and procedural complications were evaluated.
Results: Eleven (91.7%; 11/12) patients were successfully treated in 19 (median 2; range 1-3) sessions including LL (n=16) and EHL (n=3) to achieve ductal clearance (Clinical success). The technical success rate was 94.7% (18/19). Six (50%; 6/12) patients with pancreatic duct stones were successfully treated at the first session of cholangiopancreatoscopy-assisted lithotripsy. Adverse events (47.4%) after the procedure occurred in 9 patients, including fever (n=3), abdominal pain (n=5), and pancreatitis (n=5) without hemodynamic instability, bacteremia or other severe complications. The median length of hospital stay was 4 (2-9) days.
Conclusions: Cholangiopancreatoscopy-assisted lithotripsy is an effective and safe modality for difficult pancreatic duct stones.

⑳

膽道鏡導引碎石術清除率的影響因素
INFLUENTIAL FACTORS AFFECTING THE EFFICACY OF CHOLANGIOSCOPY-GUIDED ELECTROHYDRAULIC LITHOTRIPSY

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Background: Peroral cholangioscopy (POC)-guided electro-hydraulic lithotripsy (EHL) lithotripsy effectively treats difficult biliary stones. Factors influencing its efficacy in one session to achieve primary duct clearance remain unclear
Aims: Factors influencing its efficacy in one session to achieve primary duct clearance remain unclear
Methods: We performed a retrospective analysis of the patients referred for POC between January 2022 and Oct 2023. we demonstrated the outcomes associated with complete or partial biliary stone clearance achieved with electrohydraulic lithotripsy (EHL) in 24 patients.
Results: Twenty-four patients underwent POC with EHL. Complete ductal clearance was obtained in 22/24 patients (91.6%). In total, 20/24 patients (83.3%) achieved stone clearance in a single session. In the multivariate analysis, stone size and Intrahepatic duct (IHD) stone was independently associated with the failure to achieve primary ductal clearance (odds ratio = 1.257, 95% confidence interval: 1.035–1.364, p = 0.001; odds ratio = 3.224, 95% confidence interval: 1.735–4.782 , p = 0.001). The mean procedural time was 115.4 ± 53.1 minutes.
Conclusions: POC with EHL is highly effective for difficult biliary stones. Most patients achieved primary ductal clearance in one session, which was significantly more likely for stones < 20 mm. IHD stone was significantly associated with failure to achieve primary ductal clearance. The importance of considering stone size and location when planning and conducting POC with EHL for optimal treatment outcomes

主題：肝硬化及其他肝病

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飲酒與酒精性肝硬化之間的關聯：一項全國性人口研究
ASSOCIATION BETWEEN ALCOHOL CONSUMPTION AND ALCOHOLIC LIVER CIRRHOSIS: A NATIONWIDE POPULATION STUDY

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Background: Liver cirrhosis and its subsequent hepatocellular carcinoma account for the major cause of liver-related mortality. Alcohol, chronic hepatitis B virus (HBV) infection, and chronic hepatitis C virus (HCV) infection are the major causes of liver cirrhosis. Owing to nationwide HBV vaccination program and the improvements in the management of viral hepatitis, viral hepatitis-related morbidity and mortality have been significantly reduced in recent years. However, the overall and annual per adult alcohol consumption are increasing globally. The prevalence of alcoholic liver disease (ALD) and its disease severity have been reported to be increasing in different US nationally representative databases. ALD-related mortality and morbidity are increasing worldwide. Although previous studies reported that increased alcohol consumption were related to alcoholic liver cirrhosis related mortality, the relationship between alcohol consumption and the incidence of alcoholic liver cirrhosis (ALC) are yet to be confirmed.

Aims: Both imported and domestic alcohol might increase in Taiwan since Taiwan joined World Trade Organization (WTO) and opened private winemaking in 2002. Therefore, we aimed to conduct a nationwide cohort study to investigate the correlation between alcohol consumption per capita and the incidence of alcoholic liver cirrhosis.

Methods: For evaluate per capita alcohol consumption, we calculated the consumption of alcohol in Taiwan according to the data of the statistics of the Ministry of Finance's Financial Information Bureau and the Ministry of Finance's General Administration of Customs in Taiwan and we screened subjective who aged 15 or more based on the Housing Registry of the Ministry of the Interior in Taiwan from 2002 to 2017. For evaluate the incidence and severity of alcoholic liver cirrhosis, we retrieved Comprehensive health care information from Taiwan's National Health Insurance Research Database (NHIRD) from 2002 to 2017. Chi-Squared test and Kaplan-Meier method were used for comparing the comorbidity and mortality rate of alcoholic liver cirrhosis in male and female. Linear regression model was used to evaluate the trends of per capital alcohol consumption and incidence of alcoholic liver cirrhosis. Pearson correlation coefficient was used to analyze the correlation between average alcohol consumption and the incidence of alcoholic liver cirrhosis.

Results: From Jan. 2002 to Dec. 2017, a total of 25,850 new ALC patients were hospitalized in Taiwan. Among these ALC patients, 91% was male and only 9% was female. The average per capita alcohol consumption in Taiwan increased from 3.1 liters in 2002 to 4.4 liters in 2017. Per capita alcohol consumption increased by 0.098 litter per year (95%CI: 0.077-0.120, $p<0.001$). Among different beverages, spirits accounted for the most increased beverage and per capita spirit consumption increased by 0.042 litter per year (95%CI: 0.021-0.062, $p<0.001$). Based on the NHIRD during the period from 2002 to 2017, the standard incidence of ALC increased from 8.17 per 100,000 persons in 2002 to 14.45 per 100,000 persons in 2017. It increased by an average of 0.219 per year (95%CI: 0.150-0.288, $p<0.01$). The standard incidence of ALC in middle aged person increased by an average of 0.222 yearly (95%CI: 0.162-0.282, $p<0.001$). In addition, the number of newly hospitalized patients due to ALC increased by 77 %. The trend of the annual incidence of ALC was strongly related to that of per capita alcohol consumption (Pearson's correlation coefficient: 0.82, 95%CI: 0.575~0.935). Our studies disclosed each additional liter of alcohol consumption increases the standard incidence of ALC by 1.91 (95%CI: 1.145-2.676, $p<0.0001$).

Conclusions: The incidence of alcoholic liver cirrhosis was significantly related to increased alcohol consumption per capita. The findings of this study may help to monitor the public health policy.

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在健康成人群體中肝臟發炎及全身炎症反應對於左心室質量的影響：CHIEF HEART STUDY
HEPATIC AND SYSTEMIC INFLAMMATION FOR LEFT VENTRICULAR MASS IN PHYSICALLY FIT ADULTS: CHIEF HEART STUDY

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Background: Both low-grade systemic and hepatic inflammation could result in increased left ventricular mass (LVM) in the general population.
Aims: the associations, which might be modified by exercise, have not been clarified in physically active young adults.
Methods: The study included 2,004 military males aged 18–43 years in eastern Taiwan. Systemic and hepatic inflammation was defined by the upper tertiles of blood white blood cell (WBC) counts (7.51-11.00 x 103/μL) and serum alanine aminotransferase (ALT: 30-120 U/L), respectively. LVM indexed for the body height ≥49 g/m^2 .7 was defined as left ventricular hypertrophy (LVH) based on echocardiography. Multiple logistic regression analysis adjusting for age, smoking, alcohol intake, physical fitness, and metabolic syndrome was utilized to determine the associations.
Results: As compared to the lower WBC/lower ALT group, there tended to have an increased risk of LVH with the higher WBC/lower ALT group, the lower WBC/higher ALT group, and the higher WBC/higher ALT group [odds ratios: 0.89 (95% confidence intervals (CI): 0.41-1.94), 1.90 (95% CI: 0.86-4.22) and 2.48 (95% CI: 1.04-5.92); p-value for trend = 0.01].
Conclusions: Our study suggested that in physically active males, those with hepatic inflammation rather than low-grade systemic inflammation had a higher risk of LVH. Hepatic injury might be relevant to LVH as an early sign of end-organ damage regardless of physical fitness in young adults.

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食道靜脈瘤初級預防可延緩末期肝癌病患肝功能失代償
PRIMARY PREVENTION OF ESOPHAGEAL VARICES CAN DELAY HEPATIC DECOMPENSATION IN ADVANCED HEPATOCELLULAR CARCINOMA

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Background: The prevalence of esophageal varices (EV) is high in patients with hepatocellular carcinoma (HCC) and portal vein thrombosis (PVT). However, the prevention strategy and outcomes in HCC patients with PVT and EV is not well studied.
Aims: The present study aimed to investigate the clinical prognoses and prevention strategy of HCC patients with PVT and EV.
Methods: A total of 445 patients with HCC and PVT, who received esophagogastroduodenoscopy (EGD) while HCC been diagnosed, were retrospectively enrolled between Jan 2013 to Dec 2022. The diagnosis and severity of EV were reviewed by three gastroenterologists. Prognostic factors were analyzed using Cox proportional hazards model.
Results: EV was noted in 273 (60%) patients. High risk varices (HRV) was noted in 170 (38.2%) patients. Of the 170 patients had HRV in the meantime of HCC diagnosed, 80 (47%) of them did not receive any prophylactic treatment for HRV, 45 (26.5%) patients underwent EVL and 45 (26.5%) patients was prescribed with NSBB. One hundred and thirty-six patients (80%) developed hepatic decompensation and 149 patients (87.6%) expired during a median follow-up time of 109 days. Time to hepatic decompensation was higher in non-prophylaxis group than prophylaxis group (49 days vs. 71 days, p=0.007). More EVB episodes were noted in non-prophylaxis group (15.6% VS. 48.8%, P<0.001). On multivariate analysis, primary prophylaxis with NSBB or EVL (HR 0.605, p=0.005) and immunotherapy (HR 0.546, p=0.031) were associated with longer decompensation free survivals. There was no significant difference in time to decompensation and OS between EVL and NSBB group.
Conclusions: Primary prevention with NSBB or EVL in HCC patients with PVT and HRV can delay hepatic decompensation. The primary prevention method is not associated with OS or time to hepatic decompensation in patients with HRV.

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威爾遜氏症：以台灣中部醫療中心醫院的病例係列

WILSON'S DISEASE: A CASE SERIES OF A SINGLE MEDICAL CENTER HOSPITAL IN CENTRAL TAIWAN

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Background: Wilson's Disease (WD) is an inherited disorder affecting copper metabolism, resulting in pathological copper accumulation. Caused by mutations in ATP7B, it disrupts copper homeostasis, leading to overload in the liver, brain, and other organs. Clinical manifestations vary, including neurological and psychiatric symptoms. Treatment options involve chelation therapy and zinc salts, addressing copper overload through distinct mechanisms.

Aims: To evaluate the treatment efficacy of current Wilson's disease medications in a medical center hospital and the clinical spectrum and management of WD cases at CCH, shedding light on advancements in early detection for improved patient outcomes

Methods: We obtained cases with diagnosis of Wilson disease at CCH from 2018 to 2023, and analyzed the medical records (including age, sex, Ceruloplasmin and response to medications) of these patient retrospectively

Results: In this case series involving 21 patients, the age range spanned from 17 to 64 years, with 12 males and 9 females. The majority presented with predominant neurological symptoms, leading to continuous follow-up in the neurology department. Some cases progressed to liver cirrhosis. Especially the 64 years old patient had passed away due to acute fulminant hepatic faliure with decompensation, and multiple organ failure. Notably, one patient, post-liver transplantation, ceased medication use and exhibited stable symptomatology. Ceruloplasmin levels in the existing patient cohort were uniformly below 13 mg/dL, with a significant proportion registering below 6 mg/dL, rendering precise numerical values indiscernible due to exam limitations. The mainstream therapeutic approach involved the use of zinc (Zn) and trientine, either in isolation or combination. Only two cases continued to receive penicillamine. Approximately one-third of the cases underwent genetic testing, revealing ATP7B mutations in the majority. The clinical efficacy and safety of the current therapeutic modalities, especially the continued use of penicillamine, report stable disease control and warrant further investigation in larger cohorts

Conclusions: The cases emphasize the significance of neurology clinic monitoring and all have well control under current medication use with only few progress to liver cirrhosis and , in select instances, the potential for stabilizing symptoms post-liver transplantation without ongoing pharmacotherapy Liver biopsy for hepatic copper quatify is no more important currently compared with 24-hour urinary copper excretion, ceruloplasmin levels and genetic analysis of ATP7B.

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自發性腦膜淋巴管新生預防肝腦病變
NATURAL GROWTH OF MENINGEAL LYMPHATIC VESSELS PREVENTS HEPATIC ENCEPHALOPATHY IN LIVER CIRRHOSIS

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Background: Hepatic encephalopathy (HE) is a lethal complication of liver cirrhosis resulting from neuroinflammation and hyperammonemia. Enhanced meningeal lymphangiogenesis in early cirrhosis has shown to alleviate neuroinflammation and HE.
Aims: his study aimed to assess the meningeal lymphatic system in rats with advanced liver cirrhosis and evaluate the role of meningeal lymphatic flow in cirrhotic patients.
Methods: Male Sprague-Dawley rats were used to induce liver cirrhosis through common bile duct ligation. After 4 or 6 weeks post-operation, rats developed early or advanced cirrhosis, respectively. In the case of advanced cirrhosis, inhibition of meningeal lymphatic drainage was conducted either by ligation of deep cervical lymph nodes or via lenvatinib treatment. The human study involved prospectively enrolling cirrhotic patients with or without HE in a medical center, evaluating meningeal lymphatic flow using magnetic resonance imaging along the lymphatic vessels around the sigmoid sinus.
Results: Rats with advanced liver cirrhosis displayed more severe portal hypertension, increased portosystemic collaterals, and higher levels of hyperammonemia. Meningeal lymphangiogenesis (P=.047) and meningeal lymphatic drainage (P=.001) were also notably higher in the advanced cirrhosis group compared to the early cirrhosis group. However, locomotor function and neuroinflammation did not significantly differ between the early and advanced cirrhotic rats. Inhibiting meningeal lymphatic drainage through deep cervical lymph node ligation or suppressing lymphangiogenesis with Lenvatinib exacerbated locomotor function and neuroinflammation in rats with advanced liver cirrhosis. In a preliminary human study, cirrhotic patients with HE exhibited reduced flow through meningeal lymphatic vessels around the sigmoid sinus compared to patients without HE (n=5, 7, intensity to time curve, 15.6±2.2 vs. 26.4±1.9).
Conclusions: Meningeal lymphangiogenesis develops in advanced liver cirrhosis, acting as a protective mechanism against the deterioration of neuroinflammation and HE. Cirrhotic patients with HE appear to have impaired meningeal lymphatic flow. Natural growth of meningeal lymphatic vessels emerges as a crucial compensatory mechanism for HE in liver cirrhosis.

主題：上消化道疾病（三）

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食道無效性收縮對口咽吞嚥生理的影響
IMPACT OF INEFFECTIVE ESOPHAGEAL MOTILITY ON OROPHARYNGEAL SWALLOWING PHYSIOLOGY

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Background: Ineffective esophageal motility (IEM) is a common esophageal motility disorder. It is unclear whether oropharyngeal swallowing physiology would alter in patients with IEM.

Aims: This study aimed to investigate the hypothesis of whether altered oropharyngeal swallowing physiology can be demonstrated in patients with IEM.

Methods: All participants were recruited from outpatients and advertisements. Each participant underwent both esophageal and pharyngeal high-resolution impedance manometry (HRiM) study. HRiM catheter was inserted into the esophagus and pharynx. Manometric and impedance data for pharyngeal motility were recorded during swallowing thin and thick liquid administration. Data were then exported for further analysis on the Swallow Gateway online platform (www.swallowgateway.com).

Results: Fourteen patients with IEM (age 30-58 yrs, mean:39.4 yrs, male 64%) and 10 healthy adults (age 29-44 yrs, mean 34.9 yrs, male 80%) with normal esophageal motility were recruited. All subjects completed HRiM study. Healthy adults had significantly higher mesopharyngeal contractile integral than patients with IEM, especially during 10mL thin liquid swallows ($p = 0.027$) and 5mL thick liquid swallows ($p = 0.049$). There were no correlations between esophageal distal contractile integral and mesopharyngeal contractile integral either in the patients($r=-0.152\sim0.184$, $p=0.243\sim0.901$) or in the healthy adults($r=0.226\sim0.359$, $p=0.308\sim0.531$). All of the other pharyngeal manometric parameters were not different between IEM patients and healthy adults.

Conclusions: Patients with IEM have similar pharyngeal manometric metrics to healthy adults except for decreased mesopharyngeal contractile integral. Our study suggests that the contraction of the tongue base and pharyngeal constrictor may be affected by esophageal hypomotility in patients with ineffective esophageal motility, but its mechanism awaits further elucidation.

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功能性消化不良和胃輕癱症狀患者的多模式評估：將體表胃圖映射整合到胃排空呼氣試驗中
MULTIMODAL ASSESSMENT FOR PATIENTS WITH FUNCTIONAL DYSPEPSIA AND GASTROPARESIS-LIKE SYMPTOMS: INTEGRATING BODY SURFACE GASTRIC MAPPING INTO GASTRIC EMPTYING BREATH TEST

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Background: Functional dyspepsia (FD) and gastroparesis are prevalent gastroduodenal disorders. While gastric emptying (GE) tests are commonly used for assessing gastric motor function in both conditions, the test alone is unable to capture the full spectrum of underlying pathophysiology. Accurate cutaneous high-resolution gastric bioelectrical recording may provide additional insights into gastric neuromuscular function.

Aims: To investigate myoelectrical abnormalities in patients presenting with symptoms of gastroparesis and functional dyspepsia.

Methods: Consecutive patients with chronic gastroduodenal symptoms with negative endoscopy undergoing a GE breath test (250 kcal solid meal) were invited to participate. Exclusion criteria were organic gastrointestinal diseases and history of abdominal surgery. BSGM (Gastric Alimetry, Alimetry, New Zealand) was performed 30 minutes before and 4 hours during the GE test (30m fasting, 4h postprandially). Symptoms of nausea, bloating, upper gut pain, heartburn, epigastric burning, and excessive fullness by 0-10 visual analog scales were logged at 15m intervals in a validated app and combined to form a “Total Symptom Burden” score. GPLS (nausea and/or vomiting ≥1 day/week and simultaneous PDS), FD (PDS or EPS) and subcriteria dyspepsia (dyspeptic symptoms but not fitting ROME IV) were defined based on the Rome IV diagnostic questionnaires. BSGM data included BMI-Adjusted amplitude, Principal Gastric Frequency, Gastric Alimetry Rhythm IndexTM (GA-RI) and Fed:Fasted Amplitude Ratio (ff-AR). Data are presented as median (interquartile range). Mann-Whitney U and Pearson’s chi-

square tests were performed.
Results: 123 eligible patients (51 GPLS, 57 FD, 15 subcriteria dyspepsia) were included. 28.5% of patients had delayed GE (half GE time >109 min) which was associated with higher symptom severity scores for early satiety, excessive fullness and total symptom burden (all $p<0.05$). An additional 20.3% of patients with neuromuscular dysfunction were identified through BSGM spectral abnormalities (predominantly low rhythm stability and high frequency of slow waves). Several specific time-of-test symptom patterns were reported in patients with normal spectral metrics. Comparing the GPLS and FD group, no significant differences were observed in delayed GE and spectral abnormalities (both $p>0.05$).
Conclusions: The inclusion of BSGM as a complementary measurement increases the diagnostic yield for detecting gastric neuromuscular dysfunction in patients with FD or GPLS. These two entities cannot be distinguished through GE and BSGM.

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神經調節劑對患有功能性食道疾病個體之影響：系統性文獻回顧與統合分析
THE IMPACT OF NEUROMODULATORS ON INDIVIDUALS WITH FUNCTIONAL ESOPHAGEAL DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: The use of neuromodulators is prevalent in various functional gastrointestinal diseases. However, data concerning the outcomes of these treatments in functional esophageal disorders (FED) remains limited and inadequate.
Aims: The aim of this study was to assess the effects of central neuromodulators on visceral hypersensitivity-related esophageal symptoms in the context of FED classified by Rome IV definition.
Methods: We searched PubMed, EMBASE, and the Cochrane library databases from inception to April 2023. Randomized controlled trials that compared the effects of neuromodulators and placebos on FED are included. The primary outcome is symptom improvement, and Rome IV criteria are used to assess eligible studies. Secondary outcomes included differences in quality of life and the rate of adverse events.
Results: Eleven randomized controlled studies (three for functional chest pain, four for reflux hypersensitivity/functional heartburn, three for globus, and one for functional dysphagia) were included in the final analysis. Neuromodulators reduced chest pain by 52%–71% in patients with functional chest pain and alleviated symptom by 46%–75% in patients with globus (n=3, Odds ratio 6.30, 95% confidence interval 4.17–9.50). However, the results were inconsistent for reflux hypersensitivity and functional heartburn. There was a lack of convincing evidence to support the use of neuromodulators for functional dysphagia. The use of neuromodulators did not have a significant impact on the quality of life.
Conclusions: Functional chest pain and globus may potentially benefit from the use of neuromodulators, but their effectiveness for other esophageal disorders remains controversial. More controlled trials are needed to confirm the therapeutic effects of these conditions.

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紅辣椒素對健康成年人其食道收縮功能之影響

CAPSAICIN INFUSION AUGMENTS VIGOR OF ESOPHAGEAL PERISTALSIS IN HEALTHY ADULTS

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Background: Capsaicin-sensitive afferents modulate gastrointestinal sensorimotor function. Capsaicin-containing red pepper sauce suspension has been demonstrated to influence esophageal secondary peristalsis in healthy adults on conventional manometry, but it remains unclear if these effects can be reproduced on high-resolution manometry (HRM), which provides a more comprehensive motor evaluation. We hypothesized that cued esophageal primary and air-distension induced secondary peristaltic responses would augment following capsaicin infusion in healthy adults.

Aims: In this study, we aimed to apply HRM to investigate the hypothesis of whether infusion of capsaicin can modulate esophageal peristalsis in healthy adults.

Methods: We utilized HRM to investigate esophageal peristaltic responses following capsaicin and saline infusions. Eleven healthy volunteers (median age 39 years, 10 male) underwent HRM by a prototype catheter with one mid-esophageal injection port. All volunteers had normal HRM. Primary peristalsis was evaluated with ten water swallows, while secondary peristalsis was stimulated using slow and rapid air injections. Both primary and secondary peristalsis were assessed following infusions of capsaicin-contained red pepper sauce (20 mL) and saline at room temperature (20 mL) for 2 minutes. HRM parameters were explored and compared between the infusion of capsaicin and saline.

Results: Infusion of capsaicin significantly increased distal contractile integral (DCI) of primary peristalsis ($p = 0.023$), as well as secondary peristalsis following rapid air distension ($p=0.001$), but not for slow air distension ($p = 0.76$). Infusion of saline significantly increased distal latency ($p =0.031$), esophagogastric junction contractile integral ($p = 0.031$), and basal lower esophageal sphincter pressure ($p = 0.035$) of primary peristalsis. After saline infusion, the DCI of primary peristalsis was similar compared to the baseline ($p = 0.81$). Saline infusion significantly increased DCI for rapid air distension ($p = 0.003$) but not for slow air distension ($p = 0.47$). Infusion of capsaicin or saline did not affect any of the other parameters of primary or secondary peristalsis. All participants experienced a heartburn sensation following capsaicin infusion, while a cold sensation was reported after saline infusion.

Conclusions: We demonstrate that in healthy adults, both capsaicin and saline facilitate secondary peristalsis in response to rapid air distension, indicating that augmentation of distension-induced secondary peristalsis can be modulated by activation of capsaicin-sensitive afferents similar to mechanosensitive afferents. The notion that infusion of capsaicin augments primary peristalsis needs to be studied in patients with ineffective esophageal motility to determine therapeutic potential.

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探討使用經口內視鏡肌肉切除術治療芝加哥分類類型 I 和類型 II 的食道失弛緩症之術後短期結果比較：台灣南部某醫學中心回顧性研究

COMPARATIVE OUTCOMES OF POEM TREATMENT IN TYPE I AND TYPE II ACHALASIA: A SINGLE-CENTER RETROSPECTIVE STUDY IN SOUTHERN TAIWAN

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Background: Achalasia is a rare esophageal motility disorder characterized initially by occasional reflux symptoms, progressing to dysphagia, chest pain, vomiting, and significant weight loss. These symptoms severely impact patients' quality of life. Peroral endoscopic myotomy (POEM) has emerged as an effective, minimally invasive surgical intervention.

Aims: However, limited data exist comparing the efficacy of POEM between Chicago Classification subtypes Type I and Type II achalasia in terms of Eckardt score, surgical duration, hospital stay, adverse events, and weight changes. This study aims to fill this gap.

Methods: This single-center retrospective study evaluated patients diagnosed with achalasia (Eckardt score ≥4) at Kaohsiung Chang Gung Memorial Hospital from January 2020 to June 2023. We assessed high-resolution manometry (HRM) and Eckardt scores 6 months post-POEM. The primary outcome measures included Eckardt score, upper esophageal sphincter (UES) mean basal pressure, lower esophageal sphincter (LES) mean basal pressure, and integrated relaxation pressure (IRP). Secondary outcomes included one-year postoperative weight gain, operation time, length of hospital stay, and adverse event rates.

Results: Among 39 patients who underwent POEM, 17 had Type I and 22 had Type II achalasia. The median follow-up was 3.53 months (range 1.96-5.96). In the primary analysis, both Type I and Type II achalasia subtypes demonstrated statistically significant reductions in individual Eckardt score components—namely weight loss, dysphagia, retrosternal pain, and regurgitation—post-POEM intervention ($p < 0.001$ for all metrics). Nonetheless, the intergroup comparison revealed no statistically significant differential in the magnitude of Eckardt score reduction between the two subtypes ($p = 0.458$). Post-POEM, both groups exhibited statistically significant weight regain (Type I: $p = 0.023$, Type II: $p = 0.03$); however, the intergroup variance in the extent of weight modification was not statistically significant ($p = 0.693$). In terms of hospitalization duration, patients with Type II achalasia had significantly shorter stays as compared to their Type I counterparts ($p = 0.017$). Additionally, a marked decrement in LES basal pressure was observed in the Type I cohort post-POEM ($p = 0.007$), a trend not reaching statistical significance in the Type II cohort ($p = 0.068$).

Conclusions: POEM effectively improves Eckardt scores and weight gain in both Type I and Type II achalasia, with no significant differences in these primary outcomes between the subtypes. However, Type II patients experienced shorter hospital stays, suggesting quicker postoperative recovery. The study's limitations include a small sample size and its single-center design, warranting further research with larger cohorts.

主題：脂肪肝相關疾病

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MASLD 比 MAFLD 較少遺漏高風險患者
METABOLIC ASSOCIATED STEATOTIC LIVER DISEASE MISSES LESS HIGH-RISK PATIENTS THAN METABOLIC ASSOCIATED FATTY LIVER DISEASE

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Background: A new name of metabolic associated steatotic liver disease (MASLD) was proposed to replace non-alcoholic fatty liver disease (NAFLD) in 2023. Metabolic associated fatty liver disease (MAFLD) proposed in 2020 has different diagnostic criteria of metabolic dysfunction.
Aims: The comparison between two disease names and diagnostic criteria is unknown.
Methods: We recruited participants from the Taiwan Bio-bank database, excluding those with hepatitis B, hepatitis C, and "frequent drinkers". MASLD and MAFLD were diagnosed based on different criteria of metabolic dysfunction. Those who met the diagnostic criteria for MASLD but not for MAFLD were referred to as the "missing" group. Cryptogenic steatotic liver disease (SLD) was used as the control group. We used NAFLD fibrosis score (NFS) as an indicator for liver fibrosis.
Results: This study included 17,595 patients in the final analysis. There were 7,274 (41.3%) participants with MASLD, and 6,905 with MAFLD. The cryptogenic SLD group consisted of 264 (1.5%) patients, while the "missing" group had 369 patients. A total of 94.9% were overlapping between MASLD group and MAFLD group. There were no differences in metabolic parameters, liver markers and the percentage of carotid plaques between these two groups. When comparing the "missing" group to the control group, the "missing" group had higher NFS and higher proportion of carotid plaques.
Conclusions: In this large population-based study, the "missing" group having higher risks of liver fibrosis and atherosclerosis than controls is not advisable to exclude. MASLD misses less high-risk patients than MAFLD without other etiologies.

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經切片證實之脂肪肝病的臨床與組織學特徵
CLINICAL AND HISTOLOGIC FEATURES OF BIOPSY-PROVEN STEATOTIC LIVER DISEASE

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Background: Steatotic liver disease (SLD) causes a significant disease burden with increasing prevalence worldwide. The new disease definition of metabolic dysfunction-associated steatotic liver disease (MASLD) was proposed in 2023, but its clinical and histologic features are not fully understood.
Aims: This study aimed to investigate the clinical impacts of the different subtypes of SLD, including MASLD, alcohol-associated liver disease (ALD), overlap of MASLD/ALD (MetALD), and others, and compared them with the old criteria of non-alcoholic fatty liver disease (NAFLD).
Methods: Patients with histology-confirmed hepatic steatosis (≥ 5%) were consecutively enrolled from 2009 to 2023 at National Taiwan University Hospital. The diagnoses of NAFLD, MASLD, ALD/MetALD, and SLD of other etiologies were made based on the corresponding disease definitions. Those with incomplete clinical information were excluded.
Results: 199 SLD patients were finally included. Among them, the majority fulfilled the dual diagnosis of NAFLD plus MASLD simultaneously (55.8%), while small portions were NAFLD-only (4.5%), MASLD-only (20.1%), ALD/MetALD (5.3%), and others (14.6%). After excluding those with dual diagnosis and other etiologies, MASLD patients were older and had higher metabolic burdens than NAFLD and ALD/MetALD patients. Regarding the histologic features, NAFLD Activity Score (NAS) ≥ 3 was more prevalent in ALD/MetALD (60.0%) and MASLD (35.0%) patients than in NAFLD (11.1%) patients (p = 0.061). Furthermore, the criteria of MASLD and ALD/MetALD identified significant proportions of advanced fibrosis (F3-

F4) patients, 62.5% and 55.6%, respectively, while none (0%) was included in the NAFLD-only group (p = 0.006).
Conclusions: The new disease definitions of MASLD and ALD/MetALD identify more patients with a higher liver disease severity than NAFLD. Refraining from excessive alcohol intake and aggressively monitoring metabolic dysfunctions are crucial for preventing liver disease progression in SLD patients.

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肝細胞特異性腎素（原）受體剔除可減緩小鼠飲食誘發之脂肪變性
HEPATOCYTE-SPECIFIC (PRO)RENIN RECEPTOR KNOCKOUT ATTENUATED DIET-INDUCED STEATOSIS IN MICE

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Background: (Pro)renin receptor (PRR) is reportedly involved in lipid metabolism and PRR knockdown protects mice against hepatosteatosis and inflammation. PRR is also essential for autophagy and emerging evidences showed that hepatic autophagy is impaired in metabolic dysfunction-associated steatotic liver disease (MASLD). However, the impact of hepatocyte-specific PRR knockout on MASLD remain unclear.
Aims: To investigate the impact of hepatocyte-specific PRR knockout on MASLD in mice
Methods: Hepatocyte-specific PRR knockout mice were generated by crossing PRR floxed mice with albumin-Cre transgenic mice. MASLD was generated by high fat diet (HFD) feeding for 12 weeks.
Results: Hepatocyte-specific PRR knockout decreased body weight and total body fat weight with improved insulin resistance and increased metabolic rates in mice fed with HFD. Hepatic steatosis was attenuated by hepatocyte PRR knockout with upregulated peroxisome proliferator-activated receptor-alpha (PPARα), peroxisomal acyl-coenzyme A oxidase 1 (ACOX1) and cytochrome p450 4A14 (CYP4a14) expression. In vitro, primary hepatocytes from knockout mice showed increased abundance of proteins regulating fatty acids oxidation in proteomics and western blots.
Conclusions: Our findings revealed that PRR knockout in hepatocytes attenuated steatosis in mice with MASLD.

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糖尿病患者以非侵入性評估法進行肝纖維化風險分層及其相關因子分析
RISK STRATIFICATION OF LIVER FIBROSIS BY NONINVASIVE ASSESSMENTS AND THE ASSOCIATED FACTORS IN DIABETIC PATIENTS

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Background: Approximately 70% of patients with type 2 diabetes have hepatic steatosis and approximately 15% have clinically significant liver fibrosis (stage ≥ 2). Development of liver fibrosis is a predictor of liver-related outcomes. The identification of diabetic patients with the risk of developing liver fibrosis using point-of-care assessment in clinical practice can not be overemphasized.
Aims: To stratify the risk of liver fibrosis by noninvasive methods in diabetic patients.
Methods: Diabetic patients with liver biochemical tests, lipid and sugar profiles and liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) were retrospectively reviewed using electrical medical records from 2015 April to 2022 March. Body mass index (BMI), insulin resistance (IR), fibrosis 4 index (FIB-4), and history of chronic viral hepatitis and hypertension were recorded. Liver fibrosis stratification was performed using FIB-4 and VCTE. The associated factors for high risk to liver fibrosis were identified by univariate and multivariate logistic regression analysis.
Results: A total of 310 diabetic patients were recruited. The mean age was 61.2 years and 190 (61.3%) were males. We first used FIB-4 levels to stratify the fibrosis risk and yielded 117 in low-risk (<1.3), 150 in indeterminate-risk (1.3-2.67) and 43 in high-risk (>2.67) groups. LSM by VCTE was applied subsequently to the indeterminate-risk group and further stratified 150 patients into 105 in low-risk (<8 kPa), 28 in indeterminate-risk (8-12 kPa) and 17 in high-risk (>12 kPa) groups. Finally, we got 222, 28 and 60 in low, indeterminate and high-risk groups, respectively. We divided 310 patients into non-high risk (N=250) and high-risk (N=60) groups for statistical analysis. The patients in high-risk group were significantly older (66.2 vs 60 years, p<0.001), had significantly higher levels of LSM (12.9 vs 5.9 kPa, p<0.001), AST (42 vs 28 U/L, p<0.001), ALT (43 vs 30 U/L, p=0.009), and FIB-4 score (3.09 vs 1.35, p<0.001) and had significantly lower levels of platelet (154 vs 231 109/L, p<0.001), triglyceride (116 vs 134 mg/dL, p=0.018), and albumin (4.3 vs 4.6 gm/dL, p<0.001) than those in non-high risk group. Age [odds ratio (OR) 1.072, p=0.025], platelet (OR 0.954, p<0.001), albumin (OR 0.149, p=0.041), AST (OR 1.180, p<0.001) and ALT (OR 0.956, p=0.047) were the associate factors for high risk to liver fibrosis in multivariate logistic regression analysis.
Conclusions: Sequential noninvasive assessment methods can effectively focus the population of different liver fibrosis risk groups. Age and the levels of platelet, Albumin, AST, and ALT are significant factors for high risk in liver fibrosis.

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脂質體學分析在病態肥胖病人非酒精性脂肪肝的應用

THE APPLICATION OF LIPIDOMIC ANALYSIS ON NONALCOHOLIC FATTY LIVER DISEASE IN MORBIDLY OBESE PATIENTS

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Background: Nonalcoholic fatty liver disease (NAFLD) is a spectrum of liver disease including simple hepatic steatosis (NAFL) and nonalcoholic steatohepatitis (NASH) with or without fibrosis or cirrhosis. Approximately 25% of the global population has NAFLD.

Aims: This study aims to use untargeted lipidomic analysis to investigate lipidomic profile features in liver and serum among patients with NASH with mild fibrosis, NASH with significant liver fibrosis, and healthy individuals.

Methods: Lipidomics analysis was performed using ultra-high-performance liquid chromatography–tandem mass spectrometry on serum and liver samples from a prospective cohort study involving morbidly obese patients who underwent sleeve gastrectomy at Taipei Medical University Hospital between September 2016 and December 2020. Ultrasonography (US) and transient elastography (E score) were performed before surgery. Wedge liver biopsy was performed during surgery and significant liver fibrosis was defined as a fibrosis score >2. Based on these criteria, We selected 10 patients without NAFLD (C), 20 patients with NASH in fibrosis stage 0-1 (M) and 20 patients with NASH in fibrosis stage 2-4 (S).

Results: From the data of lipidome, significant changes were observed in sixty-eight lipid species in the liver and ninety lipid species in the serum. Lipids classification includes glycerolipids (GL), glycerophospholipids (GP), sphingolipids (SP), and sterol lipids (ST) that were identified and quantified with false discovery rate (FDR)-adjusted significant P values less than 0.05. Fourteen overlapping lipid species were found in the liver and serum. The heatmap shows that the relative abundance of lipid species in the liver and serum does not follow the same trend as the severity of liver fibrosis. The correlations of the lipid species in serum with clinical, metabolic features and with NAFLD parameters are presented. DG 32:0, TG 56:4, LPC 6:0, PC 40:8, PE 34:2, PE O-38:4, PE O-40:4,and CL 76:1 are positively correlated with the specific clinical characteristics; on the contrary, MG 18:1, DG 44:8, PA 28:3;O2, LPC 20:1 are negatively correlated with the specific clinical characteristics. Variable importance plots (VIP) and area under the receiver operating characteristic (AUROC) curves are shown. Multiple predictive models were developed based on the top 3 high-VIP-score metabolites and dimorphic data for detecting NASH with significant liver fibrosis detection. The AUROC (0.904, P=0.005) was highest with the features of mixed lipid biomarkers and non-invasive serum markers.

Conclusions: The concentrations of particular lipid species were associated with severity of fibrosis of the liver in NASH. Higher PE O-38:4, PE 34:2, and CL 76:1 in serum were associated with higher risk of significant liver fibrosis. The AUROC was highest with mixed lipid biomarkers and non-invasive serum markers.

主題：幽門螺旋桿菌

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以混合療法作幽門螺旋桿菌感染之第一線治療時影響除菌失敗的獨立危險因子
INDEPENDENT RISK FACTORS PREDICTING ERADICATION FAILURE OF HYBRID THERAPY FOR THE FIRST-LINE TREATMENT OF *HELICOBACTER PYLORI* INFECTION

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Background: Hybrid therapy is a recommended first-line anti-*H. pylori* treatment option in the American College of Gastroenterology guidelines, Bangkok Consensus Report on *H. pylori* management, and Taiwan *H. pylori* Consensus Report. However, the cure rates of the eradication therapy in some countries are suboptimal, and the factors affecting treatment efficacy of hybrid therapy remain unclear.

Aims: To search the independent risk factors predicting eradication failure of hybrid therapy in the first-line treatment of *H. pylori* infection.

Methods: A retrospective cohort study was conducted on 589 *H. pylori*-infected patients who received 14-day hybrid therapy between September 2008 and December 2021 in ten hospitals in Taiwan. The patients received a hybrid therapy containing a dual regimen with a proton pump inhibitor (PPI) plus amoxicillin for initial 7 days and a quadruple regimen with a PPI plus amoxicillin, metronidazole and clarithromycin for final 7 days. Post-treatment *H. pylori* status was assessed at least 4 weeks after completion of treatment. The relationships between eradication rate and 13 host and bacterial factors were investigated by univariate and multivariate analyses.

Results: In total, 589 patients infected with *H. pylori* infection were included in the study. The eradication rates of hybrid therapy were 93.0% (95% confidence interval [CI]: 90.9% - 95.1%), 94.4% (95% CI: 93.8% - 97.2%) and 95.5%% (95% CI: 93.8% - 97.2%) by intention-to-treat, modified intention-to-treat and per-protocol analyses, respectively. Univariate analysis showed that the eradication rate of clarithromycin-resistant strains was lower than that of clarithromcyin-susceptible strains (83.3% [45/54] vs. 97.6%% [280/287]; P < 0.001). Subjects with poor drug adherence had a lower cure rate than those with good adherence (73.3% [11/15] vs. 95.5% [534/559]; P = 0.005). The other factors such as smoking, alcohol drinking, coffee consumption, tea consumption and type of PPI were not significantly associated with cure rate. Multivariate analysis revealed that clarithromcyin resistance of *H. pylori* and poor drug adherence were independent risk factors related to eradication failure of hybrid therapy with odds ratios of 4.8 (95% CI: 1.5 to 16.1; P = 0.009) and 8.2 (95% CI: 1.5 to 43.5; P = 0.013), respectively.

Conclusions: A 14-day hybrid therapy has a high eradication rate for *H. pylori* infection in Taiwan, while clarithromycin resistance of *H. pylori* and poor drug adherence are independent risk factors predicting eradication failure of hybrid therapy.

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14日之「VONOPRAZAN三合療法」與「RABEPRAZOLE反轉式混合療法」在幽門螺旋桿菌第一線除菌治療上優於「VONOPRAZAN高劑量二合療法」
BOTH 14-DAY VONOPRAZAN TRIPLE THERAPY AND 14-DAY RABEPRAZOLE REVERSE HYBRID THERAPY ARE SUPERIOR TO 14-DAY VONOPRAZAN HIGH-DOSE DUAL THERAPY FOR THE FIRST-LINE ANTI-*H. PYLORI* TREATMENT

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Background: Acid inhibition efficacy of vonoprazan, a potassium-competitive acid blocker (PCAB), is superior to that of proton pump inhibitor (PPI). Currently, whether vonoprazan-based anti-*H. pylori* therapies are more effective than PPI-based therapies recommended for populations with high rates of antibiotic resistance remains unclear.

Aims: To compare the efficacies and safety of 14-day PCAB-based triple therapy, 14-day PCAB-based high-dose dual therapy and 14-day PPI-based reverse hybrid therapy for the first-line treatment of *H. pylori* infection.

Methods: In the multi-center, randomized, open-label, superiority trial, we recruited adult *H. pylori*-infected patients from eight centers in Taiwan. Subjects were randomly assigned (1:1:1) to 14-day vonoprazan triple therapy, 14-day vonoprazan high-dose dual therapy or 14-day rabeprazole reverse hybrid therapy. Eradication status was determined by 13C-urea breath test. The primary outcome was the eradication rate of *H. pylori* assessed in the intention-to-treat population.

Results: Between August 2021 and October 2023, 720 patients were randomly treated by 14-day vonoprazan triple therapy, vonoprazan high-dose dual therapy, or rabeprazole reverse hybrid therapy. The proportions of resistant strains to clarithromycin, amoxicillin, and metronidazole in the study population were 17.4%, 0.6%, and 28.5%, respectively. The intention-to-treat eradication rates were 93.3% (224/240; 95% confidence interval [CI]: 90.1 to 96.5%) for vonoprazan triple therapy, 86.3 (207/240; 95% CI: 82.0 to 90.6%) for vonoprazan high-dose dual therapy, and 92.1% (221/240; 95% CI: 88.7 to 95.5%) for rabeprazole reverse hybrid therapy. Both vonoprazan triple therapy (difference: 7.0%; 95% CI: 1.6 to 12.4%; p=0.010) and rabeprazole reverse hybrid therapy (difference: 5.8%; 95% CI: 0.3 to 11.3%; p=0.040) were superior to vonoprazan high-dose dual therapy, and were similar to one another. The frequency of adverse events of vonoprazan triple therapy, vonoprazan high-dose dual therapy and rabeprazole reverse hybrid therapy were comparable (17.1% [41/240], 12.9% (31/240), and 17.9% (43/240), respectively).

Conclusions: The interim report data suggest that eradication rates of 14-day vonoprazan triple therapy and 14-day rabeprazole reverse hybrid therapy are higher than that of 14-day vonoprazan high-dose dual therapy for the first-line treatment of *H. pylori* infection in populations with high rates of antibiotic resistance.

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依抗生素敏感性引導之含鉍劑 14 天 4 合療法在第二線胃幽門桿菌除菌治療獲得絕佳的效益

14-DAY BISMUTH CONTENT SUSCEPTIBILITY-GUIDED THERAPY ACHIEVES EXCELLENT ERADICATION RATES IN THE SECOND-LINE TREATMENT OF *HELICOBACTER PYLORI* INFECTION

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Background: Susceptibility-guided treatment (SGT) has been proposed as a promising strategy for enhancing *Helicobacter pylori* eradication rates. Current practice guidelines recommend utilizing *H. pylori* culture with susceptibility testing as third-line rescue therapy for eradication. However, evidence regarding its efficacy as a second-line therapy is limited.
Aims: This study sought to investigate the effectiveness of culture-guided therapy as a second-line treatment of *Helicobacter pylori* infection.
Methods: Between October 2019 and August 2023, we retrospectively enrolled *H. pylori*-infected patients who had experienced treatment failure during their initial attempts at eradication. Second-line anti-*H. pylori* therapy, 14-day bismuth content quadruple therapy (esomeprazole, bismuth, and two kinds of antibiotics based on the results of antimicrobial sensitivity tests) was administered. A total of five different regimens were employed, and analyses were conducted on eradication rates, adverse effects, and patient's compliance.
Results: Among the 38 enrolled patients, the intention-to-treat eradication rates of bismuth-containing SGT as a second-line treatment were 94.7%. Subgroup analysis revealed 100% cure rate in groups undergoing the EBTL, EBTM, EBAL 14-day regimen. Low eradication rates were observed in patient received EBCA and EBAT 14-day therapies, standing at 50% and 75%, respectively.
Conclusions: The 14-day bismuth content susceptibility-guided regimens, employed as a second-line rescue therapy demonstrated a high eradication rate.

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AB 優酪乳攝取對幽門螺旋桿菌、代謝和情緒健康的影響：一個雙盲、隨機對照試驗

EFFECTS OF DAILY CONSUMPTION OF UNI-AB YOGURT ON *HELICOBACTER PYLORI*, METABOLIC PARAMETERS, AND EMOTIONAL WELL-BEING: A DOUBLE-BLINDED, RANDOMIZED CONTROLLED TRIAL

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Background: *Helicobacter pylori* (*H. pylori*) infection has been associated with metabolic syndrome, insulin resistance, and dysbiosis. Conversely, probiotics have shown the potential to inhibit *H. pylori*, improve dysbiosis, and enhance insulin resistance. However, their impact on metabolic parameters and mental health in *H. pylori*-infected patients remains unclear.
Aims: To investigate the effects of daily consumption of Uni-AB unsweetened yogurt on reducing *H. pylori* infection and improving metabolic parameters and mental health.
Methods: Adults aged 20-70 with *H. pylori*, defined as carbon-13 urea breath tests (C13 UBT) > 10%, were randomly assigned to either the yogurt or placebo group for an 8-week intervention. C13 UBT, blood tests, and the Brief Symptom Rating Scale (BSRS) were conducted at baseline, week 4, and week 8.
Results: Out of 187 individuals screened, 27 participants with *H. pylori* (14 in the yogurt group, 13 in the placebo group) were enrolled. Additionally, 23 individuals without *H. pylori* were recruited as healthy controls. Both yogurt and placebo groups showed no significant differences in the change of C13 UBT (P = 0.86), weight, BMI, waist circumference, blood pressure, blood glucose, and insulin at the end of the 8th week. In week 4, the yogurt group showed a significant drop in ALT (-1.9 ± 5.4 vs. 1.8 ± 3.6, p = 0.050) compared to the placebo group, and in week 8, there was also a significant decrease in AST (-2.0 ± 9.7 vs. 1.7 ± 3.0, p = 0.034). An improvement in BSRS scores was noted in the yogurt group at week 4 compared to the placebo group (-1.9 ± 2.1 vs. -0.3 ± 1.2, p = 0.026). A transient increase in CRP levels (0.08 ± 0.15 vs. 0.00 ± 0.05, p = 0.017*) was observed in the yogurt group compared to

the placebo at week 4, abut this effect reversed and became insignificant by the end of week 8. In contrast, a notable elevation in LDL (9.1 ± 19.8 vs. -4.9 ± 8.6, p = 0.006) and cholesterol (13.0 ± 23.0 vs. -6.0 ± 11.3, p = 0.006) was observed in the yogurt group compared to the placebo at week 8. Compared to adults without *H. pylori*, individuals with *H. pylori* exhibited an elevation in creatinine (0.03 ± 0.06 vs. 0.00 ± 0.04, p = 0.043) and CRP levels (0.15 ± 0.41 vs. -0.24 ± 0.7, p = 0.006) at week 8.

Conclusions: Daily intake of 200 mL Uni-AB unsweetened yogurt did not suppress *H. pylori* but improved liver inflammation and contributed to emotional stability. Nevertheless, it had a negative effect on lipid profiles.

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幽門桿菌陰性患者後續感染幽門桿菌的機率
THE PROBABILITY OF SUBSEQUENT *HELICOBACTER PYLORI* INFECTION IN *HELICOBACTER PYLORI*-NEGATIVE PATIENTS

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Background: The presence of *Helicobacter pylori* is associated with many diseases; therefore, understanding the probability of new-onset *Helicobacter pylori* infection is crucial.

Aims: This study examined the probability of subsequent *Helicobacter pylori* infection in *Helicobacter pylori*-negative patients and analyzed its associated risk factors.

Methods: We collected data from a group of 8,297 individuals at our institution who tested negative for *Helicobacter pylori* in the period from 2003 to 2019. This investigation explores the probability of future *Helicobacter pylori* infection and its associated potential factors in this cohort.

Results: In this long-term follow-up study, it was observed that over a 17-year period, the likelihood of transitioning from *Helicobacter pylori* negativity to positivity was 25.5%, approximately corresponding to an annual infection rate of 1.5%. Multivariate analysis identified factors that influenced the probability of subsequent new *Helicobacter pylori* infections, including the year of examination (odds ratio, 0.96; 95% CI, 0.93-0.99; P=0.002), patient age (odds ratio, 1.03; 95% CI, 1.02-1.04; P<0.001), and the presence of peptic ulcers at the initial examination (odds ratio, 0.75; 95% CI, 0.59-0.96; P=0.025).

Conclusions: The potential factors influencing the subsequent *Helicobacter pylori* infection in *Helicobacter pylori*-negative patients include the year of examination, the presence of peptic ulcers at the initial examination, and age.

主題：下消化道疾病（一）

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換水法大腸鏡檢查合併人工智慧息肉偵測系統的評估：一項為前瞻性隨機分組試驗進行的先導研究成果

PERFORMANCE OF REAL-TIME COMPUTER-AIDED POLYP DETECTION USING WATER EXCHANGE COLONOSCOPY: A PRELIMINARY PILOT STUDY

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Background: Computer-aided detection (CADe) systems in randomized controlled trials (RCTs) using gas insufflation invariably reported performance improvement (significant increases in polyp/adenoma detection). However, pragmatic clinical observations and RCTs by colonoscopists experienced in gas insufflation did not confirm the improvement. Since our reports of the water exchange (WE) outperformed gas insufflation in significantly enhancing adenoma detection, the current research team has embraced routine use of WE. The advent of CADe led us to evaluate the interaction between WE and CADe. We reported that WE (with salvage cleaning to reduce false positives) and CADe (with reduction of human errors/omissions) complemented the strength and weakness of each other in optimizing detection by the analysis of pre-recorded video in a RCT (GIE 2022;95:1198-206).

Aims: Our aim was to assess if using WE might confirm CADe performance improvement in pragmatic clinical observations. We collected data with CADe used with WE and compared the results with previously acquired WE colonoscopy data.

Methods: This study was conducted in two hospitals with separate commercially available CADe systems from Italy (Endo-AID, Olympus, EU) and Taiwan (CAD EYE, Fujifilm, Japan) between February and June, 2023. Data were collected prospectively on all WE plus CADe colonoscopies performed in ≥45 y/o patients with all indications (CADe group). A similar number of patients undergoing WE alone was used as a historical control group. The primary outcomes were the ADR and mean number of adenomas per colonoscopy (APC). The secondary outcome was the sessile serrated lesion (SSL) detection rate.

Results: A total of 715 patients (367 with CADe) were enrolled, with similar baseline demographics and indications for colonoscopy. The overall withdrawal time and bowel preparation quality were comparable. There were no significant differences in the ADR and APC between the CADe and control groups (56.4% [95% confidence interval (CI), 51.3%─61.4%] vs. 58.3% [95% CI, 53.1%─63.4%], P = 0.602 [ADR]; 1.31 ± 1.80 vs. 1.14 ± 1.38, P = 0.152 [APC]). The use of CADe significantly increased the SSL detection rate in the proximal colon (5.2% [95% CI, 3.3%─8.0%] vs. 2.3% [95% CI, 1.2%─4.5%, P = 0.044), along with the mean number of proximal SSLs per colonoscopy (0.10 ± 0.58 vs. 0.03 ± 0.22, P = 0.036).

Conclusions: Compared with WE alone, the combination of WE and CADe numerically increased the overall APC and significantly improved SSL detection rate and the mean number of SSLs per colonoscopy in the proximal colon. WE permitted CADe performance improvement to be demonstrated in our pragmatic clinical observations. The complimentary benefits of combining WE and CADe on the APC and SSL detection deserve further study.

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比較充氣法和右側大腸換水對大腸腺瘤發現率的影響 - 一隨機對照試驗
RIGHT COLON WATER EXCHANGE INCREASED ADR COMPARED WITH AIR INSUFFLATION – A RANDOMIZED CONTROLLED TRIAL

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Background: Insertion water exchange (WE) is characterized by infusing water, which is immediately removed mainly during the insertion phase, to guide the advance of the colonoscope in an airless lumen. WE has been shown to improve the overall and right colon adenoma detection rate (ADR) compared to traditional air insufflation. However, WE has been criticized for prolonged insertion time. A meta-analysis showed WE took an average of 3 minutes longer than air insufflation to reach the cecum.

Aims: In this study, we tried to evaluate whether right colon WE can retain the benefit of improving ADR without prolonging insertion time.

Methods: Patients undergoing colonoscopy were randomized in 1:1 ratio to either the traditional air insufflation (air) group or right colon water exchange (WE) group. In the WE group, air insufflation was used to assist the insertion until the scope reached the hepatic flexure, where the air pump was turned off and WE used to get to the cecum. In the air group, air insufflation was used throughout the insertion phase. Air was turned on when the cecum was reached in both groups. The primary outcome was overall ADR. The insertion time, the withdrawal time, Boston bowel preparation scale and other procedural data were recorded.

Results: A total of 164 patients were randomized to either group. The baseline characteristics of the patients in both groups were similar. The overall ADR (63 % vs. 42.7 %, P = 0.01) were significantly higher in the WE group than the air group. The right colon ADR was numerically higher in the right colon (29.3% vs. 24.7%, P = 0.51) but not statistically significant. The WE group had slightly but significantly longer insertion time (8.9 ±4.3 min vs. 7.0 ± 4.7 min, P < 0.001) The WE group had higher BBPS scores in the right colon than the air group (2.6 ± 0.5 vs. 2.1 ± 0.7, P < 0.001).

Conclusions: Right colon WE increased overall ADR at the expense of a slightly longer insertion time. The method can be considered for colonoscopists who are interested in improving the quality of their colonoscopy examinations but pressed for time.

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冷及热圈套息肉切除有莖型大腸息肉(≤ 10MM) 出血風險的比較：大型隨機對照臨床試驗的次群組分析

THE BLEEDING RISK OF COLD VERSUS HOT SNARE POLYPECTOMY FOR SMALL (≤ 10MM) PEDUNCULATED COLORECTAL POLYPS: SUBGROUP ANALYSIS FROM A LARGE RANDOMIZED CONTROLLED TRIAL

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Background: Cold snare polypectomy (CSP) has been adapted as the standard of care for small colorectal polyp. However, the concern of bleeding still exists for pedunculated (0-Ip) lesion.

Aims: This study aims to compare the bleeding risk between CSP and hot snare polypectomy (HSP) for 0-Ip polyp with size ≤ 10mm.

Methods: Patients with 0-Ip polyp ≤ 10mm were extracted from a large randomized controlled trial comparing CSP vs HSP in small colorectal polyp. Immediate post-polypectomy bleeding (IPPB), defined by peri-operative use of clip for bleeding, was evaluated in each 0-Ip polyp ≤ 1cm (polyp level analysis). Delayed post-polypectomy bleeding (DPPB), defined as bleeding that develops within 2 weeks after procedure, was analyzed in patients with all polyps ≤ 10mm and at least one 0-Ip polyp (patient level analysis).

Results: Total 648 0-Ip polyps (CSP: 306; HSP: 347) were included for IPPB analysis, and 386 patients (CSP: 192; HSP: 194) for DPPB analysis. The characteristics were similar between either group. CSP had more IPB than HSP (10.8% vs 3.2%, p < 0.001) but no significant adverse events happened. The procedure time was shorter in CSP group (123.0 +/- 117.8 sec. vs 167.0 +/- 238.0 sec., p = 0.003), and similar in polyps with immediate bleeding (CSP: 250 +/- 140.2 sec. in 26 polyps vs HSP: 224.4 +/- 126 sec. in 11 polyps, p = 0.594). DPPB developed in 3 (1.5%) patients and one (0.5%) need endoscopic hemostasis in HSP group, but zero in CSP group develop IPPB (Table 1).

Conclusions: Although CSP has more immediate bleeding events than HSP for 0-Ip polyp, it doesn't lead to significant adverse events or longer procedure time. In addition, no patients develop delayed bleeding. Therefore, this support CSP as the standard of care for small pedunculated polyp.

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透過生成式人工智能檢視臨床實務，優化大腸鏡報告：初期研究成果
ENHANCING COLONOSCOPY REPORTING THROUGH GENERATIVE AI: ASSESSING BEST PRACTICE ADHERENCE IN COLONOSCOPY

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Background: Colonoscopy is a key tool for managing colorectal diseases. Traditional reporting methods offer structured data but often lack immediate quality assessment and feedback, leading to varied patient outcomes. The rise of artificial intelligence (AI), notably generative models like OpenAI's ChatGPT, introduces new opportunities to enhance medical report audits, potentially addressing these limitations.

Aims: This pilot study assesses ChatGPT-4's effectiveness in auditing colonoscopy reports, focusing on its accuracy, comprehensiveness, and adherence to clinical guidelines.

Methods: We acquired anonymized colonoscopy reports from a single center, conducted by 11 endoscopists between October 1 and October 15, 2023. The methodology involved developing a specialized training model for ChatGPT-4, which emphasized key facets of colonoscopy reporting. This included patient age, bowel preparation quality, procedure duration, and detailed lesion information such as location, size, and Paris classification, along with snare polypectomy techniques. ChatGPT-4 was tasked to assess each report against 13 crucial clinical criteria, providing detailed, actionable feedback. Subsequent to the AI audit, experienced endoscopists reviewed ChatGPT-4's evaluations to verify their clinical accuracy, thoroughness, and real-world utility.

Results: ChatGPT-4 audited a total of 116 colonoscopy reports, uncovering various areas of concern. These included inappropriate ages for screening (15%), non-optimal bowel preparation regimens (33%), insufficient bowel preparation quality (16%), and inadequate withdrawal durations (34%). Additionally, the AI identified a 17% omission rate of the Paris classification in polyp descriptions, the use of hot snare or biopsy for small polyps (3-9mm) in 1% of cases, unnecessary employment of hemoclips in 3% of cold snare polypectomies, and a significant lack of post-procedure surveillance recommendations (80%). ChatGPT-4's insights provided constructive and actionable feedback for these suboptimal aspects. When compared with expert endoscopist evaluations, these AI-detected issues demonstrated approximately 60% accuracy in consistency with the established audit criteria.

Conclusions: This study demonstrates ChatGPT's capabilities in standardizing report audits, and offering meaningful feedback for quality improvement. Despite its potential, there are limitations to note. ChatGPT-4 currently lacks the capacity to process high volumes of reports concurrently, and some of its audit outcomes were not entirely aligned with the established criteria. Future developments should aim to improve its batch processing abilities. This pilot study establishes a foundational base for further research and the progression of AI auditing tools in healthcare. It not only highlights AI's role in working collaboratively with human expertise but also underscores its potential in enhancing medical education and training.

主題：肝腫瘤（一）

㊺

惡性小腸腫瘤：單一醫學中心腸鏡的研究
MALIGNANT SMALL INTESTINAL TUMORS: A SINGLE-CENTER ENTEROSCOPY-BASED STUDY

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Background: The prevalence of small bowel (SB) malignancies is low; common types are adenocarcinoma, gastrointestinal stromal tumor (GIST), lymphoma, and neuroendocrine tumor (NET). With the development of various enteroscopic tools, SB malignancies can be diagnosed.
Aims: The aim of this study was to analyze clinical and enteroscopic features of malignant SB tumors found during enteroscopic examination.
Methods: Between January 2004 and August 2023, 541 patients underwent deep enteroscopy at Changhua Christian Hospital. Malignancies were diagnosed in 45 patients, whose data were analyzed in this retrospective study
Results: From 2004 to 2013, we identified forty-five SB malignancies diagnosed through 541 enteroscopic examinations. The patients had an average age of 62.2 years with male predominance. The most common malignancy was adenocarcinoma (37.78%), followed by GIST (26.67%) and lymphoma (17.78%). Adenocarcinoma often presented with obstructive symptoms, while the others were associated with gastrointestinal (GI) bleeding. Significant differences were observed in enteroscopic features among these malignancies: adenocarcinoma commonly displayed lumen stenosis, GIST often appeared as submucosal lesions, and lymphoma presented as ulceroinfiltrative lesions. The ulceroinfiltrative lesions were the most frequently incorrectly predicted malignancies based on enteroscopic features, frequently misdiagnosed as adenocarcinoma when they were actually lymphomas. The overall 5-year mortality rate was 55.5%, with lymphoma having the highest rate (87.5%), followed by adenocarcinoma (64.71%), and GIST having the lowest rate (16.67%).
Conclusions: Despite SB cancers being very uncommon, the current investigation sheds light on their various clinical, endoscopic, and radiographic presentations from our institution. This study could help in the clinical treatment of this rare condition in the future.

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接受免疫檢查點抑制劑之慢性 B 型肝炎癌症病人的功能性治癒之研究
FUNCTIONAL CURE OF HEPATITIS B IN CANCER PATIENTS UNDERGOING IMMUNE CHECKPOINT INHIBITORS

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Background: Immune checkpoint inhibitors (ICIs) can restore exhausted T cell immunity not only for cancer treatment but also potentially for curing chronic hepatitis B (CHB). The impact of ICIs on Hepatitis B surface antigen (HBsAg) seroclearance in cancer patients was unclear.
Aims: We aim to survey the impact of ICIs on Hepatitis B surface antigen and factors associated with HBsAg loss.
Methods: Consecutive cancer patients from 2016 to 2020 (Cohort 1, n=118), and hepatocellular carcinoma (HCC) patients from 2020 to 2022 (Cohort 2, n=44, as validation) receiving ICIs and positive for HBsAg were retrospectively recruited. Factors associated with HBsAg loss or combining HBsAg decline >1 log were analyzed.
Results: With median follow-up of 17.5 months, 8 (6.8%) in cohort 1 and 4 (9.1%) in cohort 2 achieved HBsAg seroclearance, and additional 4 in cohort 1 and 1 in cohort 2 had HBsAg decline >1 log. In multivariate analysis, HBsAg level <100 IU/mL was the factor associated with HBsAg seroclearance (HR=6.274, p=0.028) or combining HBsAg decline >1 log. In the validation cohort, the cumulative incidence of HBsAg loss at months 12 and 24 was 13.0% and 38.4% for baseline HBsAg titer <100 IU/ml. Of the 17 cases achieved HBsAg loss and decline >1 log, 16 (94.1%) had nucleos(t)ide analogs treatment. The median cycles of ICIs were 15 (ranged 7 to 32), and the median time to HBsAg loss or HBsAg decline was 16.5 months (ranged 9.6 to 27.5).
Conclusions: ICIs accelerate HBsAg seroclearance in cancer patients with baseline HBsAg <100 IU/ml. This finding may provide important information for future trial design of ICIs to achieve functional cure in CHB patients.

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免疫檢查點抑制劑對於晚期肝細胞癌具低甲型胎兒蛋白患者之療效

EFFICACY OF IMMUNE CHECKPOINT INHIBITORS FOR PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA AND LOW ALPHA-FETOPROTEIN LEVEL

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Background: Alpha-fetoprotein (AFP) is an important prognostic factor in patients with hepatocellular carcinoma (HCC) receiving immune checkpoint inhibitors (ICI) therapy. However, the efficacy of ICI therapy for HCC patients with low baseline AFP level remains unclear.
Aims: The aim of this study was to evaluate the efficacy of ICI therapy for HCC patients with low baseline AFP level.
Methods: Consecutive 307 patients with advanced HCC receiving ICI therapy in Taipei Veterans General Hospital were enrolled, including 58 patients treated with atezolizumab plus bevacizumab. Patients were classified as high AFP (AFP >20 ng/mL, n=217, 70.7%) and low AFP (AFP ≤20 ng/mL, n=90, 29.3%) groups. Factors associated with progression-free survival (PFS) and overall survival (OS) were evaluated.
Results: Patients with low AFP were significantly male predominant, had smaller tumor size and higher ALBI score. The objective response rate (ORR) in the low and high AFP groups were 19% and 33.5%, respectively (p=0.025). The low AFP group had comparable PFS (5 vs 6.3 months, p=0.730) but significantly better OS (19.1 vs 11.5 months, p=0.012) than the high AFP group. In the overall cohort, HBV infection (hazard ratio (HR)=0.672, p=0.010), AST >40 U/L (HR=2.226, p<0.001), ALBI grade 2-3 (HR=1.840, p<0.001), neutrophil-lymphocyte ratio >5 (HR=1.470, p=0.015) and AFP >400 ng/mL (HR=1.508, p=0.007) were independent predictors of OS. In the low AFP group, ALBI grade 2-3 (HR=5.333, p<0.001), NLR >5 (HR=2.153, p=0.024) and platelet count >150 x 109/L (HR=3.111, p=0.001) were independent predictors of OS. There was no significant predictor of PFS in the overall cohort and the low AFP group.
Conclusions: Patients with advanced HCC and low baseline AFP level had lower ORR but better OS after ICI therapy. ALBI grade, NLR and platelet count are the main predictors of OS in patients with low AFP level.

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UP-TO-SEVEN 標準和血清 α- 胎兒蛋白可預測接受動脈栓塞化學治療的中期肝癌患者的總體存活率

UP-TO-SEVEN CRITERIA AND SERUM ALPHA-FETOPROTEIN LEVEL COULD PREDICT OVERALL SURVIVAL OF PATIENTS WITH INTERMEDIATE-STAGE HEPATOCELLULAR CARCINOMA UNDERGOING TRANSARTERIAL CHEMOEMBOLIZATION

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Background: Patients with Barcelona Clinic Liver Cancer (BCLC) stage B hepatocellular carcinoma (HCC) and high tumor burden may not be ideal candidate for transarterial chemoembolization (TACE) because of the risk of liver function deterioration after TACE. The up-to-7 criteria, have been widely used worldwide to define the extent of tumor burden.
Aims: We aimed to use up-to-7 criteria and serum alpha-fetoprotein (AFP) level to predict overall survival (OS) of patients with BCLC stage B HCC undergoing TACE.
Methods: We recruited patients with BCLC stage B HCC and Child-Pugh class A liver disease undergoing TACE between 2011 and 2021 at our institution. We subclassified patients into three groups: group 1 was defined as within up-to-7 criteria (n=58); group 2 was defined as beyond up-to-7 criteria and AFP< 400 ng/ml (n=146); group 3 was defined as beyond up-to-7 criteria and AFP ≧ 400 ng/ml (n=66).
Results: The median OS were 2.66 [95% confidence interval (CI)=2.11-3.22], 2.38 (95%CI=1.80-2.96) and 1.06 (95%CI=0.77-1.35) years for group 1-3, respectively (p<0.001). There was not significantly different in OS between group 1 and 2 (p=0.368); however, there was significantly different in OS between group 1 and 3 (p<0.001) and group 2 and 3 (p<0.001). Using group 1 as reference, multivariate analysis showed that group 2 was not associated with inferior 5-year OS (p=0.284), whereas group 3 was associated with inferior 5-year OS (p<0.001).
Conclusions: The up-to-7 criteria combined with AFP level could stratified OS in patients with BCLC stage B and Child-Pugh class A liver disease undergoing TACE.

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現實世界中無法切除肝癌病人使用癌自癒加癌思停與樂衛瑪治療結果比較
COMPARING TREATMENT OUTCOMES OF ATEZOLIZUMAB PLUS BEVACIZUMAB VERSUS LENVATINIB IN REAL-WORLD PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA

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Background: Atezolizumab plus bevacizumab (Ate/Bev) and lenvatinib (Len) have received approval as first-line therapies for unresectable hepatocellular carcinoma (uHCC). However, there is limited data comparing treatment outcomes between these two regimens in real-world scenarios.

Aims: Hence, we conducted this study to investigate and clarify the efficacy and safety of Ate/Bev and Len for uHCC.

Methods: From April 2018 to December 2022, we retrospectively evaluated 346 patients with uHCC who had undergone Ate/Bev (n=80) or Len (n=266) first-line treatment in our hospital. PFS (Progression-Free Survival) and OS (Overall Survival) were assessed after adjusting for confounding factors using inverse probability weighting (IPW).

Results: In comparison to the Len group, the Ate/Bev group showed a higher incidence of patients with Child-Pugh class B (14.1% vs. 5.7%, p=0.014), beyond up-to-seven criteria (80% vs. 57.9%, p<0.001), or main portal vein invasion (25% vs. 12.8%, p=0.008). The occurrence of treatment-related adverse events was notably lower in the Ate/Bev group (56.3% vs. 72.3%, p=0.007). More patients in the Len group underwent concurrent treatments (40.6% vs. 20%, p=0.001). There were no significant differences observed in the objective response rate (ORR) (20% vs. 20.5%, p=0.923) and OS (13.3 months vs. 16.6 months, p=0.261) between the Ate/Bev and Len groups. However, the Len group exhibited a superior PFS compared to the Ate/Bev group (6.8 months vs. 3.0 months, p=0.006). Patients who experienced failure with Ate/Bev showed a comparable proportion to the Len group (53.8% vs. 46.9%, p=0.294). Lenvatinib (n=22, 29.3%) and immunotherapy (n=35, 15.7%) were the most frequently administered sequential therapies following Ate/Bev and Len, respectively. Post-adjustment using IPW, the Ate/Bev group demonstrated similar ORR, PFS (3.7 months vs. 5.2 months, p=0.255), and OS (13.3 months vs. 13.1 months, p=0.971) in comparison to the Len group.

Conclusions: In real-world clinical practice, patients with u-HCC who received first-line Ate/Bev appeared to have a lower liver function reserve and more advanced tumor characteristics compared to those who underwent treatment with Len. However, the treatment outcomes and safety profiles were similar between these two groups.

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非病毒性肝癌合併糖尿病患者接受熱射頻消融術後有較高之晚期復發風險
DIABETES MELLITUS ASSOCIATED WITH LATE RECURRENCE AFTER RADIOFREQUENCY ABLATION IN PATIENTS WITH NON-VIRAL HEPATOCELLULAR CARCINOMA

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Background: The impact of diabetes mellitus (DM) on the recurrence of hepatocellular carcinoma (HCC) after radiofrequency ablation (RFA) remains unclear.
Aims: The aim of this study was to evaluate the role of diabetes mellitus (DM) on the early- and late-recurrence after RFA in patients with non-viral HCC.
Methods: Consecutive 140 patients with non-viral HCC receiving RFA were retrospectively enrolled, including 66 (47.1%) patients with DM. Factors associated with early or late recurrence-free survival (RFS) and overall survival (OS) were evaluated.
Results: Diabetic patients had significantly higher body mass index, higher creatinine level, and larger tumor size. Diabetic patients had significantly higher risk of late recurrence (late RFS 56.5 months vs. not reached, p=0.002), while comparable early recurrence rate (2-year recurrence rate 46.4% vs. 41%, p=0.943) and OS (62.5 vs. 57.9 months, p=0.727) as compared to patients without DM. By multivariate analysis, tumor size >3 cm (hazard ratio (HR)=2.859, p=0.001) was an independent predictor of early recurrence, while DM (HR=3.238, p=0.017), tumor size >3 cm (HR=3.464, p=0.043) and AST to Platelet Ratio Index (APRI) >0.5 (HR=3.724, p=0.008) were independent predictors of late recurrence. Tumor size >3 cm (HR=1.681, p=0.046), AFP >10 ng/mL (HR=2.368, p=0.001), ALBI grade >1 (HR=2.773, p<0.001), Fibrosis-4 score >2.5 (HR=2.468, p=0.003) and neutrophil-lymphocyte ratio >5 (HR=2.678, p=0.022) were independent predictors of OS.
Conclusions: DM is an independent risk factor for late recurrence in patients with HCC receiving RFA. The impact of anti-diabetic agents and DM control on HCC recurrence in diabetic patients warrants further research.

主題：上消化道疾病（二）

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運用內視鏡吞嚥功能檢查：針對長期管灌的腦神經病患吸入性肺炎風險評估
FLEXIBLE ENDOSCOPIC EVALUATION OF SWALLOWING (FEES) IN NEUROLOGICAL PATIENTS ON LONG-TERM TUBE FEEDING TO PREDICT RISK OF ASPIRATION PNEUMONIA

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三軍總醫院胃腸科

Background: Nasogastric tube (NGT) and percutaneous endoscopic gastrostomy (PEG) are widely used techniques for feeding neurological patients with oropharyngeal dysphagia. However, aspiration pneumonia is the leading cause of death in enteral tube-fed patients.
Aims: Therefore, this study aimed to evaluate the role of oropharyngeal dysphagia in the risk stratification of pneumonia requiring hospitalization in neurological patients on long-term enteral feeding.
Methods: Flexible endoscopic evaluation of swallowing (FEES) using upper gastrointestinal endoscopy was performed to evaluate oropharyngeal dysphagia in neurological patients. We conducted a prospective 2-years follow-up of patients requiring hospitalization for pneumonia. A total of 226 orally-fed and 152 enteral tube-fed patients were enrolled. Multivariate analyses were performed to identify risk factors for pneumonia requiring hospitalization.
Results: Multivariate analyses showed a significantly increased risk of pneumonia in patients with previous history of pneumonia and receiving enteral tube-feeding. Subgroup analysis showed that among enteral tube-fed patients with oropharyngeal dysphagia, the risk of pneumonia requiring hospitalization was significantly lower in those who underwent PEG than in those using a NGT (P < 0.001). Kaplan–Meier curves showed that among patients with oropharyngeal dysphagia, the cumulative proportion of pneumonia requiring hospitalization was significantly lower in the PEG group than in the NGT group (P < 0.001) during long-term follow-up.
Conclusions: Flexible endoscopic evaluation of swallowing can be performed to evaluate oropharyngeal dysphagia. Among neurological patients with oropharyngeal dysphagia, PEG significantly decreases the risk of pneumonia requiring hospitalization compared with NGT for long-term enteral tube feeding.

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破解食道尖銳異物在側頸 X 光的熱點及影響辨識度因素

REVEALING HOTSPOTS AND FACTORS INFLUENCING IDENTIFIABILITY OF SHARP-POINTED ESOPHAGEAL FOREIGN BODIES ON LATERAL NECK RADIOGRAPHS

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Background: Esophageal foreign body (FB) ingestion, particularly sharp-pointed objects like fish bones, demand urgent management. The European Society of Gastrointestinal Endoscopy recommends emergent endoscopic procedures for esophageal sharp-pointed objects within 6 hours. While lateral neck radiography (LNR) is a common first-line modality due to its efficiency, challenges arise from complex neck anatomy which need precise impaction site identification.

Aims: This retrospective study from 2021 to 2023 aims to evaluate the clinical application for LNR to identify impaction sites of sharp-pointed esophageal FBs. Analyzing impaction hotspots and factors influencing FB detection on radiographic images may help to enhance diagnostics, improve clinical decisions, and facilitate precise interventions.

Methods: Enrollment began by identifying emergency department patients with FB ingestion diagnosis undergoing endoscopy. Impaction sites were determined using LNR or Neck CT finding. The detection frequency of visible FBs in specific C spine to T1 spine regions was recorded. Statistical analyses included $\chi 2$, Fisher exact test, and independent sample t-test ($P<0.05$). Uni- and multivariate logistic regression identified predictive factors for FB detection by LNR.

Results: Among 112 patients with proven sharp-pointed FB ingestion, 96 patients (85.7%) had impaction on esophagus. Due to limited detection below T1 on LNR, only 78 patients with impactions above T1 were included for analysis. Among 78 patients, 62 patients (79.5%) had identifiable FBs on LNR. Distribution of the FBs were 7 (9.0%) in the hypopharynx, 42 (53.8%) in the cervical esophagus, and 29(37.2%) in the upper esophagus. The hotspot for sharp-pointed FB impaction was the cervical esophagus, especially at C6 and C7 levels (detection frequency rate was53% and 47% subsequently) in our series. Sixteen patients were excluded only showing identifiable FBs on Neck CT, with the similar distributions as LNR ($P>0.05$). FBs identifiable only on CT were significantly shorter than those on LNR (median=2.0 vs. 2.4 cm, $P=0.034$). No significant associations were found between impaction location, gender, or age on detection of FB by LNR.

Conclusions: Our study underscores the successful identification of 79.5% of sharp-pointed esophageal FBs on LNR, with increased identifiability for the longer objects. The cervical esophagus, particularly at C6 and C7, emerged as hotspots for FB impaction on LNR. Our investigation did not reveal additional factors influencing the identifiability of foreign bodies on LNR.

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靜脈瘤處理：食道靜脈瘤結紮術與胃靜脈瘤注射硬化劑先後順序之策略比較
VARICEAL BLEEDING INTERVENTIONS: COMPARING EVL AND EIS SEQUENCING STRATEGIES

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Background: Esophageal varices (EV) and gastric varices (GV) in portal hypertension pose a risk of fatal bleeding, necessitating prompt intervention. Esophageal variceal ligation (EVL) and endoscopic injection sclerotherapy (EIS) are standard treatments. Concurrent EV and GV cases may undergo both procedures.

Aims: This study aims to assess rebleeding rates and all cause mortality, comparing outcomes when EVL precedes or follows EIS, providing insights into optimal intervention sequencing.

Methods: Patients diagnosed with concurrent EV and GV via endoscopy underwent initial treatment: EVL for EV bleeding or EIS for GV bleeding. Subsequently, patients received EIS and EVL for residual GV and EV, regardless of bleeding, between December 2009 and September 2023 at MacKay Memorial Hospital. Baseline data, rebleeding rates (at 6 months, 1 year, and 2 years), and all-cause mortality were analyzed. Statistical significance was set at $p < 0.05$, and analyses were conducted using SPSS 22.0.

Results: The patients (n=44) were divided into two groups: Group 1 (38.6%) underwent EVL followed by EIS, while Group 2 (61.4%) received EIS followed by EVL. Baseline characteristics showed no significant differences in age, sex, Child-Pugh classification, total bilirubin, INR, ascites, and encephalopathy. Group 1 had higher F1 (11.76%) and F3 (64.71%) esophageal varices (p=0.023 and 0.042), while Group 2 had more F3 (59.26%) gastric varices (p=0.002). The 6-month rebleeding rate was significantly higher in Group 1 (58.82% vs. 20.83%, p=0.034), and the 2-year rebleeding rate remained more prominent (94.12% vs. 60.87%, p=0.082). Notably, mortality rates did not significantly differ over the 3-year follow-up. Further analysis revealed that 30/40 patients with 2-year rebleeding had advanced liver cirrhosis (Child-Pugh class C, 46.67%, p=0.038). No significant differences were observed in other parameters.

Conclusions: Initiating treatment with EVL followed by EIS is associated with higher short-term rebleeding rates. Individualized strategies considering variceal classification and cirrhosis severity are crucial, guiding clinicians to optimize intervention sequencing for improved patient outcomes. Larger cohorts and extended follow-up periods are needed for further validation and refinement of these observations.

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在腎上腺素注射術後，比較併用氬氣電漿凝固術或併用止血夾兩者對於消化性潰瘍出血的止血療效之隨機控制試驗

A RANDOMIZED, CONTROLLED TRIAL OF ARGON PLASMA COAGULATION PLUS DILUTED EPINEPHRINE INJECTION VERSUS HEMOCLIPPING PLUS DILUTED EPINEPHRINE INJECTION FOR TREATMENT OF HIGH–RISK PEPTIC ULCER BLEEDING: AN INTERIM REPORT

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Background: Endoscopic treatment is recommended for initial hemostasis in nonvariceal upper gastrointestinal bleeding. Many endoscopic devices have been demonstrated to be effective in the hemostasis of bleeding ulcers. However, the additional hemostatic efficacy of argon plasma coagulation (APC) after endoscopic injection therapy has not been widely investigated.

Aims: The study aim is to compare APC plus diluted epinephrine injection (APC group) with clipping plus diluted epinephrine injection (Clip group) in treating high-risk peptic ulcer bleeding.

Methods: From Jan. 2019 to Nov. 2023, consecutive patients with high-risk bleeding ulcers, characterized by active bleeding, non-bleeding visible vessels and adherent clots, were admitted to our hospital. They prospectively randomly underwent either APC therapy plus diluted epinephrine injection or hemoclipping plus diluted epinephrine injection. Pantoprazole infusion was conducted during the fasting period after endoscopy and orally for 8 weeks to encourage ulcer healing. Episodes of rebleeding were retreated with endoscopic combination therapy. Patients who did not benefit from retreatment underwent emergency surgery or arterial embolization. The data were expressed as mean+SD. Quantitative variables were compared according to Student t-test, and qualitative variables were compared using the Chi-square test and Fisher's exact test when appropriate to compare the location of the bleeding lesions, initial hemostasis, rebleeding, emergency surgery and mortality of both treatment groups. All hypothesis tests were performed against a two-sided alternative, where appropriate. A $p < 0.05$ was viewed as statistically significant. Analyses were undertaken using SPSS software (SAS, SPSS Inc., Chicago, Ill., USA).

Results: In all, 163 eligible patients were analyzed. Hemostatic efficacy in 78 patients treated with APC plus diluted epinephrine injection was prospectively compared with 85 patients treated with hemoclipping plus diluted epinephrine injection. The two treatment groups were similar with respect to all baseline characteristics. Initial hemostasis was accomplished in 77 patients treated with APC combined with diluted epinephrine injection therapy, and 85 patients with hemoclipping plus diluted epinephrine injection therapy (98.7% vs. 98.8%, P = 1.000). Bleeding recurred in 6 patients in the APC group, and in 8 patients in the Clip group (7.7% vs. 9.4%, P = 0.784). No significant differences were observed between the 2 groups in surgery (1.3% vs. 1.2%, p = 1.000), TAE (1.3% vs. 2.4%, p = 1.000) and mortality (1.3% vs. 1.2%, p = 1.000). No significant differences were observed between the 2 groups in hospital stay and transfusion requirement.

Conclusions: Endoscopic therapy with APC plus diluted adrenalin injection is similarly effective as hemoclipping plus diluted adrenalin injection for preventing rebleeding in the treatment of high-risk bleeding ulcers. Both treatment methods also have similar safety during therapeutic endoscopy.

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利用胃內水交換減輕上消化道內視鏡檢查中患者的不適感 - 一項隨機對照試驗。
USING WATER EXCHANGE IN STOMACH TO REDUCE PATIENT DISCOMFORT DURING ESOPHAGOGASTRODUODENOSCOPY – A RANDOMIZED CONTROLLED TRIAL.

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Background: Unsedated esophagogastroduodenoscopy (EGD) is a common procedure used for diagnosing diseases in the upper gastrointestinal tract. However, discomfort experienced during the procedure might deter patients from undergoing the procedure. Sedated EGD, albeit alleviating the discomfort, increases the cost and the risk of complication. Water exchange (WE) has been shown to reduce discomfort during colonoscopy. The use of WE during EGD has never been reported.
Aims: The aim of the study was to evaluate whether the use of WE can reduce discomfort during EGD.
Methods: Patients undergoing unsedated EGD were enrolled. Patients were randomized to either the traditional air insufflation group or water exchange group when the scope reached the lower esophagus by opening a sealed envelope. In the air group, air insufflation was used to open the lumen of the stomach. In the WE group, distilled water was infused with a 50-ml syringe as the air was turned off. The infused water was aspirated immediately to keep the gastric lumen collapsed. The air was opened at the pylorus or duodenum. The endoscopists and the patients evaluate the tolerance and discomfort of the patients, respectively, during the procedure. The discomfort of the intubation was rated by the patients separately when the scope passed the throat and afterward. The primary end point was the discomfort (0, no discomfort; 10 worst discomfort) after the scope passing the throat as reported by the patient.
Results: A total of 250 patients were randomized to either air (n =120) or WE (n = 130) group. The baseline characteristics of the patients in the two groups were similar. The discomfort and tolerance of the patients when the throat was intubated were similar between the two groups. Patients in the WE group reported lower discomfort score after the scope passed through the throat (2.4 ± 2.4 vs. 3.1 ± 2.4, P=0.026). The endoscopists also found patients in the WE group had better tolerance than the air group (1.3 ± 1.4 vs. 1.6 ± 1.4, P = 0.045). Patients in the WE group had higher satisfaction score than the air group (9.4 ± 1.0 vs. 8.9 ± 1.5, P= 0.024). Patients in the WE group had less number of belching than the air group (1.8 ± 2.7vs. 2.6 ± 3.3, P=0.020).
Conclusions: Using WE technique during unsedated EGD improved patients discomfort and satisfaction.

主題：其他消化道疾病（一）

⑯

糞便鈣衛蛋白與發炎指數於潰瘍性大腸炎病患中的關聯性
THE CORRELATION BETWEEN FECAL CALPROTECTIN AND THE INFLAMMATORY INDEX OF PATIENTS WITH ULCERATIVE COLITIS

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Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by diffuse and continuous mucosal inflammation of the colon and rectum. Unlike Crohn's disease, which can involve all layers of the gastrointestinal tract, UC inflammation is often limited to the superficial rectal or colonic mucosal layer in continuity. Generally, endoscopic Mayo score can be used to evaluate the inflammation of the mucous membrane during colonoscopy. This scoring system stands as a robust tool for stratifying disease severity and guiding therapeutic decisions. Pathologically, UC is defined by crypt abscesses and mucosal ulcerations. The pathological evaluation of UC can be conducted using the Nancy score. Fecal calprotectin (FC), a sensitive and specific marker of colonic inflammation, plays a pivotal role in the non-invasive assessment of UC activity. Derived from neutrophils, calprotectin is released into the colonic lumen during inflammation, allowing for quantification in stool samples. Elevated levels of FC correlate with mucosal inflammation in UC. Clinically, FC not only assists in distinguishing between inflammatory and non-inflammatory causes of gastrointestinal symptoms but also serves as a useful tool in disease monitoring.

Aims: In this study, we aim to explore the correlation between FC levels and other inflammation parameters of UC, including the Mayo score, Nancy score, and serum inflammation markers.

Methods: We collected laboratory data and colonoscopy images from Taipei Medical University Hospital. This study spanned from January 2015 to December 2023, involving a total of 69 patients diagnosed with UC through colonoscopy. Exclusion criteria encompassed patients with an unclear diagnosis of colitis and those lacking data for Mayo and Nancy score evaluations. Subsequently, 58 patients were included in the final analysis. This cohort consisted of 22 women and 36 men. We gathered colonoscopic and pathological images for these patients, and assessed both Mayo and Nancy scores. Serum C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and hemoglobin (Hgb) levels were also collected. Subsequently, we conducted Pearson correlation analyses using IBM SPSS Statistics.

Results: In our analysis, we observed a moderate positive correlation between FC levels and ESR, with a Pearson's correlation coefficient of 0.36. Additionally, there was a negative correlation between FC levels and Hgb, indicated by a Pearson's correlation coefficient of -0.54. Furthermore, our investigation revealed a moderate positive correlation between the Mayo score and CRP, with a Pearson's correlation coefficient of 0.38. The Nancy score exhibited a moderate negative correlation with Hgb, as reflected by a Pearson's correlation coefficient of -0.36. These findings suggest that FC levels may be associated with systemic inflammatory markers such as ESR and Hgb, while the Mayo and Nancy scores exhibit correlations with CRP and hemoglobin, respectively.

Conclusions: In summary, our analysis suggests a potential association between colonic inflammation and systemic inflammatory markers, as indicated by the positive correlation observed between FC and serum ESR, as well as the correlation between Mayo score and CRP. The negative correlation between FC levels and Hgb, along with the correlation between Nancy score and Hgb levels, underscores the impact of inflammation on anemia in patients with UC. This study significantly contributes to a deeper understanding of the pathophysiology of UC, offering insights into FC as a UC marker for disease activity and severity. Further data are necessary to elucidate the associations between Mayo score, Nancy score, and other systemic inflammatory conditions.

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糞便鈣衛蛋白於兒童發炎性腸炎診斷及處置之效益 – 一項先導型研究
FECAL CALPROTECTIN HELPS IN DIAGNOSIS AND MANAGEMENT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE: A PILOT STUDY

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Background: Fecal calprotectin (FC) is a non-invasive biomarker of intestinal inflammation used to distinguish active inflammatory bowel disease (IBD) from chronic non-inflammatory gastrointestinal disorders, such as irritable bowel syndrome, other chronic diarrhea, or functional abdominal pain.

Aims: In this pilot study, we aim to investigate the clinical application of FC for children with warning symptoms of IBD in one medical center of south Taiwan.

Methods: The pediatric FC database was setup since April 2023 in our hospital. All of the enrolled subjects were aged less than 18 years old, and had a history of suspicious IBD including chronic diarrhea and/or weight loss, recurrent bloody stool, previous appendicitis-like episode, persistent right lower quadrant pain or tenderness, and severe intra-abdominal infection of unknown etiology. Clinical manifestations, laboratory and image findings, colonoscopy and pathological data, diagnosis, management and outcomes were retrospectively analyzed.

Results: Between April and December 2023, a total of 19 patients (10 males and 9 females) were eligible for the study. Eleven children (57.9%) were younger than 10 years old and 6 patients (31.6%) were less than 6 years old. Abnormal FC levels, defined as > 200 mg/kg, were documented in 8 subjects (42.1%). Among them, two patients were diagnosed as ulcerative colitis; two patients were Crohn's disease; one 6-year-old boy was monogenic IBD with underlying chronic granulomatous disease; one 4-year-old boy was eosinophilic colitis and suspicious IBD unclassified; one 6-year-old girl was steroid-responsive abdominal pain, suspecting upper gastrointestinal Crohn's disease; and one 1.5-year-old male toddler had salmonellosis and *Clostridium difficile* colitis but was lost for follow-up after antibiotics and probiotics treatment. Patients with bloody diarrhea (6/19, 31.6%) had significant higher FC (208~ > 6000 mg/kg, mean 2483.3 mg/kg) than other gastrointestinal symptoms. Concomitant intestinal infections were noted in 4 patients (2 rotavirus, 2 salmonella). In addition, normal FC (< 50 mg/kg, 9/19 patients, 47.4%) was found with functional abdominal pain (2 children) and irritable bowel syndrome (5 adolescents). However, dynamic change of FC levels should be concerned in clinical interpretation. One 8-year-old girl with Crohn's disease had initial normal FC (8 mg/kg) but elevated levels (433 mg/kg) when recurrent severe abdominal pain and diarrhea. Another 14-year-old male had previous appendicitis-like episode and normal FC (19 mg/kg) with minor symptoms but abdominal CT revealed IBD change.

Conclusions: Abnormal FC > 200 mg/kg is associated with pediatric IBD, especially when presented with bloody diarrhea and provides guidance of anti-inflammatory treatment. Combined modality diagnosis by using relevant history, FC, blood inflammatory markers, and image / colonoscopy evaluation helps in the management of IBD in children.

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飲食與發炎性腸道疾病風險之關聯性：台灣回顧性世代研究
DIET AND THE RISK OF INFLAMMATORY BOWEL DISEAS: A RETROSPECTIVE COHORT STUDY IN TAIWAN

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Background: The incidence of inflammatory bowel disease (IBD) rapidly increases in Asia, and western dietary pattern is suspected to be the major risk factor. Despite this, there has been a lack of studies analyzing the relationship between dietary patterns and IBD in Taiwan.

Aims: This study examines the dietary habits of Taiwanese individuals with and without IBD to inform clinical dietary recommendations for patients with IBD

Methods: A comprehensive survey utilizing structured questionnaires to collect baseline characteristics and dietary information from both patients with IBD and healthy controls from February and August 2022. The dietary habits of IBD patients in this study were focused on the three months leading up to their IBD diagnosis. Numerical data were presented as mean ± standard deviation, while categorical data were expressed as absolute numbers and percentages. Statistical analysis involved the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical data. Statistical significance was defined as $p < 0.05$, and all analyses were performed using SPSS version 22.0.

Results: Overall, 282 participants, including 98 with IBD (46 with Crohn's disease [CD] and 52 with ulcerative colitis [UC]) and 184 healthy controls, were enrolled in this study. Demographic analysis revealed a male predominance in both the CD and UC groups. Cigarette smoking was significantly more common in the IBD group (29.5% vs. 12.6%; $p = 0.001$). Distinct dietary patterns were observed between the groups. The control group demonstrated a higher consumption of whole foods, which included rice ($p = 0.005$), whole grains ($p < 0.001$), legumes ($p = 0.004$), mushrooms ($p = 0.004$), burdock ($p = 0.001$), poultry ($p = 0.049$), and fresh milk ($p < 0.001$). They also had a greater intake of antioxidants. By contrast, the IBD group consumed more processed food products than the control group. The consumption of red meat, seafood, and nuts was comparable between the groups.

Conclusions: Whole foods and antioxidants may be linked to a lower risk of IBD in Taiwan. Nonetheless, a larger sample size is needed to validate these observations and offer more substantial insights into the relationship between dietary factors and IBD.

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台灣炎症性腸道疾病孕婦的懷孕與周產預後：一項以人口為基礎的出生回溯性研究
PREGNANCY AND PERINATAL OUTCOMES OF INFLAMMATORY BOWEL DISEASE MOTHERS IN TAIWAN- A POPULATION-BASED BIRTH COHORT STUDY

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Background: Data from Asia for the pregnancy and perinatal outcomes of women with inflammatory bowel disease (IBD) is limited and it remains to be further dissected whether there are differences between the ulcerative colitis (UC) and Crohn's disease (CD) groups.
Aims: This study aims to use Taiwan's nationwide database to investigate the pregnancy and perinatal outcomes of pregnant women with IBD in Taiwan and compare the outcomes between UC and CD groups.
Methods: We conducted secondary data analyses using four national representative health and welfare databases: 1) Maternal and Child Health Database, 2) Birth Certificate Database, 3) National Health Insurance Database, and 4) Catastrophic Illness Database. We extracted all cases of newborns born between 2004 and 2018, identified mothers with a major catastrophic illness diagnosis code for IBD, and IBD mothers were defined by the registered IBD diagnosis (CD: ICD 9=555, ICD 10= K50.00-K50.919; UC: ICD 9=556.0-556.6 and 556.8-556.9, ICD 10= K51.00-K51.919) in the Catastrophic Illness Database. The control group of healthy pregnant women were matched with 1:10 ratio with the same birth year and maternal age as the IBD mothers. Additionally, we compared the neonatal outcomes of patients with UC and CD. For the comparison of prognosis based on the interval between disease confirmed diagnosis and delivery, we divided the intervals into "<2 years," "2~5 years," and ">5 years" groups and analyzed their neonatal outcomes. Statistical analyses were done by chi-square tests, t-test and conditional logistic regression models.
Results: Among the 3,059,647 births between 2004 and 2018, 146 newborns (126 UC; 20 CD) were born by mothers with a registered IBD diagnosis. No statistically significant differences were observed in stillbirth, preterm birth, cesarean delivery, low birth weight, small-for-gestational-age (SGA), large-for-gestational-age (LGA), and low Apgar scores when compared to the 1,460 matched healthy mothers (Table 1). Multivariate conditional logistic regression analysis also showed no significant differences in the perinatal outcomes among IBD mothers and matched control group. For the comparison between CD and UC groups, there was no statistically significant difference in the outcomes (Table 2). The association of the interval between onset and delivery on neonatal outcomes also showed no statistically significant difference among the "<2 years," "2~5 years," and ">5 years" groups).
Conclusions: Through this comprehensive analysis of long-term health and welfare databases in Taiwan, we found comparable perinatal outcomes between women with IBD and matched healthy women. And, there is no difference in neonatal outcomes between mom with UC or CD, as well as different intervals between disease confirmed diagnosis and delivery.

⑹

單發性缺陷瘤息肉：單一醫學中心 20 年全面回顧性研究
SOLITARY HAMARTOMATOUS POLYP: A SINGLE-CENTER COMPREHENSIVE 20- YEARS RETROSPECTIVE STUDY ON CLINICAL CHARACTERISTICS

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Background: In the context of increasing endoscopic accessibility, the identification of harmatomatous polyps has become more attainable, shedding light on a distinct variant known as solitary hamartomatous polyps. Unlike Peutz-Jeghers Syndrome , this variant lacks mucocutaneous pigmentation and familial history. Recognizing this solitary entity is pivotal for accurate diagnosis and management.
Aims: This retrospective study, aims to elucidate the clinical characteristics of solitary hamartomatous polyps in central Taiwan. With a focus on patients devoid of extraintestinal manifestations or a family history.
Methods: Patient data diagnosed with solitary hamartomatous polyps between January 2004 and November 2023 were extracted from the hospital database. Exclusions were made for those with extraintestinal symptoms, cancer history, or multiple hamartomatous polyps. Demographic information, initial symptoms, polyp size, location, and endoscopic findings were recorded. Statistical analyses included descriptive statistics for demographic and clinical characteristics.
Results: Over the 20-year period, 135 patients with hamartomatous polyps were identified. Thirteen participants were excluded from the study; eight were primarily excluded due to the cancer cases, and five were excluded on account of multiple hamartomatous polyps. Males constituted 50% of the study group. The most frequently encountered location is the gastric body, found in 39% of cases, with a total of 48 patients. The antrum is identified in 16% of patients, totaling 19 cases. The sigmoid represents 15% of cases with 18 patients. Following closely, the rectum accounting for 14% of cases and involving 17 patients. Moving to less common occurrences, the ascending colon is observed in 6% of cases, totaling 7 patients. The descending colon follows at 4%, identified in 5 cases. The cardia is reported in 2% of cases, with 3 patients associated with this location. Both the hepatic flexure and cecum show the lowest probability, each with a 1% occurrence and one patient associated with each location. In terms of excision methods, polypectomy accounts for 63% with 77 cases, biopsy constitutes 23% with 23 cases, and endoscopic submucosal dissection or endoscopic mucosal resection is represented by 12% with 15 cases. A patient underwent laparoscopic resection for the excision of a hamartomatous polyp located in the sigmoid colon, for the inability to successfully resection by colonoscopy.
Conclusions: This 20-year retrospective study contributes valuable insights into the epidemiological features of solitary hamartomatous polyps in central Taiwan. The unique regional distribution of polyps underscore the importance of tailored diagnostic and management strategies. While our study improves understanding.

主題：下消化道疾病（二）

㊶

COVID-19 對台灣大腸直腸癌診治影響
THE IMPACT OF COVID-19 ON THE DIAGNOSIS AND TREATMENT OF COLORECTAL CANCER IN TAIWAN

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Background: The COVID-19 pandemic caused a worldwide decline in cancer screenings, leading to an increase in more advanced cancer cases. Taiwan, South Korea, Japan, and other countries experienced reduced screening rates, which affected early cancer detection. However, some studies indicated minimal long-term effects of screening suspension on colorectal cancer mortality. The full impact of the pandemic remains uncertain due to the lack of comprehensive studies on colorectal cancer in Taiwan.

Aims: This study focuses on the impact of the COVID-19 pandemic on colorectal cancer in Taiwan, with three objectives: 1. Comparing stage distributions of colorectal cancer before and during the pandemic. 2. Evaluating survival outcomes across these periods. 3. Assessing changes in emergency visits and hospital admissions related to colorectal cancer. These aims will provide crucial insights for future healthcare strategies, especially in managing cancer during pandemics.

Methods: Conducted at Chi Mei Medical Center, this retrospective timeframe is divided into two phases: pre-COVID-19 pandemic (January 2017 to December 2019) and during the pandemic (January 2020 to December 2022). Data from hospital-based cancer registries included patient demographics, cancer stages, and treatment histories. Patients with inconsistent registry data or incorrect death dates were excluded. Statistical analyses utilized Pearson's chi-square, Fisher's exact test for categorical variables, and T-tests for continuous variables.

Results: From January 2017 to December 2022, 59,368 individuals were screened for colorectal cancer, with 3,373 positive fecal immunochemical tests (Figure 1). Before the pandemic, 1,804 of these individuals underwent colonoscopy, leading to 96 diagnoses of colorectal cancer (89 post-2019). No significant differences were found in baseline characteristics (Table 1) or in clinical stages (Table 2) between patients diagnosed before and during the pandemic. Additionally, no significant changes were observed in hospitalizations (Figure 2) and emergency department visits (Figure 3). The Kaplan-Meier curves (Figure 4) showed a non-significant divergence in survival rates between the two groups over one year.

Conclusions: Despite a reduction in screenings, colorectal cancer management in Taiwan remained resilient during the pandemic. This study underscores the need for flexible healthcare strategies to maintain effective cancer care in future health crises.

⑫

糞便潛血與死亡風險的關聯
UNCOVERING A DOSE-RESPONSE RELATIONSHIP BETWEEN POSITIVE FECAL IMMUNOCHEMICAL TEST (FIT) AND ALL-CAUSE, CARDIOVASCULAR AND CANCER-RELATED MORTALITY

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Background: Fecal immunochemical test (FIT) is for colorectal cancer (CRC) screening. Its association with non-CRC mortality has been overlooked. Given the quantitative FIT values, its dose-response relationships with different causes of deaths and years of life shortened were assessed.

Aims: We assessed the association of positive FIT with different causes of mortality, like all cancers and CVD, and establish the dose-response relationship for mortality risk expressed per unit of FIT increase. We also sought to link the FIT concentrations with the shortening of life expectancy expressed in the number of years lost.

Methods: This retrospective study included 546,214 adults aged ≥ 20 who attended a health surveillance program from 1994 to 2017 and were followed up until the end of 2020. FIT ≥ 20 μg Hb/g was defined as positive. The Cox model was used to assess adjusted hazard ratios (aHR).

Results: Positive FIT was associated with increased all-cause mortality (aHR: 1.34, 95% CI: 1.25-1.44) and all-cancer mortality (aHR: 1.71, 95% CI: 1.55-1.89), with a reduction of life expectancy by 4 years. The association remained even with CRC excluded. With each 10 μg Hb/g increase in FIT above 20 μg Hb/g, life expectancy was reduced by one year, and mortality increased by 4%. About 18.6% of deaths with positive FIT were attributed to cardiovascular disease (CVD), followed by CRC (13.5%) and upper gastrointestinal (GI) cancers (4.5%). The all-cause mortality rate after excluding CRC for positive FIT was 3.56/1,000 person-year, comparable to the all-cause mortality rate of 3.69/1,000 person-year for hypertension.

Conclusions: Positive FIT was associated with increased mortality in a dose-response manner and shortened life expectancy by 4 years, an overlooked risk comparable to hypertension, even with CRC excluded. After a negative colonoscopy, subjects with positive FIT should undergo a workup on CVD risk factors and look for other upper GI cancers.

⑬

以免疫法糞便潛血檢查濃度為指引的大腸息肉切除後個人化監測策略 - 一前瞻性族群研究
PERSONALIZED SURVEILLANCE AFTER POLYPECTOMY GUIDED BY FAECAL HEMOGLOBIN CONCENTRATION - A PROSPECTIVE COHORT STUDY

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Background: Population-based colorectal cancer (CRC) screening program using fecal immunochemical test (FIT) can reduce CRC risk through identifying subjects with adenoma followed by polypectomy in confirmatory colonoscopy. To keep CRC risk at the level of average population, surveillance colonoscopy with regular intervals is recommended. Current guidelines on surveillance intervals are devised by using the number, size, and histological findings of index adenoma.

Aims: Given the potential of fecal hemoglobin concentration (fHbC) in predicting CRC risk, this study aimed to develop a personalized surveillance interval for this population guided by fHbC level measured by FIT.

Methods: A prospective cohort design was applied by enrolling subjects received polypectomy identified in Taiwan National Colorectal Cancer Screening Program with biennial FIT test between 2010 and 2015. Subjects with fHbC higher than 20 were referred for confirmatory colonoscopy. Incident CRCs for this cohort were identified through Taiwan Cancer Registry up to the end of 2018. The CRC risk following polypectomy stratified by fHbC level and the size and histological types of adenoma were evaluated, based on which a risk-based surveillance intervals guided by fHbC were proposed. The crude and adjusted hazard ratios for each risk factor associated with incident colorectal cancer (CRC) were estimated using an accelerated failure time (AFT) model.

Results: Among 89771 subjects, an increasing trend of CRC risk by fHbC level ranging from 2.2 (20-49) to 4.0 (>=450) was observed. Using accelerated failure time (AFT) model, average CRC risk of surveillance population was 5.9 per 1000 in 3 years and 20.3 per 1000 in 7 years. For CRC risk stratified by FHbC, the estimated surveillance interval was from 2.4-3.5 years compared with 3-year CRC risk and 5.6-8.1 years compared with 7-year CRC

risk. Among non-advanced adenomas, 9.7 to 5.8 years can be applied for the fHbC level of 20-49 to >=450. As for advanced lesions, 5.0-1.9 years. Also by using personalized surveillance strategy, approximately 2,250 colonoscopies can be saved annually on a per 100,000 population basis.

Conclusions: For surveillance population of CRC, we observed gradient effect between baseline fHbC and the risk of CRC. Personalized surveillance interval in both low-risk and high-risk lesions may be guided by the level of fHbC. Also the capacity of colonoscopies may be reduced by personalized surveillance strategy.

⑭

人工智慧光學診斷系統對大腸微型息肉進行”光學診斷 - 息肉留置”與”光學診斷 - 逕行切除不送檢”策略可行性評估：一項實際運用人工智慧系統的臨床研究

EVALUATING THE PERFORMANCE OF A COMPUTER-AIDED DIAGNOSIS SYSTEM IN IMPLEMENTING DIAGNOSE-AND-LEAVE AND RESECT-AND-DISCARD STRATEGIES FOR DIMINUTIVE COLORECTAL POLYPS: A REAL-WORLD PRAGMATIC STUDY

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Background: For acceptance of computer-aided diagnosis (CADx) of diminutive (≤5 mm) polyps, CADx diagnosis should match the established Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) standards to implement the diagnose-and-leave and resect-and-discard strategies. However, available validation data in a real-world setting are limited.

Aims: We aimed to assess whether the CADx optical diagnosis of diminutive colorectal polyps met the criteria to be implemented in a clinical setting.

Methods: This was a retrospective study with an approved CADx system (CAD EYE, Fujifilm, Japan) conducted in a community hospital in Taiwan. Consecutive colonoscopy patients aged ≥40 years were included. The CADx system differentiated adenomas from non-adenomas using blue-light non-magnified imaging. For each polyp, CADx output was matched against the histology gold standard. In the CADx group, the follow-up interval after colonoscopy and polypectomy was determined by combining CADx diagnosis for diminutive polyps and histological diagnosis for ≥6 mm polyps. The primary outcomes were CADx performance in the diagnose-and-leave strategy for rectosigmoid diminutive polyps and in the resect-and-discard strategy for all diminutive polyps.

Results: Between March and August 2023, a total of 1249 polyps were detected and resected in 471 patients (mean age 55.2 years; 47% male). The indication of colonoscopy was primary screening, surveillance, diagnostic, and positive fecal immunochemical test in 49%, 39%, 5%, and 7%, respectively. Of these, 311 (25%) diminutive rectosigmoid polyps were retrieved for histology. There

were 247 of 311 polyps (79%) that were diagnosed by CADx as non-adenomatous and were amenable for the diagnose-and-leave strategy. The negative predictive value (NPV), sensitivity, specificity, and accuracy of CADx for rectosigmoid diminutive polyps were 83.8% (95% confidence interval [CI], 78.7%-87.9%), 54.5% (95% CI, 44.2%-64.5%), 92.8% (95% CI, 88.7%-95.5%), and 82.0% (95% CI, 77.3%-85.9%), respectively. Overall, 1084 diminutive polyps were retrieved throughout the colon. Based on the CADx output, 837 polyps were amenable to the resect-and-discard strategy, resulting in an 80.3% (95% CI, 76.4%-83.6%) and 94.7% (95% CI, 92.3%-96.4%) agreement between the CADx- and histology-based surveillance intervals according to American and European guidelines. The NPV, sensitivity, specificity, and accuracy of CADx for all diminutive polyps were 76.1%, 51.1%, 90.1%, and 75.8%, respectively. The CADx accuracy for diminutive polyps proximal to the sigmoid colon was lower than that for rectosigmoid location (73.4% vs. 82.0%; P = 0.003).

Conclusions: In this study, CADx fell short of the PIVI thresholds for implementation in the diagnose-and-leave strategy and resect-and-discard strategy according to US Multi-Society Task Force guidelines. Further research is warranted to improve the performance of CADx.

⑥⑤

評估 POWER BI 在腺瘤發現率上的影響
ASSESSMENT OF THE IMPACT OF POWER BUSINESS INTELLIGENCE ON ADENOMA DETECTION RATE: A PROSPECTIVE OBSERVATIONAL TRIAL

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Background: Interval cancer rates during colonoscopy screenings have varied from 2.9% to 9%, demonstrating a correlation with a low adenoma detection rate (ADR). Previous research indicates that providing adenoma detection rate feedback to endoscopists can improve ADR. Nevertheless, existing feedback mechanisms often lack automation, interactivity, real-time presentation, and effective data visualization.

Aims: This study aims to bridge the existing gap in ADR improvement by using Power Business Intelligence (Power BI, Microsoft TM Co., Redmond, USA). Developed by Microsoft, Power BI is an interactive data visualization software designed to provide real-time visualized data for endoscopy room managers. The objective is to facilitate the assessment of colonoscopy quality and deliver timely feedback to endoscopists, thereby evaluating the impact of Power BI on ADR.

Methods: By employing Power BI, colonoscopy quality data for each endoscopist was consistently displayed on the screen in the endoscopy room throughout 2022. A comparative assessment was conducted by comparing the quality data of 2022, utilizing Power BI, with that of 2021, which did not involve Power BI. Logistic regression analysis was then applied to identify independent factors influencing ADR.

Results: A total of 5,788 colonoscopies were conducted between 2021 and 2022. In the year when Power BI was employed, the patient population skewed younger, and fewer patients exhibited positive stool occult blood indications. The results of multivariate logistic regression analysis indicated no significant difference in ADR between cases with and without Power BI (47.1% vs. 45.7%, P = 0.280). Two modified endoscopist factors, specifically the use of the water method (odds ratio [OR], 1.454; 95% confidence interval [CI], 1.262-1.675; P < 0.001) and withdrawal time ≥ 6 minutes (OR, 5.463; 95% CI, 4.530-6.589; P < 0.001), were associated with adenoma detection,

with reference to a designated category. Patient-related factors linked to a high ADR included male gender (OR, 1.493; 95% CI, 1.331-1.676; P < 0.001), age (OR, 1.751; 95% CI, 1.557-1.968; P < 0.001), high body mass index (OR, 1.252; 95% CI, 1.100-1.426; P = 0.001), positive stool occult blood (OR, 1.969; 95% CI, 1.672-2.319; P < 0.001), and a high Boston bowel preparation score (OR, 1.165; 95% CI, 1.028-1.320; P = 0.017).

Conclusions: The results suggest that, even with feedback by utilizing Power BI, ADR did not show a significant improvement when colonoscopy methods and withdrawal time remained unchanged. Further optimization strategies may be needed to focus on the observation behavior change.

主題：肝腫瘤（二）

⑯

以電腦斷層影像建立肝癌腫瘤形態分類的人工智慧模型

AN ARTIFICIAL INTELLIGENCE-DERIVED MODEL FOR CLASSIFICATION OF TUMOR MORPHOLOGY BASED ON COMPUTED TOMOGRAPHY IMAGES IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Background: Tumor morphology pattern had significant impact on the treatment response and survival in patients with hepatocellular carcinoma (HCC). However, the classification of tumor morphology is time-consuming and labor-intensive.

Aims: The aim of this study is develop an artificial intelligence (AI)-derived model for automatic classification of tumor morphology using dynamic computed tomography (CT) images from HCC patients.

Methods: Dynamic CT images before transarterial chemoembolization (TACE) treatment in 515 HCC patients were used for model development (n=307) and validation (n=208). Another cohort of 643 patients receiving surgical resection were used to validate the prognostic value of AI-predicted morphology. Tumor morphology patterns were classified as low-risk (simple nodular type), intermediate-risk (simple nodular type with extranodular growth), and high-risk (confluent multinodular or infiltrative type) morphology. A ResNet-based deep-learning model (HCC-MorphoNet model) was developed to classify the tumor morphology of HCC.

Results: The HCC-MorphoNet model achieved the overall accuracy of 86.3% and 86.1% in predicting tumor morphology in the training set and the test set, respectively. The accuracy for predicting low-, intermediate-, and high-risk morphology was 83%, 89.9% and 95.3%, respectively. The AI-classified tumor morphology could significantly discriminate the radiologic response (p<0.001) and overall survival (p<0.001) after TACE, and the predicted outcomes were similar to those from human-classified

tumor morphology. The AI-classified tumor morphology also significantly discriminated recurrence-free survival ($p<0.001$) and overall survival ($p<0.001$) in HCC patients receiving surgical resection.

Conclusions: We developed an HCC-MorphoNet model based on dynamic CT images for classification of tumor morphology in patients with HCC. The AI-classified morphology significantly discriminated the outcomes of HCC after TACE and surgical resection.

⑰

KDM 家族對肝細胞癌的預後意義及免疫浸潤的綜合分析
COMPREHENSIVE ANALYSIS OF PROGNOSTIC SIGNIFICANCE AND IMMUNE INFILTRATION IN THE KDM FAMILY FOR HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma (HCC) is a highly prevalent and aggressive malignancy globally, characterized by poor prognosis. Previous studies have highlighted the importance of abnormal gene expression within the histone demethylase (KDM) family, establishing connections between epigenetic changes and enzymatic imbalances in the progression of cancer.

Aims: This study aimed to explore the expression patterns of KDMs, assess their prognostic significance, and examine their potential relationship with immune infiltration in individuals diagnosed with HCC.

Methods: In this study, multiomics analyses were utilized to analyze differential expression, prognostic value, genetic alteration, protein-protein interaction, associated biological pathways, and immune cell infiltration of lysine (K)-specific demethylase 1/3 in patients with HCC.

Results: The intricate genetic modifications and complex network of biological interactions involving KDM1 enzymes provide detailed insights into their dysregulated activity in individuals with HCC. Investigating the signaling pathways associated with KDM1 and their miRNA targets holds promise as both potential therapeutic avenues and markers of tumor progression. Elevated mRNA expression of KDM1 enzymes exhibited a significant correlation with the presence of diverse immune cell populations in HCC. Among HCC patients, the expression of KDM3A-C was notably elevated, showing variation based on tumor grade and pathology, when compared to normal tissue samples. Particularly noteworthy was the strong connection between heightened KDM3A expression and unfavorable survival outcomes in HCC patients, whereas KDM3B and KDM3C did not demonstrate such relationships. Additionally, genetic alterations within the KDM3A-B subgroup had a considerable impact on survival in HCC patients. By

analyzing KEGG pathways and miRNA targets associated with KDM3A and KDM3B in the context of HCC, valuable insights into tumor behavior and potential treatment strategies could be gleaned. The distinct expression patterns within the KDM3 family displayed a robust and meaningful correlation with the levels of various immune cell types present in HCC, including B cells, CD8+ T cells, CD4+ T cells, macrophages, neutrophils, and dendritic cells.

Conclusions: This research suggests that KDM1A, KDM1B, and KDM3A could hold promise as valuable molecular targets for HCC treatment, both as prognostic biomarkers and potential therapeutic focuses.

⑱

比較標靶藥物與標靶藥物結合免疫療法對晚期肝癌患者的存活效益評估

SURVIVAL BENEFITS BETWEEN TARGET THERAPY AND COMBINATION OF TARGET THERAPY WITH IMMUNOTHERAPY FOR PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA

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Background: The prognosis for patients diagnosed with advanced hepatocellular carcinoma (HCC) is dismal. At present, treatment options consist of target therapy (e.g., lenvatinib and sorafenib) and combination therapy (e.g., atezolizumab in conjunction with bevacizumab). We are interested in conducting a study endeavor to assess the comparative effectiveness of target therapy alone versus target therapy combined with immunotherapy.

Aims: The objective of this study is to assess the comparative effectiveness of target therapy alone vs the combination of targeted therapy plus immunotherapy in advanced HCC.

Methods: Our retrospective study comprised 744 patients with advanced HCC who were treated at Taipei Veterans General Hospital (VGH) between July 2010 and December 2022. A cohort consisting of 640 patients received targeted therapy alone. A cohort of 104 patients were treated with a combination of targeted therapy and immunotherapy. As targeted therapies, bevacizumab, lenvatinib, and sorafenib are available for use. The components of immunotherapy are nivolumab, pembrolizumab, and atezolizumab.

Results: The median overall survival is significantly lower in patients who receive target therapy alone compared to those who receive a combination of target therapy, with a duration of 6.3 months versus 7.91 months ($P < 0.001$). In the subgroup analysis, lenvatinib exhibited a marginally higher median overall survival compared to sorafenib (6.96 months vs. 6.12 months, $P = 0.044$). However, the addition of pembrolizumab to lenvatinib did not yield any benefit in terms of the median overall survival when compared to lenvatinib alone (7.86 months v.s. 6.96 months, $P = 0.084$).

Conclusions: Patients diagnosed with advanced hepatocellular carcinoma (HCC) demonstrated significantly extended survival when treated with a combination of targeted therapy and immunotherapy, as compared to those who just received targeted therapy.

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LENVATINIB 合併 PEMBROLIZUMAB 與 ATEZOLIZUMAB 合併 BEVACIZUMAB 用於不可手術切除晚期癌：傾向分數配對分析

LENVATINIB PLUS PEMBROLIZUMAB COMPARED WITH ATEZOLIZUMAB PLUS BEVACIZUMAB FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA: A PROPENSITY SCORE ANALYSIS

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Background: Atezolizumab in combination with bevacizumab stands as the primary treatment option for unresectable hepatocellular carcinoma (uHCC) in the first-line setting currently. Nevertheless, not all patients are eligible for bevacizumab therapy. Another immuno-checkpoint inhibitor (ICI) combination regimen, lenvatinib plus pembrolizumab, despite it failed in the Phase III study compared with sorafenib, impressive response rates and survival outcomes still suggests the potential clinical benefits in certain patients. Whether these two ICI combination therapy will have a better outcome is still unknown.

Aims: The study tried to evaluate the treatment response and outcomes of lenvatinib plus pembrolizumab and atezolizumab plus bevacizumab for uHCC in real-world first-line setting.

Methods: From Sep. 2019 to Nov, 2023, 144 patients who received lenvatinib plus pembrolizumab or atezolizumab plus bevacizumab for uHCC in the first-line setting within Child-Pugh class B7 liver function in Taipei Veteran General Hospital were retrospectively enrolled. A 1:1 propensity score matching (PSM) analysis was performed using prospectively collected data. The tumor responses were assessed with Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

Results: Of the 144 uHCC patients, 97 patients received lenvatinib plus pembrolizumab, 47 patients received atezolizumab plus bevacizumab. With the use of propensity scores, 46 pairs of matched uHCC patients selected from each treatment groups. After matching, patients were comparable in age, gender, severity of cirrhosis, etiology of HCC, and BCLC stage at baseline. In the PSM model, patients received lenvatinib plus pembrolizumab had significantly higher objective response rate (45.7% vs. 23.9%, p=0.029) and disease control rate (82.6% vs. 56.5%, p=0.007) compared to patients treated with atezolizumab plus bevacizumab. And no statistically significant difference in overall survival (13.5 vs. 15.9 months, p=0.879) and progression-free survival (7.1 vs. 3.3 months, p=0.405) were observed between lenvatinib plus pembrolizumab with atezolizumab plus bevacizumab.

Conclusions: Although with higher response rate, lenvatinib plus pembrolizumab showed no significantly different survival outcomes compared with atezolizumab plus bevacizumab for uHCC patient in the first-line setting.

⑦⓪

治療中慢性 B 型肝炎且伴隨脂肪肝病發生肝細胞癌之預測因子
PREDICTORS OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH TREATED CHRONIC HEPATITIS B AND STEATOTIC LIVER DISEASE

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Background: Chronic hepatitis B (CHB) is the primary factor contributing to the development of hepatocellular carcinoma (HCC). However, treated CHB does not show an association with increased incidence of HCC in the context of steatotic liver disease (SLD).
Aims: We aimed to explore the impact of concurrent SLD on the risk of HCC in patients with CHB undergoing oral antiviral therapy.
Methods: This study included patients with CHB who received oral antiviral therapy between 2004 and 2022. It identified SLD through ultrasound or biopsy evidence of hepatic steatosis. Various cardiometabolic traits were recorded, including obesity (body mass index [BMI] ≥ 23), prediabetes or diabetes, hypertension, hypertriglyceridemia, and low levels of high-density lipoprotein (HDL). Additionally, we analyzed predictors of HCC using Cox regression analysis.
Results: A total of 1,012 patients with CHB, who had undergone oral antiviral therapy, were enrolled in the study. Over a median treatment duration of 5.5 years, 73 HCC events occurred. Patients with CHB and SLD (n = 579) were younger, had a lower proportion of cirrhosis, lower FIB-4 values and HDL-C levels, and higher BMI, ALT, and platelet counts at baseline, compared to the non-SLD group (n = 433). In the cardiometabolic criteria-based model 1, SLD was independently associated with a 57% reduced risk of HCC (adjusted hazard ratio [aHR] 0.43, 95% confidence interval [CI] 0.258–0.700, P = 0.001). Conversely, alcohol consumption (aHR = 1.72), AFP levels ≥5 ng/mL (aHR = 1.71), and FIB-4 ≥3.25 (aHR = 1.71) were associated with an increased risk of HCC. Furthermore, steatosis and cardiometabolic traits had distinct effects on HCC in the cardiometabolic traits-based model 2. Notably, pre-diabetes and diabetes increased the risk of HCC (aHR 1.86, 95% CI 1.17–2.97, P = 0.009).
Conclusions: Concurrent hepatic steatosis is independently associated with a reduced risk of HCC. However, metabolic dysfunction, especially pre-diabetes and diabetes, exacerbates the risk of HCC in patients with CHB who are receiving antiviral therapy.

主題：其他消化道疾病（二）

⑦①

組織學癒合可減少中度至重度且使用過生物製劑治療的潰瘍性結腸炎患者的內視鏡復發：一項全面的回顧性研究
HISTOLOGICAL REMISSION LEADS TO LESS ENDOSCOPIC FLARE-UP IN MODERATE-TO-SEVERE, BIOLOGICS EXPERIENCED ULCERATIVE COLITIS PATIENTS: A COMPREHENSIVE RETROSPECTIVE COHORT STUDY

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Background: In the management of inflammatory bowel disease (IBD), adopting a treat-to-target strategy has proven beneficial. Current therapeutic targets primarily focus on achieving endoscopic remission. However, the significance of histological remission as a potential target. However, it remains underexplored in Asian populations.
Aims: We aimed to investigate the role of histological remission in clinical outcomes among ulcerative colitis (UC) patients already in endoscopic remission.
Methods: In this retrospective cohort study, we enrolled moderate to severe, biologics experienced UC patients with endoscopic remission, defined as endoscopic Mayo subscore 0 point during June 2017 and September 2023 in Chang Gung Memorial Hospital, Linkou. Then the patients were divided into histological remission (HR) and non-histological remission (non-HR) groups according to histological Nancy index (NI). HR was defined as NI 0 point, and others belonged to non-HR group. Comparative analyses were performed between two groups regarding baseline characteristics, one year follow up and end of follow-up clinical outcomes. The location of biopsy was active inflammatory lesion, if no active lesion, we performed routine biopsy over rectum, 15cm level from anal verge. We took at least 4 pieces biopsy over each location.
Results: We enrolled 42 moderate-to-severe, biologics experienced UC patients (HR group, 23 patients and non-HR group, 19 patients) with endoscopic remission. The average follow-up duration was 17.6 months. In non-HR group, NI scores were categorized as follows: 1

point (42.1%), 2 points (31.6%), 3 points (21.1%), and 4 points (5.3%). Baseline characteristics showed no significant differences between the two groups. In terms of outcomes, the HR group demonstrated a significantly lower endoscopic relapse rate (26.1% vs. 68.4%, P=0.006) and better results in Kaplan-Meier survival analysis (log-rank P=0.015) at the end of the follow-up period. The HR group also exhibited a reduction in clinical relapses, emergency department visits, and hospital admissions. Although these differences did not attain statistical significance, this phenomenon is likely attributable to the study's constrained sample size.

Conclusions: In moderate-to-severe UC patients who are biologics-experienced and in endoscopic remission, achieving histological remission is associated with a reduced rate of endoscopic relapse.

⑫

上消化道克隆氏症臨床特徵與結果：回顧性世代研究

CLINICAL CHARACTERISTICS AND OUTCOMES OF CROHN'S DISEASE WITH UPPER GASTROINTESTINAL INVOLVEMENT: A COMPREHENSIVE RETROSPECTIVE COHORT STUDY

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Background: Crohn's Disease (CD) affects the entire gastrointestinal tract, predominantly involving the terminal ileum and colon. However, the incidence and implications of upper gastrointestinal tract involvement in CD are often underestimated and underreported, especially in Asian populations.

Aims: This study provides a comprehensive evaluation of the clinical characteristics and outcomes associated with UGI involvement in CD

Methods: We conducted a retrospective cohort study at Chang Gung Memorial Hospital, Linkou, from January 2001 to September 2023, including CD patients with consistent follow-up records. Patients were categorized into two groups based on UGI involvement: Montreal L4 and non-L4. Comparative analyses were performed between the groups regarding baseline characteristics, new-onset complications post L4 disease diagnosis, and clinical outcomes.

Results: The study included 223 CD patients, 114 in the L4 group and 109 in the non-L4 group, with an average follow-up of 40.6 months. Initially, the L4 group showed higher smoking prevalence (21.1% vs. 5.5%, P<0.001), higher Crohn's Disease Activity Index (CDAI) scores (302.6±85.6 vs. 272.8±106.3, P=0.023), increased stricture disease (Montreal B2) incidence (55% vs. 48.2%, P<0.001), and more frequent use of biologics (12.3% vs.3.7%, P=0.021) and proton pump inhibitors (64.9% vs. 52%, P=0.014). They also had lower albumin levels (3.6±0.8 vs.

3.9±0.7, P=0.011) and reduced peri-anal (14.9% vs. 26.8%, P=0.026) and fistulizing disease incidences (14% vs. 26.6%, P=0.016). At follow-up end, the L4 group continued to exhibit higher CDAI scores (153.6±98.7 vs. 114.4±71.8, P = 0.001), increased hospitalization rates (0.6±1.1 vs. 0.3±0.5 times/year, P=0.009), elevated C-reactive protein levels (15.2±37.8 vs. 6.9±15.1, P=0.036), and decreased albumin levels (4±0.7 vs. 4.2±0.4, P=0.018). Though they had a lower incidence of new-onset perianal fistula (6.7% vs. 3.7%, P=0.041), the L4 group had higher incidences of most new-onset CD-related complications, including strictures (44% vs. 20.2%, P<0.001), enter enteral fistulae (11.9% vs. 3.5%, P=0.036), and intraabdominal abscesses (17.4% vs. 5.3%, P=0.009). Upper gastrointestinal involvement (OR 2.307, 95% CI 1.173-4.538) and the presence of structuring (OR 3.466, 95% CI 1.771-6.78) disease at the time of diagnosis are independently associated with an increased risk of developing new-onset strictures.

Conclusions: CD with UGI involvement is associated with higher disease activity and an increased risk of IBD-related complications, especially new-onset stricture. Comprehensive assessments at diagnosis and aggressive treatments are crucial for these patients to mitigate poorer outcomes

⑦③

發炎性腸道疾病患者之糞便白血球脂酶濃度可預測內視鏡嚴重度、與作為替代的監測指標

FECAL LEUKOCYTE ESTERASE LEVEL CAN PREDICT ENDOSCOPIC SEVERITY AND CAN BE AN ALTERNATIVE MONITORING BIOMARKER FOR INFLAMMATORY BOWEL DISEASE PATIENTS

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Background: The urine leukocyte esterase (LE) strip is widely employed to detect leukocyte presence in human body fluids due to its simplicity, speed, cost-effectiveness, and wide availability. Our previous study demonstrated that fecal LE (FLE) correlated with fecal calprotectin (FC) levels.

Aims: This study aims to validate the previous results and assess the predicting ability of FLE for endoscopic severity in inflammatory bowel disease (IBD) patients.

Methods: This prospective study consequently invited IBD patients who would receive the ileocolonoscopy due to clinical indications at the National Taiwan University Hospital from December 2021 to November 2023. FLE and FC in the same stool sample, which was collected before and within one month of endoscopy, were analyzed. The correlation between FLE, FC, and endoscopic severity scores was assessed using the Pearson method. Active disease in ulcerative colitis (UC) and Crohn's disease (CD) patients was defined as Mayo endoscopic score (MES) ≥ 2 and simple Endoscopic Score for Crohn's Disease (SESCD) ≥ 8, respectively. Sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and the Area Under the Receiver Operating Characteristic curve (AUROC) were analyzed by using SPSS.

Results: A total of 177 IBD patients (93 with UC, 84 with CD) were included. The correlation between FLE and FC levels was significantly positive (r=0.305, p<0.001). The correlation between FLE and endoscopic severity in UC and CD patients was 0.442 (p<0.001) and 0.293 (p=0.007), respectively. Among UC patients, the area under the receiver operating characteristic curve (AUROC) for

predicting MES ≥ 2 by FLE, FC and CRP were 0.717, 0.776 and 0.582 with an optimal cutoff of 2+ for FLE and 42.5 mg/kg for FC, respectively. At this cutoff point, FLE demonstrated a sensitivity, specificity, PPV, and NPV for predicting MES ≥ 2 as 52.3%, 81.6%, 71.8%, and 65.6%, respectively. For CD patients, the AUROC for predicting SESCD ≥ 8 by FLE, FC and CRP were 0.758 and 0.883 and 0.462, with an optimal cutoff of 2+ for FLE and 225 mg/kg for FC, respectively. FLE exhibited a sensitivity, specificity, PPV, and NPV of 81.8%, 64.4%, 74.3%, and 95.9% for predicting SESCD ≥8 respectively, at this cutoff.

Conclusions: Our results validated that FLE correlated with FC and can predict endoscopic activity. Compared to FC, FLE is a cheaper and more widely available monitoring tool, which could be an alternative to FC for IBD monitoring.

⑦④ 比較膠囊內視鏡及單氣囊小腸鏡作為第一線探查大量不明原因消化道出血之應用價值

COMPARISON OF VIDEO CAPSULE ENDOSCOPY AND SINGLE-BALLOON ENTEROSCOPY FOR FIRST-LINE EXPLORATION OF MASSIVE OBSCURE GASTROINTESTINAL BLEEDING

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Background: The position of video capsule endoscopy (VCE) relative to single-balloon enteroscopy (SBE) in the diagnostic algorithm of massive obscure gastrointestinal bleeding (OGIB) is unclear, as previous studies involved the use of both techniques in all patients.

Aims: The aim of this study was to compare the diagnostic yield and clinical outcomes of the two approaches.

Methods: We retrospectively enrolled patients who had undergone VCE or SBE for massive OGIB between January 2017 and March 2023 at a tertiary referral academic center. The alternative method was only used if the first-line method revealed no definite bleeding source, or if required for clinical reasons during follow-up. We analyzed the diagnostic yield of VCE and SBE, therapeutic intervention rate and long-term rebleeding rate.

Results: VCE and SBE, used as the first-line exploration, identified a bleeding source in 30 of 40 patients and 34 of 49 patients, respectively (75% vs 69.4%; P =0 .639). The most frequent positive findings at VCE were erosions/ulceration (15 patients, 37.5%) followed by angiodysplastic/vascular lesions (9, 22.5%). The most frequent findings at SBE were angiodysplastic/vascular lesions (20 patients, 40.8%) followed by erosions/ulceration (12, 24.5%). Therapeutic intervention was performed in 55% and 65.3% of patients in the VCE and SBE groups, respectively (P=0.385). In patients with OGIB, the overall rebleeding rate was 32.5% (13/40) in VCE group and 38.8% (19/49) in SBE group during a median follow-up of 12 months (range 6-64 months). Multivariate analysis showed that only hemoglobin ≤7 g/dL before OGIB study (hazard ratio [HR] 2.543, 95% confidence interval [CI] 1.236-5.196, P = 0.011) was independent risk factor associated with rebleeding.

Conclusions: High detection rates of the causes of massive OGIB are feasible with VCE-first and SBE-first approaches. The ulceration and angiodysplasia were two common findings for OGIB. Rebleeding is common during the long-term follow-up of patients with OGIB. Careful follow-up is required for these patients after hospital discharge.

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與非法中藥鉛中毒相關的胃腸道疾病
GASTROINTESTINAL DISORDERS RELATED TO LEAD POISONING FROM ILLEGAL CHINESE MEDICINE

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Background: Lead poisoning is known to cause multi-organ damage in humans, resulting in conditions including gastrointestinal (GI) disorders, anemia, and neuropathy. This study was prompted by an outbreak of lead poisoning events caused by the ingestion of illegal lead-containing traditional medicine.

Aims: This study aims to investigate the impact of lead poisoning on the human body, with a particular focus on liver function.

Methods: Adult patients diagnosed with lead poisoning due to the ingestion of illegal Chinese herbal medicine were retrospectively enrolled at China Medical University Hospital between April 2020 and June 2023. Lead poisoning was defined based on elevated blood lead levels (PbB) surpassing 10 micrograms per deciliter (μg/dL), accompanied by associated symptoms or evidence of organ damage. Exclusion criteria were applied to patients with pre-existing conditions such as cirrhosis, liver tumors, absence of blood liver function test, or lead poisoning unrelated to Chinese herbal medicine. We analyzed the clinical and laboratory data of these patients. Subsequently, we divided them into two groups: the hepatitis group and the non-hepatitis group, identifying distinct features between the two groups.

Results: Between April 2020 and June 2023, a total of eighteen adult patients were diagnosed with lead poisoning related to illegal Chinese medicine containing lead, after excluding one patient with a liver tumor and one patient who had not undergone a blood liver function test. The most common GI symptoms were abdominal pain (n = 12) and abdominal fullness (n = 10), followed by constipation and nausea (Table 1). Hepatitis related to lead poisoning was diagnosed in 8 out of 18 cases, with a median serum glutamic pyruvic transaminase (SGPT) level of 144.5 IU/L (interquartile range (IQR) 59; 445). Among the 8 hepatitis patients, 6 exhibited hyperbilirubinemia with a median (IQR) blood total bilirubin level of 2.73 mg/dL (1.45; 3.13), all of which were conjugated hyperbilirubinemia. The median (IQR) of ratio of blood direct bilirubin to total bilirubin was 28.8% (21.7%; 36.1%). In contrast, no patients in the non-hepatitis group exhibited hyperbilirubinemia. Furthermore, the median (IQR) PbB in the hepatitis group was 89.3 μg/dL (62.6; 159.5), whereas in the non-hepatitis group, it was 57.9 μg/dL (48; 61.2). A Mann-Whitney test revealed a significantly higher PbB in the hepatitis group compared to the non-hepatitis group (P = 0.027). Meanwhile, the median (IQR) Hb level in the hepatitis group was 8.7 g/dL (7.7; 10.9), whereas in the non-hepatitis group, it was 13.0 g/dL (11.2; 13.8). A Mann-Whitney test revealed a significantly lower Hb level in the hepatitis group compared to the non-hepatitis group (P = 0.002).

Conclusions: Gastrointestinal disorders are commonly observed in lead-poisoned patients. In patients with unexplained gastrointestinal discomfort, attention to their exposure history is crucial, and lead poisoning should be considered in the differential diagnosis. We found that compared to the non-hepatitis group, the hepatitis group demonstrated higher PbB, more severe anemia, and hyperbilirubinemia, implying a potentially greater impact of higher PbB on the liver and hematological systems. Nevertheless, due to limitations in the number of cases, a correlation or regression relationship between PbB and SGPT could not be established in this study.

主題：上消化道疾病（四）

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檢測食道癌呼吸中揮發物的比較分析：一項奈米粒子強化口罩研究
COMPARATIVE ANALYSIS OF BREATH VOLATILES IN ESOPHAGEAL CANCER DETECTION: A NANOPARTICLE-ENHANCED FACE MASK STUDY

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Background: Esophageal squamous cell carcinoma (ESCC), representing the majority (85%) of esophageal cancers, is often diagnosed late (stages III and IV), resulting in a low 5-year survival rate (10-30%). Traditional detection methods like esophagogastroduodenoscopy (EGD) are invasive and uncomfortable. In contrast, studies have shown promise in using exhaled breath volatile organic compounds (VOCs) for non-invasive cancer detection.

Aims: This pilot study explores VOC differences in ESCC patients versus a healthy group, utilizing nanoparticle-layered face masks, with the goal of developing an ESCC detection method.

Methods: In this study, 18 healthy volunteers and 12 ESCC patients participated. Each wore a specially designed medical mask for two hours. The mask contained two g-C3N4/PDMS/TFME-PP membrane strips, each measuring 1×2 cm, positioned in the second layer to capture exhaled breath VOCs. The healthy volunteers were stationed in a controlled environment, while ESCC patients stayed in their own rooms. Prior to mask wearing, a 6-hour fasting period was mandated to ensure consistency in VOC sampling. Post-wearing, the nanoparticle layers were extracted for VOC analysis. Our primary analytical technique was gas chromatography-mass spectrometry (GC-MS), targeting 28 specific VOCs identified from literature reviews for their relevance to ESCC. These included Butanal, Toluene, various Xylenes, and other alkanes. Ethical compliance was ensured with all participants providing informed consent, under the approval of the institutional review board (KMUHIRB-G(I)-20220018).

Results: The study included 18 healthy volunteers (8 male, 10 female) and 12 male ESCC patients with advanced-stage cancer. Key VOC differences were noted in Butanal, 1,2,3-trimethylbenzene, and decanal levels. ESCC patients exhibited higher Butanal but lower 1,2,3-Trimethylbenzene and Decanal levels compared to healthy subjects. Butanal's diagnostic performance (sensitivity and specificity of 0.83; AUC=0.89, p=0.01) was noteworthy. The diagnostic accuracy of these VOCs is depicted in the ROC curve.

Conclusions: This study highlights the potential of exhaled VOC analysis as a non-invasive ESCC detection method. The observed VOC distinctions between ESCC patients and healthy individuals merit further investigation in larger cohorts.

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內視鏡切除上消化道黏膜下病灶之有效性及安全性分析：一個內視鏡治療中心的經驗
EFFECTIVENESS AND SAFETY OF ENDOSCOPIC RESECTION OF UPPER GASTROINTESTINAL SUBEPITHELIAL LESIONS: A SINGLE-CENTER EXPERIENCE

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Background: Gastrointestinal (GI) subepithelial lesions (SELs) are usually discovered during routine screening or diagnostic endoscopy. The pathology ranged from benign to malignant, including lipoma, GISTs and metastatic tumors. However, tissue acquisition remains challenging due to small size and deep location. Close endoscopic surveillance frequently causes anxiety in patients and unnecessary invasive procedures. Resection is a proposed alternative that has not been validated.

Aims: We aimed to evaluate the effectiveness and safety of endoscopic resections for upper GI SELs.

Methods: This retrospective study analyzed data collected from all patients who underwent endoscopic resection for upper GI SELs at Taipei Medical University Hospital between January 2018 and December 2022. Data pertaining to patients' demographics, procedural characteristics, en bloc/R0/R1 resection rate, and complications were retrieved and analyzed. EMR, ESD, and STER were chosen by the endoscopist's consideration. All patients received ETGA for anesthesia.

Results: Twenty-two patients with 24 upper GI SELs were included, with 8 in esophagus and 16 in stomach. Fifteen SELs are smaller or equal to 2 cm, while 9 SELs are larger than 2 cm. Fifteen SELs were resected with STER, 8 with ESD, and 1 with EMR. The effectiveness outcomes revealed a high en bloc resection rate of 83.3% (20/24). For malignant SELs (6 GISTs), a low R0 resection rate of 13.3% (1/6) and an R1 resection rate of 86.7% (5/6) were recorded. The complications comprised 4 perforations, of which 3 were treated endoscopically with close monitoring and 1 was surgically repaired without leading to mortality.

Conclusions: Our study revealed high en bloc resection and low complication rate. The low R0 rate but high R1 rate is considered acceptable because of the low risk of recurrence for small GISTs. Endoscopic resection may be an alternative for SELs measuring ≤2 cm without a definite diagnosis. Our single-center study indicates that endoscopic resection is a safe and effective method for diagnosing and managing upper GI SELs in selected cases.

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內視鏡下切除胃肌肉層腫瘤之療效及安全性：單一醫學中心的經驗
EFFICACY AND SAFETY OF ENDOSCOPIC RESECTION OF GASTRIC MYOGENIC TUMOR: A SINGLE CENTER EXPERIENCE

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Background: The prevalence of gastric subepithelial tumors (SETs) is increasing due to widespread application of gastroscope examination. Among them, SETs with malignant potential, such as gastrointestinal stromal tumor (GIST), should be managed. Endoscopic muscularis dissection (EMD) and endoscopic subserosal dissection (ESSD) are minimally invasive alternatives for resection of myogenic tumor.
Aims: This study aims to evaluate the effectiveness and safety of endoscopic dissection of gastric myogenic tumors.
Methods: The study was conducted between March 2018 and September 2023 at a tertiary-care referral center, Far Eastern Memorial Hospital, in Taiwan. We consecutively enrolled patients with endoscopic ultrasound (EUS)-documented myogenic tumor of stomach. The primary outcomes were technical success and en bloc rates. The secondary outcomes included R0 resection rate, procedure time, complications, rate of shifting to endoscopic full thickness resection (EFTR), hospital stay, tumor recurrence, and mortality rate.
Results: In total, 35 patients [20 (57.1%) leiomyoma, 14 (40.0%) GISTs and one (2.9%) lipoma] were enrolled, with 19 (54.3%) patients underwent EMD and 16 (45.7%) patients underwent ESSD. The technical success and en-bloc rates were 100%. R0 resection rate was 89% whereas mean tumor size and procedure time were 11.3mm and 47.0 minutes, respectively. Five (14.3%) ESSD were shifted to EFTR with final pathology report of GIST. The mean hospital stay was 6.1 days and none of the patient had recurrence during mean follow-up period of 463.7 days. Three (8.6%) patients had complication including intra-procedural perforation (Two patients) and delayed bleeding (One patient). One (2.9%) patient died 2 months after the procedure due to acute respiratory distress syndrome after additional gastrectomy with R1 resection by ESSD. Irregular border (71% vs 15%, $p = 0.001$), heterogenous echotexture (86% vs 20%, $p < 0.001$), exophytic growth (71% vs 35%, $p = 0.037$) under EUS and rate of shift to EFTR (36% vs 0%, $p = 0.016$) were statistically higher in GIST than leiomyoma.
Conclusions: Endoscopic resection techniques, including EMD and ESSD, appeared to be an efficient and safe method for removal of gastric myogenic tumors. Additionally, EUS features can predict the malignant potential of gastric myogenic tumors.

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探討 AI 在早期胃癌診斷之準確度 - 統合性分析
THE ACCURACY OF ARTIFICIAL INTELLIGENCE IN THE ENDOSCOPIC DIAGNOSIS OF EARLY GASTRIC CANCER: POOLED ANALYSIS STUDY

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Background: Artificial intelligence (AI) for gastric cancer diagnosis has been discussed in recent years. The role of AI in early gastric cancer is more important than in advanced gastric cancer since early gastric cancer is not easily identified in clinical practice. However, to our knowledge, past syntheses appear to have limited focus on the populations with early gastric cancer.
Aims: The purpose of this study is to evaluate the diagnostic accuracy of AI in the diagnosis of early gastric cancer from endoscopic images.
Methods: We conducted a systematic review from database inception to June 2020 of all studies assessing the performance of AI in the endoscopic diagnosis of early gastric cancer. Studies not concerning early gastric cancer were excluded. The outcome of interest was the diagnostic accuracy (comprising sensitivity, specificity, and accuracy) of AI systems. Study quality was assessed on the basis of the revised Quality Assessment of Diagnostic Accuracy Studies. Meta-analysis was primarily based on a bivariate mixed-effects model. A summary receiver operating curve and a hierarchical summary receiver operating curve were constructed, and the area under the curve was computed.
Results: We analyzed 12 retrospective case control studies (n=11,685) in which AI identified early gastric cancer from endoscopic images. The pooled sensitivity and specificity of AI for early gastric cancer diagnosis were 0.86 (95% CI 0.75-0.92) and 0.90 (95% CI 0.84-0.93), respectively. The area under the curve was 0.94. Sensitivity analysis of studies using support vector machines and narrow-band imaging demonstrated more consistent results.
Conclusions: For early gastric cancer, to our knowledge, this was the first synthesis study on the use of endoscopic images in AI in diagnosis. AI may support the diagnosis of early gastric cancer. However, the collocation of imaging techniques and optimal algorithms remain unclear. Competing models of AI for the diagnosis of early gastric cancer are worthy of future investigation.

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靶向 MRC2 以克服 IL-6 介導的基质化療抵抗性：一種嶄新的胃癌治療策略
TARGETING MRC2 TO OVERCOME IL-6-MEDIATED STROMAL RESISTANCE TO CHEMOTHERAPY IN GASTRIC CANCER: A PROMISING STRATEGY

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Background: Recent studies highlight the pivotal role of cancer-associated fibroblasts (CAFs) and the tumor microenvironment (TME) in the progression and treatment outcomes of gastric cancer (GC). Our research focuses on the mannose receptor C-type 2 (MRC2) in tumor-adjacent stroma, which correlates with poor prognosis in GC patients.
Aims: This study aims to explore the modulatory roles of MRC2 in CAFs, particularly in their secretion of soluble factors like interleukin-6 (IL-6), influencing the metastasis of GC, and their contribution to chemotherapeutic resistance.
Methods: High-throughput secretomic analyses were employed to assess the impact of altering MRC2 expression levels, via both overexpression and knockdown, in conditioned media from gastric CAFs. Additionally, the study examined the effect of MRC2-modulated CAF-derived conditioned media (CAF-CM) on the chemoresistance of GC cells.
Results: Our results revealed that the secretome of CAFs, when influenced by MRC2, exhibited notable changes, particularly in IL-6 secretion. CAFs overexpressing MRC2 secreted increased levels of IL-6, while MRC2 knockdown led to a reduction in IL-6 secretion. Conditioned media from MRC2-overexpressing CAFs markedly enhanced the migratory abilities of AGS gastric cancer cells, correlated with increased STAT3 phosphorylation and raised IC50 for 5-fluorouracil. Notably, the chemoresistance conferred by CAFs to GC cells was significantly mitigated by MRC2 knockdown, highlighting the role of MRC2 affecting through IL-6/gp130/STAT3 in CAF-mediated chemoresistance.
Conclusions: This study substantiates that MRC2 within CAFs plays a significant role in promoting malignancy

and chemoresistance in GC through the IL-6/gp130/STAT3 pathway. These insights propose that targeting MRC2 in CAFs represents a viable therapeutic approach to mitigate IL-6 mediated stromal resistance in GC. Future investigations will explore the feasibility of targeting MRC2 with antibody drug conjugates for GC treatment.

主題：C 型肝炎（二）

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C 型肝炎病毒治癒患者脂肪性肝病的盛行率及其對肝臟相關併發症的影響
THE PREVALENCE AND IMPACT OF STEATOTIC LIVER DISEASE ON THE LIVER-RELATED EVENTS IN PATIENTS CURED OF HEPATITIS C VIRUS

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Background: The new fatty liver nomenclature steatotic liver disease (SLD) was proposed in June 2023. The prevalence and impact of different subclass SLDs on liver-related events (LREs) in patients with chronic hepatitis C (CHC) and achieving a sustained virologic response (SVR) to direct-acting antiviral agents (DAAs) is unknown.
Aims: We analyzed the predictors of LREs, specifically focusing on components of different SLD, in patients with CHC who have achieved an SVR to DAA therapy.
Methods: 1185 patients with cured CHC with body mass index or lipid profile data were enrolled. The cardiometabolic criteria (CMC) and alcohol consumption were defined accordingly. Variables at 12 or 24 weeks after DAA therapy (PW12) were used to identify predictors of LREs.
Results: The median age of the 1185 patients was 57 (47–65) years. Of the participants, 557 (47.0%) were men, and the median BMI was 24.13 (21.87–26.83) kg/m^2. There were 562 (47.4%), 96 (8.1%), 14 (1.2%), 78 (6.6%), and 435 (36.7%) patients who had metabolic dysfunction-associated (MASLD), MetALD (MASLD and increased alcohol intake), alcohol-related liver disease (ALD), specific-etiology or cryptogenic SLD, and no SLD, respectively. The multivariable Cox regression analysis indicated that age, alcohol consumption, per CMC (hazard ratio 1.307, 95% confidence interval: 1.070–1.596, P = 0.009), post-therapeutic albumin, alpha-fetoprotein, and fibrosis-4 were independent predictors of LREs. Kaplan–Meier analysis showed that patients with 3–5 CMCs had a higher cumulative incidence of LRE than those with 0–2 CMCs.
Conclusions: The new fatty liver nomenclature SLD could stratify CHC patients with viral eradication by DAA therapy. The risk of LREs increased by about 30% per CMC in this group of patients.

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病毒根除降低慢性 C 型肝炎患者新生肝硬化及肝臟相關併發症的發生率

VIRAL ERADICATION DECREASES THE INCIDENCES OF NEW-ONSET LIVER CIRRHOSIS AND MAJOR LIVER-RELATED EVENTS IN PATIENTS WITH CHRONIC HEPATITIS C

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Background: The risk of hepatocellular carcinoma (HCC) development in patients with chronic hepatitis C (CHC) and liver cirrhosis (LC) is around 2–7% per year. Patients with liver decompensation (DLC), including esophageal or gastric variceal bleeding, hepatic encephalopathy, and ascites, have shorter survival than those with compensated cirrhosis. Previous large-scale clinical studies have revealed that successful treatment with pegylated interferon and ribavirin (PR) may halt and reverse hepatic fibrosis in patients with CHC. The achievement of sustained virological response (SVR) with PR therapy in patients with CHC is associated with reduced liver-related mortality. Direct-acting antiviral agents (DAAs) have been the standard of care for CHC. However, large-scale real-world evidence for the efficacy of PR and DAA therapy is still limited.

Aims: We aimed to validate the effect of viral eradication on clinical outcomes in patients with CHC through this nationwide cohort study.

Methods: The Taiwanese chronic hepatitis C cohort (T-COACH) and Taiwan hepatitis C virus (HCV) registry (TACR) are prospective, observational nationwide collaborative HCV registry cohorts involving 23 and 53 primary clinics, regional hospitals, and medical centers in Taiwan, respectively. Overall, 34,027 patients with CHC who had received PR (n = 13,699) or DAA therapy (n = 20,327) for at least four weeks from January 2004 to December 2019 were enrolled. Continuous and categorical variables are reported as mean ± standard deviation and numbers (percentage). We considered death as a competing event. We modified the Kaplan–Meier method according to Fine-Gray's cumulative incidence method. We compared the incidence of new-onset LC or HCC in noncirrhotic patients and the incidence of DLC or HCC in cirrhotic patients between patients with and without SVR. Subdistribution hazard models were used to estimate the hazard ratio (HR) and 95% confidence interval (CI) to examine the independent factors associated with the significant outcomes.

Results: Of the 27,577 patients, 25,461(92.3%) patients achieved SVR, and the mean age was 58.9 ± 12.4 years. The mean follow-up duration was 51.19 ± 48.41 months with overall 118,567 person-years. In multivariable Cox proportional hazards models, the HR for incident HCC

was 1.39 (95% CI: 1.00–1.95, $P = 0.052$) among baseline noncirrhotic patients without SVR compared to those with SVR, and the HR was 1.82 (95% CI: 1.34–2.48, $P < 0.001$) among baseline cirrhotic patients without SVR compared to those with SVR after adjustment for competing mortality. The HR for liver-related events, including HCC and DLC, was 1.70 (95% CI: 1.30–2.24, $P < 0.001$) among baseline cirrhotic patients without SVR compared to those with SVR after adjustment for competing mortality. Patients with SVR had a significantly lower 10-year cumulative incidence of new-onset HCC than those without SVR in patients with or without baseline LC ($P < 0.001$) using the modified Kaplan-Meier method after adjustment for competing mortality.

Conclusions: HCV eradication with PR or DAA therapy decreased the incidence of HCC in patients with and without LC and the incidence of liver-related events in patients with LC.

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高風險患者經成功抗病毒治療後 HCV 再次感染率 - 來自醫療中心的經驗

HCV REINFECTION OF HIGH-RISK PATIENTS AFTER SUCCESSFUL DIRECT-ACTING ANTIVIRAL THERAPY – REAL-WORLD DATA FROM A MEDICAL CENTER

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Background: The curate rate of direct-acting antiviral therapy for HCV is very high. However, the reinfection of HCV in high-risk patients, such as people living with HIV (PLWH), people who use injection drugs (PWID) and hemodialysis, remain an important issue after achieving sustained virologic response (SVR).

Aims: We presented a real-world data from a medical center about reinfection rate in these high-risk patients.

Methods: The retrospective study included three high-risk groups of HCV patients who achieved SVR12 after DAA therapy between Jan 2018 and Jun 2022. The HCV RNA was rechecked ≥1 subsequent after SVR12 and the reinfection was defined as recurrent detected viremia after SVR12.

Results: We recruited 146 HCV patients including PLWH from sexual transmission (n=22), PLWH combined PWID (n=51), PWID (n=42) and hemodialysis (n=31). The median time to reinfection was 2.4 years. The reinfection rate of 13.6%, 11.8%, 14.3% and 0% in group of PLWH from sexual transmission, PLWH combined PWID, PWID and hemodialysis. The incidence of reinfection was 6.1 per 100 person-years of follow-up (PYFU), 5.3 per 100 PYFU, 6.1 per 100 PYFU and 0 per 100 PYFU of each group. There was no statistically significant difference between the reinfection among the three groups (PLWH from sexual transmission, PLWH combined PWID and PWID)

Conclusions: The reinfection rate remains high in PLWH and PWID groups. Effective HIV prevention programs and syringe services programs are still needed in such high risk populations.

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最終的抗病毒治療反應及肝臟儲備功能對於慢性 C 型肝炎肝硬化病患在接受長效型干擾素合併雷巴威林治療後長期肝臟疾病進展發生率之影響

IMPACT OF ULTIMATE ANTIVIRAL RESPONSE AND FUNCTIONAL LIVER RESERVE ON THE LONG-TERM INCIDENCE OF LIVER DISEASE PROGRESSION FOR CHRONIC HEPATITIS C PATIENTS WITH LIVER CIRRHOSIS AFTER TREATMENT BY PEGYLATED INTERFERON PLUS RIBAVIRIN

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Background: Chronic hepatitis C virus (HCV) infection is one of the leading causes of liver cirrhosis, hepatic decompensation, hepatocellular carcinoma (HCC), and liver transplantation candidacies. It has been estimated that liver cirrhosis developed approximately 10%–20% of patients over 20–30 years after HCV infection with a 3%–6% annual risk of hepatic decompensation and a 1%–5% annual risk of HCC. Successful antiviral treatment response brings huge beneficial effect on long-term outcome for patients with chronic hepatitis C (CHC). However, the risk of hepatic decompensation and future development of HCC are not entirely eradicated after cure of HCV infection, especially for patients with advanced liver disease.

Aims: To investigate the impact of ultimate antiviral response and functional liver reserve, reflected by albumin-bilirubin (ALBI) grade, on the long-term incidence of disease progression for CHC patients with liver cirrhosis after treating with Peg-IFN plus ribavirin (RBV) with or without SVR.

Methods: Between January 2011 to June 2018, a total of 79 consecutive CHC patients with compensated liver cirrhosis who treated with Peg-IFN plus RBV by the investigators were enrolled. History of HCC before the initiation of Peg-IFN, prior liver transplantation and early terminate antiviral therapy with short follow-up period (< 1 year) were excluded. For patients who failed to Peg-IFN plus RBV, all oral direct-acting antivirals (DAAs) were provided for rescue therapy and treatment responses were recorded. The primary end point analyzed was the cumulative incidence of disease progression after Peg-IFN initiation, defined as the occurrence of any of the following: (1) liver decompensation events (ascites, variceal hemorrhage, hepatic encephalopathy, or jaundice), (2) de novo HCC, (3) need for liver transplantation, or (4) death. The date of the first event was determined for cumulative failure curves. Death was categorized further as liver-related and non–liver-related. The cumulative incidence of liver disease progression was measured by Kaplan-Meier statistical method and compared by log rank test.

Results: Mean age of enrolled patients starting Peg-IFN was 59.8 ± 9.3 years, 60.8% of them was female, and mean pre-treatment HCV RNA was 5.98 ± 0.91 log10 IU/mL. After therapy with Peg-IFN plus RBV, 50.6% of them achieved SVR. The median follow-up period post first dose Peg-IFN was 109 months (mean value: 98.3 ± 32.5, range: 16 to 143 months). 32 of 39 (82.1%) patients who failed Peg-IFN plus RBV received all oral DAAs as rescue therapy, the median time from Peg-IFN failure to DAAs initiation was 37.5 months (range: 4-70), and 31 of them (96.9%) achieve SVR. A total of 39 (49.4%) patients developed liver disease progression during study period and de novo HCC is the most common event of liver disease progression. For cirrhotic patients achieved SVR by Peg-IFN + RBV or DAAs (n=71), incidence to have liver disease progression at 1, 3, 5, 8, and 11 years was 7.0%, 17.1%, 24.8%, 41.1% and 56.8%, respectively. For cirrhotic patients without ultimate SVR (n=8), the incidence to have liver disease progression at 1, 3 and 5 years was 37.5%, 66.7% and 100%, respectively (P <0.001). The ALBI grade measured at 24 weeks post Peg-IFN closely associated with the probability of liver disease progression. The cumulative incidence of liver disease progression for ALBI grade 1 or 2/3 at 2, 5, 8, and 11 years was 7.3% vs 23.8%, 15.2% vs 50.2%, 32.1% vs 62.4%, and 51.6% vs 72.1%, respectively (P =004).

Conclusions: For CHC patients with liver cirrhosis, despite viral clearance by either Peg-IFN or DAAs, the long-term risk to develop liver disease progression still existed. Ultimate antiviral response and functional liver reserve closely associated with the long-term incidence of disease progression. Continuing surveillance of HCC and other liver-related events should be arranged for patients with advanced liver disease after antiviral therapy.

主題：膽胰疾病（二）

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AKT1 透過促進感染性病毒顆粒由內質網轉移到胞內體參與 C 型肝炎病毒的釋放
AKT1 IS INVOLVED IN HCV RELEASE BY PROMOTING ENDOPLASMIC RETICULUM-TO-ENDOSOME TRANSITION OF INFECTIOUS VIRIONS

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Background: Hepatitis C virus (HCV) relies on the viral and host factors to complete its life cycle. It has evolved to profit from Akt activation at some stage in its life cycle through various mechanisms, notably by activating lipogenesis, which is crucial for infectious virions production.
Aims: To elucidate the role of Akt activation in the life cycle of HCV.
Methods: By employing an Akt-specific inhibitor, the impact of Akt on intracellular and extracellular infectivity was investigated. To ascertain the role of Akt in the HCV life cycle, the two-part cell culture-derived HCV infection protocol utilizing Akt1 small interfering RNAs (siRNAs) was implemented. The impact of Akt1 on intracellular HCV transition was determined using membrane flotation assay and proximity ligation assay coupled with Anti-Rab7 immunoprecipitation and immunofluorescence.
Results: Akt1 silencing reduced infectious virions release to a degree comparable to that of ApoE, a host component involved in the HCV assembly and release, suggesting Akt1 was critical in the late stage of the HCV life cycle. Extracellular infectivity of HCV was inhibited by brefeldin A, and the inhibitory effect was augmented by Akt1 silencing and partially restored by ectopic Akt1 expression. Immunofluorescence revealed that Akt1 inhibition suppressed the interaction between HCV core protein and lipid droplet. Akt1 silencing impeded the transition of HCV from the endoplasmic reticulum to the endosome and hence inhibited the secretion of HCV infectious virions from the late endosome.
Conclusions: Our study demonstrates that Akt1 has an impact on the lipogenesis pathway and plays a critical role in the assembly and secretion of infectious HCV.

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電腦輔助內視鏡逆行性胰膽管攝影定位壺腹乳頭和估計總膽管方向
COMPUTER-AIDED AMPULLA OF VATER LOCALIZATION AND ESTIMATION OF COMMON BILE DUCT DIRECTION FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Background: The identification of the ampulla of Vater and the direction of the bile duct during endoscopic retrograde cholangiopancreatography (ERCP) is a challenging procedure in gastroenterology and hepatology. Failure to accurately identify the direction of the bile duct can result in treatment failure and fatal complications. However, anatomical variations in the ampulla of Vater can make it difficult to accurately locate it, leading to significant delays in ERCP. In fact, if the delay exceeds 5 minutes, more than 5 cannulation attempts, or more than 2 pancreatic guidewire passages, it will result in ERCP failure.
Aims: In this study, we aim to develop a computer-assisted system for locating the ampulla of Vater and estimating the direction of the bile duct during ERCP procedures.
Methods: To address this issue, we collected 22 ERCP videos from patients treated at Shin Kong Wu Ho-Su Memorial Hospital in Taiwan between 2021 and 2022. We proposed a computer-assisted system that processed and learned the data from each frame of the videos. Using the transfer learning technique on the pre-trained EfficentNetB0 model, we classified whether the ampulla of Vater was included in every endoscopic image. Then we used the YOLOv4 object detection model to locate the ampulla of Vater. Finally, we estimated the direction of the bile duct using image processing techniques.
Results: At the first stage, the system detects the existence of the ampulla of Vater with an accuracy of 92.16%. Up to the second stage, the system locates the ampulla of Vater with an AP of 42.02% and an AP50 of 86.58%. Overall, the system estimates the direction of the bile duct with a mean angle error (MAE) of 22.77º and a mean angle error rate (MAER) of 12.65%.
Conclusions: We established the computer-assisted system for locating the ampulla of Vater and estimating the direction of the bile duct during ERCP procedures. This system can assist physicians in shortening the examination time and effectively reducing the complications caused by the inspection.

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內視鏡超音波導引細針切片與經皮超音波導引粗針切片在診斷胰臟病變的比較
COMPARISON OF ENDOSCOPIC-GUIDED FINE NEEDLE BIOPSY VERSUS ULTRASOUND-GUIDED CORE NEEDLE BIOPSY FOR THE EVALUATION OF PANCREATIC LESIONS

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Background: Pancreatic cancer stands out as one of the lowest 5-year survival rates among all cancer types. Therefore, pathological diagnosis through tissue biopsy is crucial for patients who cannot undergo surgery or need to rule out malignancy. The primary modalities guiding pancreatic biopsy include percutaneous ultrasound (US) and endoscopic ultrasound (EUS). Nevertheless, the existing data for assessing the diagnostic accuracy and complication rates of percutaneous ultrasound core needle biopsy (US-CNB) in comparison to endoscopic ultrasound fine needle biopsy (EUS-FNB) for pancreatic lesions is limited.

Aims: In this study, we aimed to evaluate the diagnostic accuracy and immediate complication rates between EUS-FNB and US-CNB in pancreatic lesions.

Methods: From January 2013 to October 2023, we conducted a retrospective analysis of 256 cases involving the use of US-CNB or EUS-FNB for pancreatic lesions at Changhua Christian Hospital. Patients were included if they underwent EUS-FNB or US-CNB due to pancreatic lesion noted on an abdominal ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) and suspicious of malignancy. Exclusions were applied for cases with incomplete information (n = 32). For US-FNB, biopsy needles ranging in size from 18 to 21-gauge were utilized under real-time echoguidance. EUS-FNB procedures utilized the Olympus EU-ME1 with the GF-UCT260 scope, employing the Boston Acquire FNB needle, with needle sizes ranging from 21 to 25-gauge. The final diagnosis was established based on biopsy, surgical pathology, or metastasis pathology of other sites, clinical course, and follow-up images.

Results: A total of 235 biopsy attempts were undertaken in 224 patients (EUS-guided FNA, n = 178; US-guided CNB, n = 57). Six patients from the EUS group and three from the US group underwent repeat biopsies due to concerns about pathological diagnosis. One patient had two pancreatic masses and underwent three separate EUS-FNB during the same examination. There were no significant differences in age, sex, tumor location, BMI or repeat biopsy between the two groups. However, significant differences were observed in pathologic diagnosis ($p = 0.006$), tumor size ($p < 0.001$), tumor size smaller than 3 centimeter(cm) ($p = 0.011$) and needle size ($P < 0.001$). In terms of diagnostic performance of malignancy, EUS-FNB showed 92.8% sensitivity and 100% specificity, with an overall accuracy of 94.4%. Meanwhile, US-CNB had a sensitivity of 89.3%, specificity of 100%, and an accuracy of 91.2%. Area under the receiver operating characteristic (ROC) curve shows no significant difference ($p = 0.560$) between the two groups. There was no immediate complication noted after both procedures.

Conclusions: For pancreatic tumors, there is no significant difference in diagnostic accuracy of malignancy between EUS-FNB and US-CNB, and both methods are acknowledged to be safe. However, smaller tumors may lead doctors to choose EUS for biopsy. In settings where EUS is unavailable, US-CNB stands as a viable alternative for biopsy.

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超音波內視鏡引導乙醇消融術之於小型胰臟神經內分泌腫瘤：系列報告
ENDOSCOPIC ULTRASOUND-GUIDED ETHANOL ABLATION FOR SMALL PANCREATIC NEUROENDOCRINE TUMOR: A CASE SERIES

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Background: Pancreatic neuroendocrine tumor (pNET) can be categorized into functional pancreatic neuroendocrine tumor (F-pNET) and non-functional pancreatic neuroendocrine tumor(NF-pNET). According to the European Neuroendocrine Tumor Society Consensus Guidelines of non-functional pNET, surgery was suggested if tumor size was larger than 2 cm. However, pNET has been found in small size recently due to advanced diagnostic image tool. Surgical intervention for the incidental discovery of small, mainly < 2cm, non-functional pNET was challenging because the resection of pNETs may lead to relatively high mortality and morbidity. Therefore, Endoscopic ultrasound(EUS)-guided tumor ablation is emerging as a new treatment modality of small pNET. However, due to the rarity of the disease, the experience of EUS- guided tumor ablation in Taiwan remained limited.

Aims: We will evaluate the safety and efficacy of EUS-guided ethanol ablation in patients with non-functional and functional pNET in Changhua Christian hospital experience.

Methods: We totally enrolled 9 patients between June 2018 and August 2023 who have definite diagnosis of neuroendocrine tumor by EUS-FNA or EUS-FNB. Besides, all tumor size was less than 2 cm and the patients refused surgery. Prophylactic antibiotics with cefazolin was used before tumor ablation. As for the endoscopic alcohol ablation technique, we use 22G or 25G FNA needles(Expect®) with priming by the 99.5% alcohol. We inject alcohol using 1 ml syringe to control the volume more precisely, and injected the agent until the hyperechoic blush extended to the margin of the tumor. And, we repeat EUS-guided alcohol ablation one or more session until no viable tumor was visualized on CT/MRI image. If no viable tumor was visualized on CT/MRI image, Contrast-enhanced endoscopic ultrasound (Sonazoid®) was used for further confirmation.

Results: We enrolled 9 patients (4 males, mean age 63.1 years) who had a total of 10 pNETs with a mean size of 13.02 mm (range 10 – 18mm) localized in the pancreatic head (2 lesions), pancreatic body (5 lesions), and tail (3 lesions), respectively. Only one patient had symptoms of insulinoma (cold sweating, generalized weakness, and tremor) and others were diagnosed with pNET incidentally. The procedure was technically successful in all patients. The mean amount of alcohol injection is 1.18 ml(range 0.6 – 2 ml). Complete remission was confirmed in seven of them in the follow-up CT or MRI (Complete ablation rate: 80%) in first injection session. After the second injection session, complete remission was confirmed in one of the two patients. However, the other patient lose follow up after the second session of EUS-guided alcohol ablation and the residual tumor was identified on the first follow-up imaging. As for the following CT/ MRI timing, two of the patients had residual tumor on the follow-up CT scan which was performed at two weeks post EUS-guided alcohol ablation in our study. However, no residual tumor was identified on the second time follow-up imaging. No any adverse events were observed in all of the patients.

Conclusions: EUS-guided ethanol ablation is convenient and effective in the treatment toward pNET which was smaller than 2cm.

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導管內乳頭狀黏液性腫瘤的增大有著更高機率胰臟外惡性腫瘤的發生 --- 一篇追蹤十年的回溯性病例對照研究

THE ENLARGING SIZE OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM (IPMN) MAY BE ASSOCIATED WITH HIGHER RISK OF EXTRA-PANCREATIC MALIGNANCY OCCURRING---A TEN YEAR FOLLOW-UP RETROSPECTIVE CASE CONTROL STUDY

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Background: Although there is a higher incidence of extra-pancreatic malignancies in patients with IPMNs than in the general population that have been proved in several studies, some recent studies told that the rate of metachronous extra-pancreatic malignancies is not superior to the general population. Additional malignancies that most occur before or concurrent IPMN diagnosed have been identified in 10%-52% of patients with IPMNs in previous studies but we found most of these studies followed patients less than five years. Previous reported factor for developing secondary malignancy is not clearly identified, only older age had been demonstrated.

Aims: 1. We want to recognize the rate of extra-pancreatic malignancy occurrence after IPMN diagnosed when longer duration of following up. 2. We want to investigate the risk factor of extra-pancreatic malignancy in IPMN patients then we can have regular screening for these population.

Methods: We retrospectively collected 196 patients with IPMN diagnosed by Magnetic Resonance Imaging (MRI) from 2010/1/1 to 2014/12/31 in Chang Gung Memorial Hospital and finally 114 patients were analyzed after excluding who had following up time less than 1 year and the pathology revealed other than IPMN. The characteristics of patients including age, gender, type of IPMN, location, cyst number and size, lab data and following up duration were all recorded. Different extra-pancreatic malignancy is demonstrated as before, concurrent or after IPMN diagnosed. The risk factors were compared between patients with or without extra-pancreatic malignancy.

Results: Total 114 patients with IPMN were analyzed with average 10.5 years following up. 46 Extra-pancreatic malignancy occurred in 42 patient (36.8%) and in which most found after IPMN diagnosed (N=26, 55.3%). The most common extra-pancreatic malignancy is lung cancer (N=8, 30.8%) followed by hepatocellular carcinoma (N=5, 19.2%). The multivariate regression test revealed that the rate of cyst progression (cm/year) is a risk factor for predictive of extra-pancreatic malignancy (p=0.038, OR=31.529, 95%CI=1.203-826.635) and the AUROC curve showed that the area under curve is 0.882.

Conclusions: Extra-pancreatic malignancy is also found after IPMN diagnosed when we prolong the following duration up to 10 years and the most of these is lung cancer. We found that the progressed size of cyst seems highly associated with the extra-pancreatic malignancy occurring.

⑨⓪

胰臟癌病患發生間質性肺炎後再挑戰藥物治療可以有更好的預後
TREATMENT RECHALLENGE IS SAFE AND LEADS TO A BETTER SURVIVAL IN PANCREATIC CANCER PATIENTS WITH INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a potentially fatal complication of cancer-related therapy. However, data regarding the possible etiologies, risk factors, and prognosis of ILD as well as the safety and benefit of treatment rechallenge following ILD recovery are scarce.
Aims: To evaluate the possible etiology, risk factors, prognosis, the safety and benefit of treatment rechallenge.
Methods: Patient diagnosed with pancreatic cancer were retrospectively enrolled and those with ILD were identified. We investigated the incidence and etiology of ILD, associations with potential risk factors, and the impact of treatment rechallenge on clinical outcomes and survival.
Results: A total of 809 patients were diagnosed with pancreatic cancer, 62 of whom (7.7%) had ILD. The incidence of ILD was higher in patients who received nab-paclitaxel therapy (odds ratio [OR]: 1.84, P = 0.04) and those with previous lung diseases, including ILD, asthma, chronic obstructive pulmonary disease, tuberculosis, primary lung cancer, metastasis or pneumonia (OR: 2.02, P = 0.03). Infection was the most common etiology (45.2%). After rechallenge therapy in 33 patients, ILD recurred in 3 (9%), with pathogens identified as the cause of recurrence in 2 patients. The median overall survival was longer in patients with ILD than in others (11.3 vs. 8.3 months, P < 0.001). Competing risk analysis revealed that nab-paclitaxel, gemcitabine, and erlotinib were independent risk factors for developing ILD.
Conclusions: Most cases of ILD were related to but not directly induced by cancer therapy. Self-protection from possible infection was recommended. Furthermore, treatment rechallenge after an ILD episode during pancreatic cancer therapy is a reasonable approach, because ILD recurrence was uncommon and treatment options are limited.

壁報展示
第一部分：肝

P.001

TENOFOVIR DISOPROXIL FUMARATE 與 ENTECAVIR 對 B 型肝炎患者食道靜脈曲張新生發展的療效比較
EFFICACY OF TENOFOVIR DISOPROXIL FUMARATE VERSUS ENTECAVIR ON DE NOVO DEVELOPMENT OF ESOPHAGEAL VARICES IN PATIENTS WITH HEPATITIS B

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Background: The comparative risk of de novo development of esophageal varices (EV) in patients with hepatitis B virus infection receiving tenofovir disoproxil fumarate (TDF) vs. entecavir (ETV) remains unclear.
Aims: To assess the association between ETV / TDF and occurrence/progression of EV.
Methods: In this retrospective cohort study conducted during 2007–2020, 600 patients were enrolled from the Chang Gung Medical System (488 and 112 in the ETV and TDF groups, respectively). The primary end point was the de novo development of EV defined by esophagogastroduodenoscopy (EGD). The inverse probability of treatment weighting (IPTW) with the propensity score was used to evaluate the association between ETV / TDF and EV occurrence/progression.
Results: Over a mean follow-up period of 35 (standard deviation: 25) months, the 6-year incidence of de novo EV occurrence was 31.3% and 10.2% in the ETV and TDF groups, respectively. Meanwhile, the 6-year progression rate of de novo EV was 35.3% and 22.4% in the ETV and TDF groups, respectively. Compared with the ETV group, the TDF group exhibited a significantly lower incidence of EV occurrence (adjusted hazard ratio [aHR]: 0.30, p = 0.007) and a significantly lower EV progression rate (aHR: 0.55, p = 0.032). Moreover, significant correlations were found between the risk of EV occurrence/progression and thrombocytopenia, liver cirrhosis, and history of hepatocellular carcinoma or cholangiocarcinoma ($p < 0.05$).
Conclusions: To the best of our knowledge, this is the first study to provide evidence on the association of TDF treatment with a decreased risk of de novo EV occurrence and progression compared with ETV treatment in a real-world context.

P.002

屏東地區以核苷酸類似物貝樂克惠立妥治療慢性 B 型肝炎相關性肝硬化其肝癌發生七年風險之比較

SEVEN-YEAR COMPARISON OF ENTECAVIR AND TENOFOVIR ON THE RISK OF HEPATOCECULLAR CARCINOMA IN PATIENTS WITH CHRONIC HEPATITIS B RELATED CIRRHOSIS IN PING-TUNG COUNTY

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Background: Chronic hepatitis B (CHB) infection is currently incurable. Nucleus(t)ide analogue (NUC) treatment with entecavir (ETV) or tenofovir disoproxil fumarate (TDF) is effective to reduce hepatic inflammation, risk of disease progression to cirrhosis, decompensation and hepatocecullar carcinoma (HCC). However, TDF treatment was more effective in lowering risk of HCC compared with ETV treatment in Korean nationwide cohort of CHB patients. Whether there is a difference between these two agents in reducing a risk of HCC in patients with cirrhosis has not been clarified in Ping-Tung County.

Aims: We aimed to compare the long term efficacy of ETV and TDF in prevention of disease progression to HCC among high risk patients with CHB related cirrhosis.

Methods: Between Jan 2014 and Jul 2022, 78 treatment naïve patients with CHB related cirrhosis on ETV or TDF in Ping-Tung County were evaluated. The treatment and follow-up period for each patient was calculated as 4.86±3.05 years and 8.15± 4.67 years. All patients who met eligibility criteria at baseline were included in the analysis. Seven years cumulative incidence was assessed using Kaplan-Meier methods and Cox proportional hazard models.

Results: Total 42 and 36 patients received ETV and TDF, respectively. The cumulative risk of HCC at 1, 3, 5 and 7 years was 3.8%, 11.5%, 14.1% and 16.7% in the ETV group, respectively; and 6.4%, 9.0%, 11.5% and 11.5%, in TDF group, respectively. TDF resulted in risk of HCC development compared to ETV with hazard ratios of 0.811 (95% CI 0.480-1.373, P=0.436).

Conclusions: Although TDF treatment showed a lower rate of HCC development, it did not reach statistical significance compared with ETV treatment. This study has demonstrated the clinical outcomes in patients with CHB related cirrhosis who received ETV or TDF treatment has no difference in the risk of HCC between those two drugs. Treatment with ETV or TDF showed a comparable long-term risk of HCC in CHB related cirrhosis.

P.003

TENOFOVIR ALAFENAMIDE 在 HBV 病人中可誘導干擾素表現進而減少 CD8+ T 細胞對肝細胞的傷害並促進病人血清轉換率
TENOFOVIR ALAFENAMIDE REDUCES CD8+ T CELLS-MEDIATED LIVER DAMAGE AND ENHANCES SEROCONVERSION RATES THROUGH INDUCING INTERFERONS EXPRESSION IN PATIENTS WITH CHRONIC HEPATITIS B

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Background: Chronic hepatitis B (CHB) leads to liver inflammation and dysfunctions, resulting in liver fibrosis and cancer. Tenofovir alafenamide (TAF), an inhibitor of CHB virus, specifically suppresses reverse transcription to diminish HBV replication. Literature has revealed an observation of seroconversion by changing HBsAg to HBsAb in the 1-2% CHB patients. However, the mechanism of seroconversion is unclear.

Aims: In this study, we hypothesize and demonstrate that TAF not only suppresses HBV, but also trigger hepatocytes to activate immune cells to enhance seroconversion.

Methods: Healthy volunteers and CHB patients treated with TAF were enrolled in this study. AST and ALT as liver function markers and HBsAg and HBsAb as seroconversion markers were measured and recorded in the clinical routine. The AST and ALT levels correlated with T cell ratio (CD4/CD8) and markers, including CD69, CD107a, CD183 (CXCR3), and CD279 (PD-1) were investigated by using flow cytometry. Meanwhile, IFNγ, IL-2, and CXCL10 in the PBMCs as immune activation markers detected by qPCR were compared between healthy volunteers and CHB patients. To mimic TAF-treated hepatocytes effect, HepG2 and HBV-infected PLC5 were treated with TAF, and the supernatant was collected and incubated with healthy PBMCs. The immune activation markers were consequently investigated by qPCR and flow cytometry.

Results: We found that TAF significantly suppressed AST and ALT levels and enhanced seroconversion rate (6%) compared to the literature report (1.15%). AST and ALT were positively correlated with CD107a in CD4+ T ($R = 0.2786$, $p = 0.0116$) and CD8+ T cells ($R = 0.3533$, $p = 0.0035$). TAF significantly increased PD-L1 in non-HBV HepG2 cells. The CHB patients with seroconversion exhibited higher CD4/CD8 ratio and IFNγ levels compared to healthy volunteers. In addition, TAF specifically triggered HepG2 and PLC5 to express IFNα and IFNγ, which increased PD-L1 expression in HepG2 and IFNγ and CXCL10 in PBMCs, particularly resulting in activation of CD4+ T cells.

Conclusions: This study revealed a potential mechanism that TAF not only suppressed HBV replication but also triggered hepatocytes to activate immune cells. TAF induced IFN expression in hepatocytes, resulting in PD-L1 expression to potentially protect CD8+ T cells-mediated liver damage. In addition, IFNs activate immune cells, particularly inducing CXCL10 to activate CD4+ T cells for seroconversion.

P.004

C 型肝炎盛行地區的 B 型肝炎感染狀態
HEPATITIS B INFECTION STATUS IN HCV-ENDEMIC AREAS

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Background: Hospital-based studies revealed the interaction between HBV and HCV, suggesting the newcomer may suppress existing viruses. However, the studies at community level are limited. HBcrAg reflects intrahepatic ccc DNA level and has been proved to be surrogate marker for chronic HBV monitor. It is uncertain whether HBcrAg could be helpful to detect HBsAg undetectable HBV carriers.

Aims: To elucidate the interaction between hepatitis B and C viruses in the community level, and to understand the availability of HBcrAg in detection of occult HBV infection.

Methods: Quantitative HBsAg (qHBsAg) and anti-HCV reflex HCV Ag were employed in a community-based study, from Oct 2018 to Dec 2019, in Lioujiao and Yijhu, townships with the highest prevalence rate of HCV infection in Chiayi county. Using available store serum of HBsAg-negative subjects, anti-HBs and anti-HBc were tested. HBcrAg was tested in subjects who were anti-HBs-negative and anti-HBc-positive. HBV DNA was measured in HBcrAg-positive sample.

Results: The prevalence of HBsAg was 12.8% and anti-HCV was 11.7% in the whole study(n=2000). The prevalence rates of HBsAg were 8.1%, 16.9%, 12.0% and 7.3% in subjects aged <40, 40~59, 60~79 and ≥ 80 years, respectively. Those of anti-HCV (+) were 5.6%, 8.9%, 15.0% and 24.8%, respectively. HBsAg carrier rate was 3.7% in subjects born after Hepatitis B vaccination policy in 1986. Neither Hepatitis B carrier status (HBsAg(+)) nor infected status (HBsAg(+) or anti-HBc(+)) was found with the subjects with positive anti-HCV or HCV Ag. Only 6 (6.7%) out of 89 subjects of anti-HBc positive alone were HBcrAg-positive. HBV DNA can be detected but low titer (<30 IU/ml) in 3 (50%) of them.

Conclusions: In this community-based study in two rural HCV-endemic townships showed that (1) HBsAg carrier rate were 12.8%, (2) HBsAg carrier rate were 3.7% in Hepatitis B vaccinated age, (3) hepatitis C infection was not correlated with hepatitis B carrier or infection status, and (4) HBcrAg was with limited utility in re-evaluation of HBsAg carrier rate. Further community-based studies and interventions for controlling sequelae of chronic hepatitis B infection would be conducted in the future.

P.005

煙氯奎寧降低 B 型肝炎患者罹患肝細胞癌之風險：回溯性研究
HYDROXYCHLOROQUINE REDUCED THE RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HEPATITIS B VIRUS INFECTION: A RETROSPECTIVE COHORT STUDY

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Background: Chronic hepatitis B virus (HBV) infection is one of the leading causes of hepatocellular carcinoma (HCC) worldwide. Hydroxychloroquine (HCQ) is a medication used to treat autoimmune disorders and recent studies have suggested that it may also have anti-cancer properties based on autophagy and non-autophagy mechanisms.
Aims: This study investigates the correlation between HCQ use and the risk of hepatocellular carcinoma in patients with chronic HBV infection.
Methods: HBV infected patients were enrolled from Taiwan's National Health Insurance Research Database (covering January 1, 2006, to December 31, 2016). The association between HCQ use and HCC risk was evaluated using the Kaplan-Meier method and Cox proportional hazards regression.
Results: 434,690 HBV patients were enrolled and individual matching with 1:10. Among 3,871 patients using HCQ (defined as ≥ 28 cumulative defined daily doses [cDDDs]), 39 developed HCC. Comparatively, among 38710 patients not using HCQ (≤ 28 cDDDs), 795 were diagnosed with HCC. HCQ use by HBV patients showed a significantly reduced HCC risk with an adjusted hazard ratio (aHR) of 0.47 (95% CI, 0.32~0.69). Furthermore, no observable dose-response relationship between HCQ use and HCC risk. Additionally, using of concurrent medications like H1-antihistamines (aHR: 0.62[CI 0.50~0.77]) and statins (aHR: 0.51[0.42~0.61]) was associated with a lower risk of HCC.
Conclusions: HCQ use appears to lower the risk of HCC among patients with HBV infection, suggesting potential benefits in preventing HCC in this population. Further research is necessary to confirm these findings and underlying mechanisms.

P.006

乙型肝炎病毒相關冷凝球蛋白血症
CHRONIC HEPATITIS B VIRUS INFECTION-RELATED MIXED CRYOGLOBULINEMIA

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Background: In addition to hepatic events including liver cirrhosis and hepatocellular carcinoma, chronic hepatitis B virus (HBV) infection may lead to extrahepatic manifestations such as mixed cryoglobulinemia.
Aims: The prevalence rate and associated factors of mixed cryoglobilinemia remain elusive in Taiwan. We aimed to investigate them.
Methods: An 8-year prospective cohort study of 721 patients with chronic HBV infection was conducted in a Taiwan tertiary referral center. Baseline factors including sex, age, mixed cryoglobulinemia, liver cirrhosis, fatty liver, alpha-fetoprotein, liver biochemistry, hepatitis B e antigen and antibody, estimated glomerular filtration rate, homeostasis model assessment-insulin resistance index, lipid profile, rheumatoid factor (RF), immunoglobulin M (IgM), IgG, complement components (C3) and C4, were investigated. The diagnosis of mixed cryoglobulinemia was based on the presence of serum mixed cryoglobulins in > 2 determinations over ≥12-week intervals.
Results: Of 721 chronic HBV-infected patients, 191(26.4%) patients had mixed cryoglobulinemia. Compared with patients without mixed cryoglobulinemia, patients with mixed cryoglobulinemia were more frequently female (53.4 vs. 43.6%, p=0.028), had higher levels of alanine transaminase (45.52+/-90.77 vs. 37.88+/-47.21 U/L, p=0.009), RF (69.77+/-193.3 vs. 18.47+/-45.71IU/mL, p<0.001) and IgM (132.5+/-63.21 vs. 86.07+/-46.41 mg/dL, p<0.001) but lower rates of fatty liver (53.4 vs. 59.8% , p=0.028). The multivariable analysis confirmed that RF (95% CI OR:1.002-1.034, OR:1.017) and IgM (95% CI OR:1.003-1.019, OR:1.011) were independently associated with mixed cryoglobulinemia.
Conclusions: In patients with chronic HBV infection, mixed cryoglobulinemia is not uncommon, with a prevalence rate of 26.4%. Both RF and IgM were independent factors for mixed cryoglobulinemia. Additionally, the links of female dominance, higher transaminase levels and fatty liver rates with HBV-related mixed cryoglobulinemia demand further investigation.

P.007

比較 TENOFOVIR ALAFENAMIDE 以及 ENTECAVIR 在急性 B 肝炎中兩者在 HBV DNA VIRAL LOAD 下降效益 - 單一醫學中心回朔性分析

THE EFFECTIVENESS OF TENOFOVIR ALAFENAMIDE VERSUS ENTECAVIR FOR DECLINING HEPATITIS B VIRUS DNA VIRAL LOAD: A SINGLE TERTIARY CENTER RETROSPECTIVE STUDY

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Background: Since May 1st 2019, tenofovir alafenamide(TAF) has been enrolled within national health care insurance in Taiwan, which gave another treatment hope for HBV hepatitis patients. However, there is still a lack of evidence head-to-head comparing efficacy of TAF and entecavir(ETV). Among all the serum markers, HBV DNA viral load is the independent marker predicting disease progression to liver cirrhosis and HCC.

Aims: This is a single center study that aims to compare the effectiveness on declining HBV DNA viral load from baseline to 6 month, 6 month to 1 year and 1 year to 1.5 years after receiving TAF or ERV in antiviral drug näive, HBV hepatitis patients.

Methods: We retrospectively enrolled patients with HBV hepatitis who qualified to receive HBV antiviral drugs under Nation Health Insurance from May 1st 2019 to June 1st 2022. The biochemical markers and liver cirrhosis status at baseline was documented. The decline range of HBV DNA viral load(log) after treatment was recorded every half year until 1.5year of treatment. A Mann-Whitney U test of <0.05 was considered statistically significant via SPSS IBM software.

Results: A total of 85 HBV antiviral drug naïve, HBV hepatitis patients were enrolled(50 patients received ETV and 35 received TAF treatment). Patients receiving TAF antiviral therapy showed significant decreases in HBV DNA viral load from baseline to half a year when compared with patients who received ETV antiviral therapy($P<0.001$). However, there is no significant difference in HBV DNA viral load reduction from 0.5 year to 1 year($P=.383$) between these two drugs. One interesting finding should be noticed, in patients who received TAF showed slightly better in HBV DNA viral clearance from 1 year to 1.5 year when compared with the ETV group.

Conclusions: In conclusion, our study showed significant HBV DNA viral load reduction from baseline to half a year in patients who receive TAF. However, no significant HBV DNA viral load reduction in the following half year to 1.5 years.

P.008

基因 6 型之 HCV 在台灣注射毒品者中的地理傳播及流行史
GEOGRAPHIC TRANSMISSION AND EPIDEMIC HISTORY OF HCV GENOTYPE 6 AMONG TAIWANESE PEOPLE WHO INJECT DRUGS

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Background: Persons who inject drugs (PWID) and their risk-related behaviors (e.g., unprotected sex and sharing of needles/syringes/other injection equipment) have given rise to serious public health concerns, especially in the rapid spread of HIV-1 and HCV.
Aims: This study aimed to reconstruct the epidemic history of HCV genotype 6 among Asian PWID.
Methods: We conducted sequence alignment analysis using the BioEdit v7.2.6.1 software with a range of reference strains sourced from the HCV database (https://hcv.lanl.gov/content/index). The MEGA X program was used to find the best-fit nucleotide substitution model and to construct phylogenetic trees using neighbor-joining (NJ) and maximum likelihood (ML) methods. Evolutionary rates were obtained using the Bayesian Markov chain Monte Carlo (MCMC) approach implemented in BEAST v2.5.1. For estimating evolutionary rates and generating tree structures, we employed general time-reversible (GTR) substitution models incorporating gamma-distributed among-site rate variation with six categories. Constantly sized, exponentially growing, and Bayesian skyline coalescent models were used for each case and each MCMC chain was run for at least 10,000,000 states and sampled in every 1000 states. Posterior probability densities were calculated, and the convergence of the chains was verified using the Tracer v1.7.1 with 10% of each chain discarded as burn-in.
Results: The GTR + G6 + I constant model was selected for data analysis, enabling us to identify the tMRCAs (time of most recent common ancestors) of HCV-6. We determined that the exponential growth model (likelihood in CS: - 9744.679, EG: - 9717.44, and BS: - 9868.01) best represents its transmission dynamics. NS5B gene-based phylogenetic analysis demonstrated the formation of a single clade comprising Asian PWID and reference strains. All genotype-6 strains from Asia (China, Myanmar, Taiwan, Vietnam) are traced back to 1928.1 (95% CR: 1890.2–1966.0). Subtypes 6a, 6n, and 6w were identified in the Taiwanese PWID population. For instance, subtype-6a emerged in Vietnam around 1993.5 (95% CR: 1977.5–2001.3) and subsequently spread to China in 1994.5 (95% CR: 1988.9–2000.9). Subtype-6n was initially introduced to China (1987.8, 1952.0–2005.0) and then spread to Myanmar (1990.4, 1954.7–2007.7). Notably, this subtype originated in Yunnan in 1987.8 (1953.1–2007.0) and spread eastward to Suzhou, Zhenjiang, and Jiangsu in the early and mid-2000s. Moreover, subtype-6w isolates from various regions in Taiwan appear to share a common source dating back to the mid-1990s (95% CR: 1985.0–2001.8).
Conclusions: The routes of drug trafficking and the resulting high prevalence of HIV-1/HCV co-infections among PWID might have contributed to the virus transmission and promoted its spread worldwide. Continuous surveillance and effective policy implementations within high-risk populations are crucial for disease management.

P.009

與治療前慢性 C 型肝炎患者的高鐵蛋白血症相關的因素分析
FACTORS ASSOCIATED WITH PRE-TREATMENT HYPERFERRITINEMIA IN PATIENTS WITH CHRONIC HEPATITIS C

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Background: Various factors causing an inflammatory response may lead to elevated serum ferritin, as it not only stimulates ferritin synthesis through cytokines and prostaglandins but also leads to the release of ferritin from damaged cells(Kernan & Carcillo, 2017). In chronic hepatitis C patients, elevated serum ferritin level is contributed to multiple factors, including liver enzymes, metabolic factors, hepatic steatosis, and liver fibrosis.(El Bacha et al.)

Aims: The objective of this study is to unveil potential correlations and influencing factors of ferritin level in HCV patients.

Methods: The cross-sectional prospective study recruited pre-treatment HCV patients, with serum HCV RNA detectable for more than 6 months. The presence of hyperferritinemia and its association with baseline demographic data, biochemical and virological variables, and fibrosis stage were analyzed.

Results: Of 2309 patients diagnosed with chronic hepatitis C, 627 were excluded from the study because of decompensated cirrhosis (n=21), history of HCC (n=75), organ transplantation (n=35), end-stage kidney disease (n=240), HIV coinfection (n=253) and iron deficiency anemia (n=3). A total of 1682 patients were included in the study (Figure 1.) The demographic, biochemical and virological data were shown in Table 1. The median age of the participants was 56 years old (48-63). The percentage of individuals aged more than 50 years accounted for 69.0% of the total study population. In terms of gender distribution, males comprised 51.4% of the population, with a total of 864 individuals. The median Body Mass Index (BMI) among the participants was 25.3 (23.0-27.6). The median ALT level was 86 U/L (51-146) and approximately 76.9% of the population exhibited exceeding 2 times the upper normal limit. The median eGFR was 79 ml/min/1.73 (68-94), and a substantial 89.5% of the population had eGFR values equals to or more than 60 ml/min/1.73. The median of HCV RNA log10 level was 6.07 IU/mL (5.37-6.56). Patients with HCV genotype 1 slightly outnumbered those without HCV genotype 1 (991 vs 691)(58.9% vs 41.1%). Out of the total patient population, 144 individuals (8.6%) had coinfection with HBV. 635 individuals (38.6%) were diagnosed with MASLD. Among them, 221(13.4%) had diabetes mellitus (DM), 407(24.7%) were overweight/obese, and 7(0.4%) were categorized as lean or having a normal weight. The fibrosis stage was assessed through liver stiffness measurement using transient elastography. Thirty-five patients without valid or reliable LSM results were excluded. Among the remaining participants, 699 (42.4%) were classified as F0-1, 416 (25.3%) as F2, 199 (12.1%) as F3, and 333 (20.2%) as F4. Factors associated with hyperferritinemia Univariate analysis revealed that patients older than 50 had an odds ratio (OR) of 1.73 for hyperferritinemia, which remained significant after adjustment in the multivariate analysis (adjusted OR 1.38). Patients with a fibrosis stage of F3 or higher had a higher likelihood of hyperferritinemia (OR 2.22), which persisted in the multivariate analysis(adjusted OR 1.36). The FIB-4 index greater than 3.25 was associated with an increased risk of hyperferritinemia (OR 2.39) in univariate analysis, and this association remained significant in the multivariate analysis (adjusted OR of 1.46). The presence of MASLD was also a significant predictor, with an OR of 1.51 in the univariate analysis and an adjusted OR of 1.43. Elevated ALT levels more than two times the upper limit of normal (ULN) presented a strong association with hyperferritinemia, having the highest OR of 3.55 in univariate and an adjusted OR of 2.87 in multivariate analysis. Other variables such as sex, HBV coinfection, HCV RNA levels, HCV genotype 1, and eGFR were not significantly associated with hyperferritinemia. In the univariate analysis, sex was not a significant predictor of hyperferritinemia (OR: 0.91, p=0.34). HBV coinfection showed an OR of 1.13, but this was not statistically significant in the unvivariate analysis (p=0.48). For HCV RNA levels, higher RNA level(> 2,000,000 IU/mL) groups had non-significant ORs (p=0.66). HCV genotype 1 yielded an OR of 1.17, which did not reach significance (p=0.11). Lastly, eGFR below 60 mL/min/1.73m² was significantly associated with hyperferritinemia (univariate OR 1.38, adjusted OR not significant).

Conclusions: In chronic hepatitis C patients, baseline age, levels of ALT, FIB-4, fibrosis stage and presence of MASLD were positively associated with hyperferritinemia, while sex, HBV co-infection, HCV RNA level, HCV genotype, and eGFR showed no significant correlation with hyperferritinemia.

P.010

不同醫療科別運用 C 型肝炎篩檢電子提示系統之分析
ANALYSIS OF HCV SCREENING BY USING AN ELECTRONIC NOTIFICATION SYSTEM IN DIFFERENT MEDICAL DEPARTMENTS

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Background: The extended HCV screening program for high-risk patients using an electronic notification system was conducted at the Far Eastern Memorial Hospital outpatient department.
Aims: To evaluate the proportion of the patients with notification over time, and finished screening in different medical departments after starting the program.
Methods: From December 2022 to April 2023, the patients with a higher prevalence of HCV infection (45 to 79 years old, DM, and CKD/pre-CKD) were enrolled. The clinics in the departments of internal medicine and family medicine started in December 2022, and other clinics from January 2023. If the patients had no previous anti-HCV data in the hospital information system and previous doctors did not answer the pop-up window would alert the doctors to choose agreement or disagreement of checkup (Reported in TDDW 2023 Poster P.08). The proportion of the patients with notification and finished blood test were analyzed in each medical department.
Results: Totally 85305 notifications (15.1%) were activated in 563712 person-times of clinic visits. After 5 months of screening, the proportion of patients with notification significantly decreased to <10% (27.6% in December 2022 to 7.9% in April 2023, P<0.001). However, the proportion was still >10% in the department of occupation medicine (18.2%), ophthalmology (17.1%), oral surgery (13.3%), ENT (11.8%), proctology (11.5%), gynecology (10.9%), urology (10.6%), cardiovascular surgery (10.4%), neurology (10.3%), and neurosurgery (10.2%). Among 21431 patients (25.1%) who finished blood tests, there were 515 patients (2.4%) with positivity of anti-HCV. For the enrolled patients in the department of internal medicine vs. non-internal medicine, the finished test rate was higher (39.4% vs. 10.1%, P<0.001) and the HCV seropositive rate was the same (2.5% vs. 2.2%, P=0.54).
Conclusions: The goal of HCV screening was >90% in the selected population. After introducing the system for 5 months, an average of >90% of the patients who visited the outpatient department needed no notification. All the departments of internal medicine and family medicine achieved the goal. Some departments in non-internal medicine may need more screening time and possibly more convenient tests or in-hospital checkup processes to promote the finished rate.

P.011

慢性 C 型肝炎患者接受小分子抗病毒藥物後之短期與長期 FIB-4 與血小板的動態變化
SHORT- AND LONG-TERM DYNAMIC CHANGES IN FIB-4 AND PLATELET COUNTS IN PATIENTS WITH CHRONIC HEPATITIS C RECEIVING ANTIVIRAL THERAPY

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Background: An accurate assessment of fibrosis status is important for managing hepatitis C virus (HCV) infection. The non-invasive fibrosis index, FIB-4, is one of the most popular methods used to reflect liver fibrosis status.
Aims: The purpose of this study was to investigate the dynamic changes in FIB-4 and platelet counts (PLT) at different time points in patients with chronic hepatitis C who received direct-acting antivirals.
Methods: We enrolled chronic hepatitis C patients who had received antiviral therapy and achieved sustained virologic response (SVR). Clinical characteristics and laboratory data were collected. FIB4 was calculated based on laboratory data. We investigated the dynamic changes of FIB4 and PLT separately during the treatment (TW0 to SVR) and follow-up periods (posttreatment 15 [P15M] to 39 months [P39M]). For analyzing short-term dynamic changes of FIB4 and PLT, we used the entire cohort. For analyzing long-term dynamic changes of FIB4 and PLT, we selected the subgroup that had complete laboratory data from TW0 to P39M.
Results: A total of 1,234 CHC patients who received antiviral therapy and achieved SVR were enrolled. The percentage of patients with cirrhosis was 12.4%. During the treatment period, FIB-4 showed a rapid decline from the baseline to its lowest value at the end of treatment (EOT). The median values of FIB-4 at TW0, TW4, EOT, and SVR were 2.00, 1.63, 1.59, and 1.60, respectively. PLT exhibited a rapid increase from baseline to its highest value at TW4, then slowly declined until SVR. The median values of PLT at TW0, TW4, EOT, and SVR were 177, 187, 184, and 182 x 10^3/μl. Compared to the treatment period, FIB-4 during the follow-up period showed a more gradual decline from the time point P15M to P39M. In the subgroup (n = 329), the median values of FIB-4 at TW0, SVR, P15M, P27M, and P39M were 2.26, 1.95, 1.72, 1.69, and 1.66, respectively. The decline in FIB-4 during the treatment period was approximately elevenfold compared to that during the follow-up period. The PLT count also showed similar trends during the treatment and follow-up periods, with greater increase during the treatment period than the follow-up period.
Conclusions: The FIB-4 index primarily declined during the first month of treatment, with the lowest value remaining at the EOT, which can be attributed not only to the rapid normalization of hepatitis but also to the marked increase in PLT at week 4. Furthermore, the decline in FIB-4 during the treatment period was approximately elevenfold compared to that during the follow-up period. Further large-scale studies are warranted for validation.

P.012

隱源性脂肪肝疾病病患之肝臟及動脈粥狀硬化風險探討
LIVER AND ATHEROSCLEROTIC RISKS OF PATIENTS WITH CRYPTOGENIC STEATOTIC LIVER DISEASE

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Background: In 2023, a new nomenclature of "metabolic associated steatotic liver disease" (MASLD) has emerged by incorporating cardio-metabolic criteria to redefine "non-alcoholic fatty liver disease" (NAFLD). Among steatotic liver disease (SLD), those having no known causes and without any one of cardio-metabolic criteria are deemed to have cryptogenic SLD.
Aims: This study aims to compare the liver and atherosclerotic risks between MASLD and cryptogenic SLD patients.
Methods: We analyzed participants with liver ultrasound data from the Taiwan Bio-Bank cohort, excluding those with positive HBsAg, positive anti-HCV, or "frequent drinker". MASLD involves hepatic steatosis and any of five cardiometabolic risk factors, whereas cryptogenic SLD features hepatic steatosis without these risk factors. Liver fibrosis severity was assessed by using NAFLD fibrosis score (NFS), while atherosclerosis was determined by carotid plaques on duplex ultrasound.
Results: Among 17,595 subjects (age 55.47±10.41; males 31.8%), 7,538 participants (42.8%) had SLD, comprising 96.5% of MASLD and 3.5% of cryptogenic SLD. Cryptogenic SLD patients are younger and had a lower percentage of male than those with MASLD. After propensity score matching for age and sex, patients with cryptogenic SLD exhibited milder glucose and lipid profiles, fewer carotid plaques, lower liver steatosis, inflammation, and fibrosis markers than those with MASLD.
Conclusions: In this large population-based study, cryptogenic SLD, the excluded group, occupy only 3.5% in NAFLD patients. It has lower liver and atherosclerotic risks than MASLD, supporting its exclusion from NAFLD and justifying the rationale for the new disease name and diagnostic criteria of MASLD.

P.013

長期飲酒對代謝性脂肪肝病的臨床影響
CLINICAL IMPACT OF CHRONIC ALCOHOL CONSUMPTION ON METABOLIC-DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE

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Background: The prevalence of alcoholic and metabolic-dysfunction associated steatotic liver disease had been increasing in Taiwan. However, alcohol consumption and metabolic dysfunction frequently co-exist in patients with steatotic liver disease. Thus, the effects of alcohol and metabolic dysfunction on metabolic-dysfunction associated steatotic liver disease cannot be fully distinguished.
Aims: The aim of this study is to evaluate the clinical effect of chronic alcohol consumption on metabolic-dysfunction associated steatotic liver disease in Taiwan.
Methods: Patients with clinically diagnosed metabolic-dysfunction associated steatotic liver disease by abdominal ultrasonography were consecutively enrolled. The clinical features, including anthropometric parameters, clinical and biochemical characteristics as well as the history of alcohol consumption were collected. According to alcohol consumption, patients were divided into chronic drinkers and non-chronic drinkers. Chronic drinkers were defined as alcohol consumption at least twice per week for more than. Statistical analyses were performed by chi-square test, Fisher's exact test, Student's t test.
Results: A total of 290 patients with metabolic-dysfunction associated steatotic liver disease were enrolled. There were 78(26.9%) chronic drinkers and 212(73.1%) were non-chronic drinkers. There were no significant difference in terms of age, BMI, waistline, prevalence of DM, hypertension, chronic hepatitis B and C between two groups. The chronic drinkers had significantly higher ratio of male gender (92.31% vs. 56.13%, P<0.0001) and higher creatinine levels (0.88±0.17 mg/dl vs. 0.81±0.22 mg/dl, P=0.016), γ-glutamyl transferase levels (73.02±115.97 U/L to 36.60±38.09 U/L, P=0.015), FIB-4 score (1.82±1.64 vs. 1.36±1.48, P=0.049) and lower alkaline phosphatase levels (64.43±18.83 U/L vs. 72.97±19.60 U/L, P=0.004) than non-chronic drinkers. In subgroup analysis, there were 140 patients (37 chronic drinkers and 103 non-chronic drinkers)

received hepatic stiffness and Controlled Attenuation Parameter (CAP) measurement by Fibroscan. There was no significant difference in CAP measurement between chronic drinkers and non-chronic drinkers (307.97±44.84 dB/m vs. 294.60±51.35 dB/m, P=0.168). The fibrosis stages distribution of chronic drinkers and non-chronic drinkers were similar (F0 in 78.4% and 84.5%, F1 in 5.4% and 8.5%, F2 in 5.4% and 1.0%, F3 in 0 and 1.9%, and F4 in 10.8% and 3.9%).

Conclusions: The synergistic effects of chronic alcohol consumption and metabolic dysfunction were observed on the clinical manifestation in patients with steatotic liver disease. Serum γ-glutamyl transferase may be used to identify chronic alcohol consumption in patients with metabolic-dysfunction associated steatotic liver disease.

P.014

不同亞型代謝性脂肪肝病的臨床特徵及纖維化嚴重程度
THE CLINICAL CHARACTERISTICS AND FIBROSIS SEVERITY IN DIFFERENT SUBTYPE OF MAFLD

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Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) is significant global health issues. According the diagnosis criteria, MAFLD can divided into three subtypes (1) Overweight/obesity (2) Presence of metabolic dysregulation despite normal weight (lean MAFLD) (3) Diabetes mellitus (DM). As the prevalence of MAFLD is increasing in Taiwan. However, the clinical characteristics and fibrosis severity in different subtypes of MAFLD need further clarification.

Aims: The aims of the study are to compare the clinical characteristics, steatosis and fibrosis severity indicators between three subtypes of patients with MAFLD.

Methods: Patients with hepatic steatosis which was diagnosed by abdominal ultrasound were consecutively enrolled according to MAFLD diagnostic criteria. The clinical features, including anthropometric parameters, clinical and biochemical characteristics were collected. Statistical analyses were performed by Kruskal-Wallis test, Dunn's test, chi-square test and Fisher's exact test.

Results: A total of 290 patients with MAFLD were enrolled. The patients were divided into 3 subtypes according to the MAFLD diagnostic criteria. Subtype 1: Overweight/obesity, 218 patients. Subtype 2: Lean MAFLD, 20 patients. Subtype 3: DM, 52 patients. There were 1.8% of patients with overweight/obesity had no metabolic risk factor. There was no significant difference between three subtypes in terms of alcohol consumption, prevalence of hypertension or chronic hepatitis B and C, platelet counts, INR, bilirubin level, alkaline phosphatase level, lipid level, alpha-fetoprotein and Fib-4 score. Among the three subtypes, patients with lean MAFLD had highest female gender (75%). Patients with DM had significantly older age (57.58±11.26 to 52.63±12.16, P=0.019), AST levels (45.61±41 U/L to 29.95±17.81 U/L, P=0.002), and NAFLD fibrosis score (0.29±2.59 to -0.74±2.55, P=0.036) than patients with obese/overweight. Patients with lean

MAFLD had significantly lower BMI (21.39±1.27 vs. 26.90±2.59 vs. 27.70±3.92, P<0.0001), lower waistline (81.00±6.25 cm vs. 93.63±7.73 cm vs. 96.92±10.78 cm, P < 0.0001), lower creatinine levels (0.69±0.11mg/dL vs. 0.83±0.19 mg/dL vs. 0.84±0.29 mg/dL, P=0.007) and γ-glutamyl transferase levels (35.06±64.05 U/L vs. 41.90±53.17 U/L vs. 71.71±119.23 U/L, P=0.002) than patients with obese/overweight and patients with DM. Patients with DM had higher level of ALT (61.14±56.48 U/L vs. 42.94±35.03 U/L vs. 31.75±18.76 U/L, P=0.005), AC glucose(141.02±65.02mg/dL vs. 95.81±9.39 mg/dL vs. 97.74±10.9 mg/dL, P < 0.0001), HbA1c (7.27±1.40% vs. 5.66±0.43% vs. 5.79±0.40, P < 0.0001), HOMA-IR (6.30±4.29 vs. 3.35±2.07 vs. 2.25±1.07, P < 0.0001) than patients with obese/overweight and patients with lean MAFLD. In subgroup analysis, there were 137 patients (104 patients in overweight/obese MAFLD, 11 patients in lean MAFLD and 22 patients in MAFLD with DM) received hepatic stiffness and controlled attenuation parameter (CAP) measurement by Fibroscan. There was no significant difference of CAP (300.08±48.19 vs. 278.73±61.97 vs. 298.55±51.94, P=0.534) and elastography stiffness (5.07±2.66 kPa vs. 4.34±1.44 kPa vs. 6.50±3.56 kPa, P = 0.067) between the three subtypes.

Conclusions: The majority of patients with MAFLD are obese/overweight subtype. MAFLD patients with DM seem to have more hepatic inflammation than the other two subtypes. However, there was no significant difference in steatosis and fibrosis severity among three subtypes. The long-term outcomes of MAFLD subtypes still need further study.

P.015

服用紅藜萃取物保健食品於成人非酒精性脂肪肝的臨床驗證
EFFECTS OF CHENOPODIUM FORMOSANUM EXTRACT SUPPLEMENTATION ON HEPATIC STEATOSIS IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS

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Background: Non-alcoholic fatty liver disease patients are increasing nowadays and there are a lot of supplementation which needed to be clarified their usefulness to attenuate non-alcoholic fatty liver disease patients' fibrosis level. In this study, we try to investigate Chenopodium Formosanum extract to be a useful nutritional strategy to attenuate CAP level in non-alcoholic fatty liver disease patients.

Aims: To investigate the effects of Chenopodium Formosanum extract supplementation on hepatic steatosis in non-alcoholic fatty liver disease patients.

Methods: All participants received blood testing and FibroScan before and after supplementation. A randomized, double-blind study design was used to assign 18 subjects into the low-dose group (n=10) or high-dose group (n=8). All participants consumed either one capsule of Chenopodium Formosanum extract for low-dose group (1 g) or three capsule for high-dose group (3 g) once per day for 12 weeks. Data was analysed by two-way mixed-design ANOVA

Results: There were no significant differences in liver function (GOT: 24.80±6.16 U/L vs. 28.75±11.44 U/L; GPT: 33.50±20.06 U/L vs. 33.75±12.45 U/L), renal function (BUN: 13.20±2.30 mg/dL vs. 13.25±2.55; Creatinine: 0.94±0.13 mg/dL vs. 0.94±0.21 mg/dL), blood lipid profile (TC: 184.10±31.50 mg/dL vs. 215.63±49.39 mg/dL; TG: 111.90±88.98 mg/dL vs. 147.75±107.69 mg/dL; HDL-C: 55.40±15.36 mg/dL vs. 49.63±10.60 mg/dL; LDL-C: 120.90±24.78 mg/dL vs. 151.63±34.93 mg/dL), and FibroScan (CAP: 293.10±44.57 dB/m vs. 322.25±45.30 dB/m; F score: 4.78±0.97 Kpa vs. 4.41±0.96) between low-dose group and high-dose group before supplementation. After supplementation, the CAP level of low-dose group and high-dose group were significantly lower than before supplementation, respectively (256.50±54.34 dB/m and 275.50±50.14 dB/m). However, there was no significant difference between two groups. In addition, the other dependent variables of two groups were no significant

differences between before and after supplementation.
Conclusions: Low-dose and high-dose Chenopodium Formosanum extract can effectively attenuate the CAP level, and has no negative benefits on liver function, renal function, and blood lipid profile. Taken together, 1 g of daily Chenopodium Formosanum extract for 12 weeks seems to be a useful nutritional strategy to attenuate CAP level in non-alcoholic fatty liver disease patients.

P.016

使用 DELPHI 共識對脂肪肝的新定義和命名法對脂肪肝族群進行分析
AN ANALYSIS OF FATTY LIVER DISEASE COHORT USING THE NEW DEFINITION AND NOMENCLATURE OF STEATOTIC LIVER DISEASE FROM DELPHI CONSENSUS

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Background: The novel definition and nomenclature proposed from a multi-society modified Delphi consensus introduces a comprehensive interpretation of steatotic liver disease (SLD). It is important to emphasize that the term nonalcoholic fatty liver disease (NAFLD), previously known as metabolic dysfunction-associated fatty liver disease (MAFLD), has been rebranded as metabolic dysfunction-associated steatotic liver disease (MASLD).
Aims: The aim of this study to elucidate the distribution and clinical characteristics of the SLD subgroups and to compare clinical features of persons meeting criteria for NAFLD, MAFLD, and MASLD.
Methods: A total of 848 patients diagnosed with fatty liver disease via abdominal ultrasound at Chang Gung Hospital in Kaohsiung from July 2022 to September 2023 were prospectively enrolled. We evaluated the presence of cardiometabolic risk factors according to predefined criteria and categorized all the participants into 5 groups according to the Delphi consensus: MASLD, MetALD (MASLD with increased alcohol intake), ALD (alcohol-related liver disease), cryptogenic SLD, and other etiologies.
Results: The prevalence of MASLD, MetALD, ALD, cryptogenic, and other etiologies of SLD was 86.8%, 9.1%, 0.5%, 2.5%, and 1.2%, respectively. In the comparison with previous definition of fatty liver disease, a total of 481 (56.7%) patients were defined as NAFLD and 784 (92.5%) patients as MAFLD. There is no significant difference between NAFLD, MAFLD and MASLD but MASLD included more patients than NAFLD. In subgroup analysis, the MetALD group had a significantly higher percentage of male gender, mean levels of waist, rGT, creatine, triglyceride, and fatty liver index than the MASLD group, but lower in high sensitivity CRP and ESR, highlighting the importance of alcohol consumption in metabolic dysfunction associated liver disease.
Conclusions: Using the new definition and diagnostic

criteria of SLD, there are more patients met the criteria of MASLD than old criteria of NAFLD. Differing from MAFLD, the Delphi consensus emphasizes the significance of alcohol consumption in metabolic dysfunction associated liver disease, categorizing it independently as MetALD with metabolic factors distinct from MASLD.

P.017

愛滋病毒合併感染顯著增加慢性 B 型肝炎患者之脂肪肝
SIGNIFICANTLY INCREASED RISK OF STEATOTIC LIVER DISEASE IN PEOPLE WITH HIV AND HBV CO-INFECTION

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Background: Steatotic liver disease (SLD) is growing prevalence in people with chronic liver disease such as chronic hepatitis B (CHB). It is unclear whether co-infection with human immunodeficiency virus (HIV) increases the risk of SLD in people with CHB.
Aims: To identify the prevalence and the associated factors with SLD in people with HIV and HBV co-infection.
Methods: We conducted a retrospective cross-sectional study to include people with HIV and HBV co-infection who were receiving tenofovir-based antiretroviral therapy at the National Taiwan University Hospital between 2006 and 2023. People with HBV mono-infection who were receiving tenofovir disoproxil fumarate (TDF) for at least one year were included as the comparison group. Propensity scores were calculated to match both cohorts by age, sex, and body mass index (BMI) in a 1:4 ratio. SLD was diagnosed by the presence of steatosis in the latest abdominal sonography. Demographic data, relevant laboratory profiles, and co-morbidities were collected. Multivariable logistic regression analyses were performed to investigate the factors associated with SLD.
Results: During the study period, 57 people with HIV and HBV co-infection and 228 people with HBV mono-infection were included. The median age and BMI were 57 years and 23.7 kg/m^2, respectively, and 97% were male. The latest liver function, blood glucose, and co-morbidities of diabetes and hypertension were comparable between the two groups. Compared with the HBV- mono-infected group, the HIV/HBV-co-infected group had a significantly higher prevalence of hyperlipidemia (56.1% vs. 25.4%, P<0.001) and SLD (63.2% vs. 44.7%, P=0.013). After adjustments made for age, sex, liver function, and hyperlipidemia, a higher BMI (adjusted odds ratio [aOR], 1.33; 95% confidence interval [CI], 1.19-1.50), a lower FIB-4 index (aOR, 0.25; 95% CI, 0.10-0.57), and HIV co-infection (aOR, 3.01; 95%CI, 1.42-6.64) were independent

factors associated with SLD.

Conclusions: The prevalence of SLD (63.2%) and hyperlipidemia (56.1%) were significantly higher in people with HIV and HBV co-infection than in patients those with HBV mono-infection. HIV co-infection was associated with a 3-fold higher risk of SLD.

P.018

在代謝相關脂肪性肝疾患族群中新型發炎指數與肝纖維化指數及丙胺酸轉胺酶濃度呈現相關

NOVEL INFLAMMATORY MARKERS CORRELATES WITH ALT LEVELS AND FIB-4 IN MASLD PATIENT

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Background: Steaototic liver disease is increasingly recognized as a significant global health concern. The American Association for the Study of Liver Diseases (AASLD) recently introduced the term Metabolic dysfunction-associated steatotic liver disease (MASLD) to emphasize the connection between Steatotic liver disease and metabolic disorders. In this study, we investigated the relationship between novel inflammatory markers and ALT levels in MASLD patients. These inflammatory markers, such as the systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI), have been shown to be predictive factors for coronary artery disease. Additionally, the triglyceride-glucose (TyG) index (CTI) has been found to correlate with insulin resistance and the severity of inflammation. Meanwhile, ALT levels are associated with the severity of liver inflammation. and FIB-4 index is a indicator for liver fibrosis. Further research is needed to uncover the correlation between liver inflammation and these novel inflammatory markers.

Aims: The aim of this study is to explore the correlation between novel inflammation markers and ALT levels in patients with MASLD. We will analyze inflammation markers such as Systemic Immune Inflammation Index (SII) and Systemic Inflammatory Response Index (SIRI), and investigate their associations with predictive factors for coronary artery disease. Additionally, we will study the correlation between the Triglyceride-Glucose Index (TyG index) and insulin resistance and the severity of inflammation. Furthermore, ALT levels are related to the severity of liver inflammation. Through further research, we hope to uncover the relationship between liver inflammation and these novel inflammation markers.

Methods: This study recruits about 10000 of MASLD patients as participants according to AASLD definitions. Their clinical data and abdominal echo were collected. Novel inflammatory indexes including Neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte

ratio (LMR), Metabolic profiles atherogenic index of plasma (AIP), Triglyceride-glucose index of insulin resistance(TyG), CRP- TyG index(CTI), Systemic immune-inflammation index(SII), Systemic Inflammatory Response Index (SIRI) and Inflammatory prognosis index (IPI) were calculated. Univarient analysis was conducted for regarding different ALT levels and different FIB-4 risk groups. Further machine learning techniques will be conducted for more precise results.

Results: Currently, Both: NLR LMR has shown to be significant regarding different FIB-4 levels and CTI BMI levels have shown to be correlated with different ALT levels. Further result was still under analyzed, pending further contact before the post

Conclusions: This study aims to investigate the correlation between novel inflammation markers and ALT levels, as well as FIB4 levels, in patients with MASLD. The findings of this study are expected to enhance our understanding of the pathogenesis of MASLD and offer new insights for the diagnosis and treatment of the disease.

P.019

日常體能狀態作為肝癌之替代預測因子—白蛋白膽紅素評分系統以及簡化版白蛋白膽紅素評分系統之臨床角色
PERFORMANCE STATUS AS A PROGNOSTIC SURROGATE IN HEPATOCELLULAR CARCINOMA: ROLE OF ALBUMIN-BILIRUBIN (ALBI) AND EASY (EZ)-ALBI GRADE

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Background: Performance status (PS) is associated with the severity of liver cirrhosis and is also an important survival determinant in hepatocellular carcinoma (HCC). Albumin-bilirubin (ALBI) grade and easy (EZ)-ALBI grade have been proposed to evaluate liver dysfunction in HCC, but their role in patients with different PS is unclear.

Aims: We aimed to investigate the prognostic role of ALBI and EZ-ALBI grade in a large HCC cohort with variable PS.

Methods: A total of 3,355 of newly diagnosed HCC patients between 2002 to 2018 were identified and retrospectively analyzed. Independent prognostic predictors associated with survival were investigated by using the Cox proportional hazards model.

Results: Patients with good PS have better long-term survival compared with those of poor PS. ALBI and EZ-ALBI grade can discriminate long-term outcome in the entire cohort as well as in patients with different PS. ALBI and EZ-ALBI are objective and feasible prognostic models to evaluate liver dysfunction in HCC patients independent of PS.

Conclusions: Patients with good PS have better long-term survival compared with those of poor PS. ALBI and EZ-ALBI grade can discriminate long-term outcome in the entire cohort as well as in patients with different PS. ALBI and EZ-ALBI are objective and feasible prognostic models to evaluate liver dysfunction in HCC patients independent of PS.

P.020

一家醫學中心肝癌患者接受經皮腫瘤燒灼治療之趨勢探討
THE TREND OF PERCUTANEOUS TUMOR ABLATION METHODS FOR HEPATOCELLULAR CARCINOMA IN A SINGLE MEDICAL CENTER

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Background: Percutaneous tumor ablation methods, such as radiofrequency ablation (RFA) and percutaneous ethanol injection therapy (PEIT) play a crucial role in the treatment of hepatocellular carcinoma (HCC). Previous studies indicate that RFA is more effective than PEIT.
Aims: Our study aims to emphasize the trend of percutaneous tumor ablation methods for HCC and reform the treatment outcome in different eras.
Methods: The medical records of patients who underwent RFA or PEIT in MacKay Memorial Hospital from January 1st, 2013 to December 31th, 2022 were reviewed retrospectively. The patients diagnosed with HCC were enrolled. Exclusion criteria encompassed cases of HCC classified as BCLC stage C or D, TNM stage IV, death resulting from causes unrelated to HCC, and patients who were lost to follow-up for more than one year. We analyzed the trends of percutaneous tumor ablation. These patients are categorized by the date of their first percutaneous tumor ablation. The clinical features of patients in different time groups (2013-2017; 2018-2022) were compared using the Fisher exact test and Mann-whitney U test. Survival analysis was calculated by using the Kaplan-Meier method.
Results: A total of 355 patients with HCC, who received percutaneous tumor ablation were collected and 60.84% of patients were male. The patients were categorized into two groups: the 2013-2017 group (n = 202) and the 2018-2022 group (n = 153). There were no significant differences between two groups in age (65.08±12.59 versus 66.82±11.23 years, P=0.306), gender, HCC etiology and ECOG performance status. However, there were significant differences in BCLC stage (p=0.016) and grade of Child Pugh classification (p=0.009). Over the past decade, there has been a noticeable decline in treatment times and case numbers, with a decline in the portion of PEIT and an increase in the use of RFA in the last 10 years. (Figure 1). Significant differences were observed in survival curves between patients in these two eras (P<0.001) (Figure 2). Linear regression analysis demonstrated a significant correlation between survival time and BCLC stage or Child-Pugh classification.
Conclusions: Our real-world data on HCC patients indicate a decreasing trend in both treatment times and the number of patients undergoing percutaneous tumor ablation. Notably, there is a significant improvement in survival time over the past 5 years. This improvement might be attributed to the better BCLC stage and liver function status in patients within the most recent 5 years.

P.021

免疫合併標靶療法在肝癌的效力與安全性
EFFICACY AND SAFETY OF PD-1/PD-L1 INHIBITORS PLUS BEVACIZUMAB IN HEPATOCELLULAR CARCINOMA: A RETROSPECTIVE COHORT STUDY

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Background: Recent trends in the management of unresectable HCC involve the combination of an immune checkpoint inhibitor and antiangiogenic agent, since the combination of atezolizumab and bevacizumab significantly prolonged overall survival (OS) and progression-free survival (PFS) in patients with unresectable HCC in the IMbrave 150 phase 3 trial in 2020. However, inclusion was restricted to patients with preserved liver function Child–Pugh score A and ECOG ≤1. While patients with advanced cirrhosis and/or poor performance status were excluded, this patient group is commonly seen in clinical practice.

Aims: This study reviewed the efficacy and safety of combined PD-1/PD-L1 inhibitors and bevacizumab compared to targeted therapy (sorafenib or lenvatinib) for unresectable HCC in a real-world cohort including patients even with impaired liver function and poor performance status. The goal is to understand the real clinical outcomes of patients who received the combination.

Methods: We retrospectively reviewed 112 HCC patients who received targeted therapy between January 1, 2018 and December 31, 2021 in Chi Mei Medical Center. The follow up cut-off date was October 18, 2023. Clinical characteristics, the information of patients, therapeutic responses including OS, PFS, radiological findings, and adverse events were recorded for analysis. Patients information from the medical records included sex, age, performance status, Child-Pugh class, AFP, HCC etiology, and prior therapy for HCC. HCC was classified using the Barcelona Clinic Liver Cancer staging system. Tumors were assessed by CT or MRI after initiation of treatment. The therapeutic response was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST). OS and PFS were calculated using the Kaplan-Meier method and statistically analyzed using the log-rank test, $p < 0.05$ was considered statistically significant. Figure 1 presents the study flowchart.

Results: A total of 23 patients were treated with PD-1/PD-L1 inhibitors plus bevacizumab and 89 patients were treated with sorafenib or lenvatinib. The characteristics of the patients are summarized in Table I. Atezolizumab, nivolumab, durvalumab, pembrolizumab and tislelizumab were 7, 3, 10, 2 and 1 patients, respectively. Sixty-three patients with ECOG performance status of 2-3 were enrolled in this study. Child-Pugh class A and B were observed in 87 and 22 patients, respectively. BCLC stage A, B and C at study entry were 5, 11, and 94 patients, respectively. The most common etiology of liver disease was viral hepatitis, including 56 (50%) with hepatitis B and 26 (23%) with hepatitis C. Forty-five (40%) patients had AFP levels more than 400 ng/ml. The radiological therapeutic response to therapy and side effect are shown in Table 2. Overall survival and progression-free survival were significantly longer within PD-1/PD-L1 inhibitors plus bevacizumab group (Figure 3). The incidence of bleeding side effect between two groups were similar. In terms of patients' demographics, male, Child-Pugh class A and AFP levels below 400 ng/ml demonstrate independent predictive factors in PD-1/PD-L1 inhibitors plus bevacizumab group (Table 3).

Conclusions: PD-1/PD-L1 inhibitors plus bevacizumab showed good efficacy and safety in HCC patients even with impaired liver function and poor performance status. The combination of PD-1/PD-L1 inhibitors with bevacizumab resulted in more favorable survival outcomes without an increased risk of bleeding adverse effects.

P.022

對無法切除的浸潤性與非浸潤性肝細胞癌施以免疫治療的療效 - 一個真實世界的比較研究

REAL-WORLD COMPARISON OF THE EFFECTIVENESS OF IMMUNOTHERAPY FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA BETWEEN THE INFILTRATIVE AND NON-INFILTRATIVE TYPES

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Background: Although patients diagnosed with infiltrative hepatocellular carcinoma (HCC) typically experience unfavorable survival outcomes, the ideal therapeutic approach for such patients remains uncertain. Immunotherapy utilizing immune checkpoint inhibitors (ICIs) has emerged as the preferred first-line treatment for advanced HCC. However, the effectiveness of this immunotherapy in patients with infiltrative HCC remains to be comprehensively understood.

Aims: This study aims to compare clinical outcomes between patients with infiltrative and non-infiltrative HCC who had been treated with ICIs.

Methods: Unresectable HCC patients who underwent immunotherapy with ICIs were retrospectively included. The study subsequently categorized this cohort into two groups: infiltrative and non-infiltrative. The primary outcomes encompassed treatment response according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria, as well as progression-free survival (PFS) and overall survival (OS).

Results: Of a total of 198 patients included, 60 were diagnosed with infiltrative HCC, while 138 had non-infiltrative HCC. Following immunotherapy with ICIs, the infiltrative HCC group exhibited an objective response rate (ORR) of 36.7% and a disease control rate (DCR) of 55.0%, with no significant difference between the infiltrative and non-infiltrative groups. Notably, patients in the infiltrative group experienced a significantly shorter median of PFS and OS following immunotherapy, with PFS and OS durations of 4.1 months (95% confidence interval: 2.5-6.7; p = 0.0288) and 10.4 months (95% confidence interval: 6.7-14.4; p = 0.0112), respectively, compared with those in the non-infiltrative group.

Conclusions: Despite the similarity in therapeutic response between the non-infiltrative and infiltrative groups, improved survival outcomes in patients with infiltrative HCC were disclosed. Further studies, both large-scale and prospective, are essential to validate these findings and explore the potential of combination therapies in patients with infiltrative HCC.

P.023

局部消融治療（包括射頻消融、微波消融、立體定位消融放射治療和粒子放射治療）於無法手術之肝細胞癌的治療效益比較：一個系統性回顧和統合分析

COMPARISON OF LOCAL ABLATIVE THERAPIES, INCLUDING RADIOFREQUENCY ABLATION, MICROWAVE ABLATION, STEREOTACTIC ABLATIVE RADIOTHERAPY, AND PARTICLE RADIOTHERAPY, FOR INOPERABLE HEPATOCELLULAR CARCINOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Hepatocellular carcinoma (HCC) is a dominant type of liver cancer with only a few patients being suitable to receive radical surgery. Radiofrequency ablation therapy (RFA) is the first-line local therapy in inoperable patients. Microwave ablation therapy (MWA), stereotactic body radiotherapy (SBRT) and charged particle therapy are tested to be an alternative option.
Aims: This study conducted an updated and comprehensive systematic review and meta-analysis of the effect of these local ablative therapies in inoperable patients with HCC.
Methods: Studies were searched from PubMed, EMBASE, and Cochrane Library databases. A single-arm meta-analysis was conducted to calculate a pooled effect size using random-effects models. The primary outcome was the local control rate. The secondary outcome included regional and distant progression rates, overall survival rate, and adverse events.
Results: This study included 6 randomized controlled trials and 20 prospective cohort studies that involved 1,937 patients with HCC. MWA ($p < 0.001$) and particle therapy ($p < 0.001$) showed better performance of local control rate compared to RFA, while SBRT ($p = 0.276$) showed non-significant trend. However, SBRT ($p = 0.002$) and particle therapy ($p < 0.001$) showed better performance than RFA and MWA in HCCs of >30 mm in size. MWA showed a similar result to RFA while SBRT and particle therapy showed a lower survival rate in the 2-, 3-, and 4-year overall survival rates. MWA had the lowest regional and distant progression rate while SBRT and particle therapy had a higher progression rate compared to RFA.
Conclusions: Our results indicate that MWA, SBRT, and particle therapy were safe with better local control rates than RFA. The local control rates of SBRT and particle therapy are significantly better than RFA in HCC of >30 mm in size. However, long-term overall survival and disease progression rates are worse in SBRT and particle therapy, probably due to the different patient profiles in the enrolled studies.

P.024

肝癌併肝外轉移之臨床特性和預後分析
CLINICAL CHARACTERISTICS AND OUTCOMES FOR HEPATOCELLULAR CARCINOMA WITH EXTRAHEPATIC METASTASES: A RETROSPECTIVE ANALYSIS IN TAIWAN

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Background: Hepatocellular carcinoma (HCC) is a significant health concern in Taiwan, ranking fifth in incidence and second in cancer-related deaths. HCC with extrahepatic metastases (EHM) impacted overall survival and systemic therapies were recommended by several guidelines.
Aims: The role of aggressive locoregional control for advanced-stage HCC with EHM remains controversial. We retrospectively analyzed a cohort of HCC patients to further investigate the clinical features and prognostic factors for HCC with extrahepatic metastasis.
Methods: A retrospective analysis of 4,161 HCC patients admitted to Kaohsiung Veterans General Hospital between 2005 and 2022 were reviewed and 552 patients with EHM at initial diagnosis were identified. Clinical characteristics and outcomes were analyzed.
Results: EHM was detected in 552 (13.3%) of patients. Metastases to lymph nodes in 266 (48.2%), lungs in 182 (33%), bones in 61 (11%), adrenal glands in 34 (6.2%), and other sites in 8 (1.4%) patients were found. Various treatments were administered, including locoregional, systemic, and combined locoregional and systemic treatments and palliative treatment. Multivariate analyses revealed alcohol use, tumor numbers more than 2, tumor size greater than 5 cm, and portal vein invasion as significant risk factors for developing EHM. Patients without EHM had a significant longer median survival than those with EHM (24 Vs. 3 months, p<0.001). In HCC patients with EHM, tumor numbers more than 2, tumor size greater than 5 cm, and portal vein invasion were independent risk factors for survival. Locoregional treatments (including operation (OP), radiofrequency ablation (RFA), radiotherapy (R/T), transarterial embolization (TAE), transarterial chemoembolization (TACE), hepatic arterial infusion chemotherapy (HAIC) or transarterial radioembolization (TARE) and systemic treatments (including target therapy or immune check point inhibitors) were associated with improved survival in EHM patients. In patients with EHM who received systemic treatments had longer survival (6 Vs. 2 months, P=0.016). In EHM patients who received systemic therapy, combined locoregional therapy demonstrated a significant survival benefit (8 Vs. 3 months, p<0.001).
Conclusions: This study disclosed the clinical features and prognostic factors of HCC with EHM. In EHM patients who received systemic therapy, combined locoregional therapy demonstrated a significant survival benefit.

P.025

重度肝癌病患接受修正 FOLFOX 配方之肝動脈化療之臨床特性和預後分析
CLINICAL CHARACTERISTICS AND OUTCOMES FOR ADVANCED HEPATOCELLULAR CARCINOMA UNDERGOING HEPATIC ARTERIAL INFUSION CHEMOTHERAPY WITH MODIFIED FOLFOX REGIMEN

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Background: Hepatocellular carcinoma (HCC) ranks fifth in incidence and second in cancer-related deaths in Taiwan. Hepatic arterial infusion chemotherapy (HAIC) has been widely performed in advanced HCC.
Aims: The aim of the study is to analyze the clinical characteristics and efficacy of HAIC with modified folfox regimen for advanced HCC.
Methods: HCC patients with tumor size more than 8cm or portal vein (PV) invasion were included. All enrolled patients received HAIC with modified folfox regimen (oxaliplatin 30 mg /M^2, leucovorin 100 mg /M^2, 5-FU 400 mg/M^2 for 3 days) followed by lipiodol embolization if needed. Clinical characteristics and outcomes were analyzed.
Results: We enrolled 21 advanced HCC who received HAIC with modified folfox regimen in Kaohsiung Veterans General Hospital from 2020/2 to 2021/11. Nineteen patients were male, 14 were HBV related and mean age was 61 years old. Eighteen patients were child's A, mean tumor size was 8.2cm, tumor numbers more than 2 were noted in 11 patients, 17 had PV invasion and 2 had extrahepatic metastasis. Forteen patients also received target therapies (11 received sorafenib and 3 received lenvatinib). Response could be evaluated in 19 patients. Complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) were found in 1 (5%), 4 (21%), 3 (16%) and 11 (58%) respectively. Median survival was 17 months (2-35months). Survival rates at 3, 6, 9, 12 months were 90%, 76%, 62% and 57% respectively. Patients with responses had better survival (P=0.005). Adverse events included anorexia in 6, vomiting in 5, fever in 5 and diarrhea in 3 patients. No patients developed significant liver dysfunction.
Conclusions: HAIC with modified folfox regimen was safe and effective for patients with advanced HCC.

P.026

身體肌肉及脂肪組成對於男性肝癌病患手術切除後的影響
IMPACTS OF MUSCLE AND ADIPOSE MASS ON MALE HEPATOCELLULAR CARCINOMA PATIENTS UNDERGOING RESECTION

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Background: Body composition is an objective assessment reflecting nutritional status and liver reserves. Curative resection, the standard treatment for early-staged hepatocellular carcinoma (HCC) is an energy-consuming major operation that would affect body composition.
Aims: In this study, we aimed to investigate the impact of muscle and adipose tissue on the outcome of HCC after curative resection in male patients.
Methods: From January 2013 to December 2016, 229 consecutive female patients undergoing curative resection for HCC in Taipei Veterans General Hospital were retrospectively reviewed. Skeletal muscle index (SMI), subcutaneous, visceral, intramuscular, and total adipose tissue index (SATI, VATI, IMATI, TATI) were calculated at L3 vertebral level from pre-operative computed tomography scan using Slice-O-matic software. Factors associated with survivals were analyzed.
Results: A significantly worse overall survival (OS) was noted in patients with pre-surgical lower SMI ($p < 0.001$), higher IMATI ($p < 0.001$), and lower SATI ($p = 0.005$). Otherwise, the OS could not be differentiated by VATI or TATI. Besides, baseline ALBI grade > (Hazard ratio [HR]: 1.889, $p = 0.035$), poorly differentiated tumor histology (HR: 2.748, $p = 0.001$), lower SMI (≤ 46.6 cm^2/m^2) (HR: 2.103, $p = 0.020$), higher IMATI (> 2.9 cm^2/m^2) (HR: 3.719, $p < 0.001$), and lower SATI (≤ 38.0 cm^2/m^2) (HR: 2.416, $p = 0.029$) were independent predictors of a worse OS.
Conclusions: Sarcopenia, myosteatosis, and subcutaneous adiopopenia can independently predict survival in male HCC patients undergoing surgical resection. These findings help to establish surveillance and nutrition support strategies to optimize patients' outcomes.

P.027

醫學中心大型單一顆無大血管侵犯的肝臟腫瘤之實際臨床經驗
SOLITARY LARGE HEPATOCELLULAR CARCINOMA WITHOUT MACROVASCULAR INVASION: AN EXPERIENCE FROM REAL-WORLD CLINICAL PRACTICE AT A MEDICAL CENTER.

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Background: There are some controversies about the BCLC staging system for a single large hepatocellular carcinoma (HCC) >5 cm in diameter. Solitary large HCC is classified in BCLC A in the western world, but classified in BCLC B in Taiwan. The categorization of solitary large HCC tumo may affect the treatment plan and epidemiologic statistical results, necessitating a revision in the BCLC classification.

Aims: This study aims to review real world experiences of the survival outcomes of patients with a single large HCC >5 cm without macrovascular invasion compared with other patients in BCLC stage A and stage B, with a particular focus on a comparison with existing data from our institute and tertiary medical centers.

Methods: This is a retrospective study targeting the patients who have a single large HCC > 5 cm which was newly diagnosed at our hospital from 2007 to 2018. Survival outcomes were analyzed. We compared our results with the survival data from our hospital (MMH) and tertiary medical centers of BCLC A and B patients.

Results: A total of 97 patients were enrolled in this study. Four patients who passed away either during or immediately after the surgery were excluded. Additionally, patients who declined treatment and lost follow-up were also excluded. After these exclusions, 90 patients remained for further analysis. After a median follow-up of 64.3 months, 40 (44.4%) patients died. The median OS was 86.4 months (IC 95%: 73.7-99.1) and the five-year overall survival was 61%. ± 5.3%. Upon reviewing survival data from MMH and other medical centers, MMH reported a five-year survival rate of 70.71% (56.42%-85.01%) for BCLC A patients and 49.83% (28.63%-71.02%) for BCLC B patients. Similarly, other medical centers reported a five-year survival of 76.44% (74.07%-78.81%) for BCLC A patients and 44.27% (40.34%-48.20%) for BCLC B patients. Importantly, our study's five-year survival rate was observed to fall between the reported rates for BCLC A and B patients at both MMH and other medical centers. We investigated the OS of patients after receiving surgical resection or loco-regional therapies as initial therapy. Patients who underwent surgical resection showed better outcomes vs. patients who received loco-regional therapies (median survival 95.98 months vs. 60.993 months, p=0.016). The 5 five-year overall survival was 70% after surgical resection and 32% after loco-regional therapies.

Conclusions: In conclusion, patients with a single large HCC >5 cm had an intermediate OS between BCLC A and B patients. As such, it might be more appropriate to classify the prognosis of these patients as a special group, with survival rate inferior to that of BCLC A patients yet superior to BCLC B patients. This group of patients should be classified as a new group as BCLC Ap (A+) or Bm (B-).

P.028

對於 3~5 公分的單一肝細胞癌，分別使用經皮穿刺射頻燒灼術與肝臟切除手術作為第一線治療的總存活率是相當的。
OVERALL SURVIVAL IS COMPARABLE BETWEEN PERCUTANEOUS RADIOFREQUENCY ABLATION VERSUS LIVER RESECTION AS FIRST-LINE THERAPY FOR SOLITARY 3–5 CM HEPATOCELLULAR CARCINOMA

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Background: Studies have reported ambiguous results regarding the efficacy of percutaneous radiofrequency ablation (pRFA) for early-stage hepatocellular carcinoma (HCC) with single tumor 3-5 cm.
Aims: To compare the long-term outcomes of liver resection (LR) and percutaneous radiofrequency ablation (RFA) for the treatment of solitary 3–5 cm hepatocellular carcinoma (HCC).
Methods: From 2011 to 2021, patients with Child-Pugh class A liver disease and solitary 3–5 cm HCC without macrovascular invasion or extrahepatic metastasis who underwent LR or percutaneous RFA were enrolled in this retrospective study. There were 310 patients undergoing LR and 114 patients undergoing percutaneous RFA. The primary end point was overall survival (OS); the secondary end point was recurrence-free survival (RFS). Propensity score matching (PSM) was used to balance baseline variables including age, sex, alpha-fetoprotein (AFP) and Model for End-Stage Liver Disease (MELD) score between the two groups.
Results: Before PSM, 5-year OS and RFS were significantly lower in the percutaneous RFA group than in the LR group (both p values were <0.001). After PSM, the 5-year OS was comparable between two modalities (p=0.367); however, the 5-year RFS was significantly lower in the RFA group than in the LR group (p=0.001).
Conclusions: Percutaneous RFA might be a first-line alternative to LR for solitary 3–5 cm HCC in selected patients, especially for patients unsuitable for LR.

P.029

罹患早期肝細胞癌之慢性 C 肝患者使用全口服抗病毒藥物治療後之腫瘤復發：治療前後甲型胎兒蛋白序列變化之預測性
TUMOR RECURRENCE FOR CHRONIC HEPATITIS C PATIENTS WITH EARLY-STAGE HEPATOCELLULAR CARCINOMA AFTER THERAPY WITH ALL ORAL DIRECT-ACTING ANTIVIRALS: PREDICTIVE VALUE BY DYNAMIC CHANGES IN AFP VALUE

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Background: The therapeutic landscape of chronic hepatitis C (CHC) evolved dramatically after the invention of all-oral direct-acting antivirals (DAAs). DAAs-induced sustained virological response (SVR) resulted in reduced future hepatocellular carcinoma (HCC) development, risk of liver-related and all-cause mortality. For patients with CHC-related HCC after anti-cancer therapy, the clinical benefits of DAAs treatment in preventing HCC recurrence and risk factors responsible for tumor recurrence after DAAs remained to be clarified. Previous studies suggested that either pre-DAAs or post-DAAs alpha-fetoprotein (AFP) level might be helpful to predict tumor recurrence.
Aims: To examine the role of dynamic changes in AFP value before and after DAAs therapy and the predictive value on recurrent HCC.
Methods: Between January 2017 and August 2021, 208 CHC-HCC patients underwent DAAs treatment at Taipei Veterans General Hospital. Among them, 94 patients met the inclusion criteria (Barcelona clinic liver cancer [BCLC] stage 0/A after treatment with complete radiological response) for analysis. History of liver transplantation or active HCC before DAAs treatment, short follow-up period (< 0.5 year) after DAAs initiation and patients with intermediate or advanced HCC (BCLC stage B, C, D) were excluded. Using a cutoff value of 10 ng/mL, the enrolled patients were categorized into different groups based on dynamic changes in AFP values before and after DAAs treatment, and investigate its impact on recurrent HCC.
Results: The mean age of the enrolled patients was 75.9 ± 8.9 years; 44.7% were male, and 94.7% were Child-Pugh class A. Before DAAs treatment, 31.9% experienced HCC

recurrence. The median follow-up after DAAs treatment was 22.1 months (interquartile range, 8.6-35.9 months). After treatment, 95.7% of the patients achieved a sustained virological response (SVR 12), but HCC recurrence occurred in 54.3%. Cumulative HCC recurrence rates after treatment were 31.1% at 1 year, 57.3% at 3 years, and 68.5% at up to 5.69 years. Notably, none of our patients experienced a transition from low (≤10 ng/mL) to high (>10 ng/mL) AFP values after DAAs treatment, leaving only three groups for analyses. Intriguingly, patients with consistently high AFP values (> 10 ng/mL) before and after DAA treatment had the highest risk of HCC recurrence. In this group, the cumulative incidence of HCC recurrence was 66.7% at 1 year, 75.0% at 2 years, 75% at 3 years, and 87.5% at 4 years, and the difference was significant compared to the other two groups (P <0.01). Conversely, patients whose AFP values declined from high (>10 ng/mL) to low (≤10 ng/mL) after DAAs treatment had the lowest incidence of HCC recurrence, with a cumulative incidence rate of 14.3% at 1 year, 29.5% at 2 years, and 40.4% at 3 years.

Conclusions: Our real-world data suggested for patients with CHC-related HCC after anti-cancer therapy with complete radiological response, DAAs treatment can reduce the elevated AFP levels attributed to the hepatitis activity of CHC, making the monitoring of carcinogenic properties easier. Our study demonstrated that the dynamic changes in AFP values before and after DAAs therapy were helpful to predict HCC recurrence.

P.030

比較白蛋白為基準的肝臟功能模型 與MELD 3.0 對肝癌合併腎功能不全合患者的預後

ALBUMIN-BASED LIVER RESERVE MODELS VS MELD 3.0 IN PROGNOSTIC PREDICTION FOR HEPATOCELLULAR CARCINOMA PATIENTS WITH RENAL INSUFFICIENCY

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Background: The severity of liver functional reserve is a crucial predictor in hepatocellular carcinoma (HCC). Four albumin-based models, albumin-bilirubin (ALBI), easy (EZ)-ALBI, platelet-albumin-bilirubin (PALBI) and platelet-albumin (PAL) score, are used to evaluate the severity of liver dysfunction. More recently, model for end-stage liver disease (MELD) 3.0 score was proposed in the liver transplant setting. However, their prognostic role in HCC patients specifically with renal insufficiency (RI) is unclear.

Aims: We aimed to investigate the predictive accuracy of the five models in these patients.

Methods: A total of 1,120 newly diagnosed HCC patients with RI were enrolled. Multivariate Cox proportional analysis was used to identify independent predictors associated with survival.

Results: In the Cox model, older age, α-fetoprotein ≥ 20 ng/mL, vascular invasion, medium and high tumor burden score, performance status (PS) 1-2, PS 3-4, ALBI grade 2 and grade 3, EZ-ALBI grade 2 and grade 3, PALBI grade 2 and grade 3, PAL grade 2 and grade 3, MELD 3.0 score between 10 and 14 and sore > 14, were all independently associated with decreased overall survival (all p<0.001). Among the five liver reserve models, ALBI score had the lowest corrected Akaike information criteria (AICc) with the highest homogeneity value, followed by PALBI and EZ-ALBI score.

Conclusions: The albumin-based liver reserve models (ALBI, EZ-ALBI, PALBI and PAL) and MELD 3.0 all are feasible prognostic markers to indicate liver injury specifically in HCC patients with RI. Among them, ALBI grade is the most robust tool for survival prediction in these patients.

P.031

不可切除肝細胞癌患者以免疫治療為基礎的一線全身治療的臨床分析—醫學中心經驗
CLINICAL ANALYSIS OF THE IMMUNOTHERAPY-BASED FIRST-LINE SYSTEMIC THERAPY FOR PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA - EXPERIENCE AT A MEDICAL CENTER

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Background: Hepatocellular carcinoma (HCC) represents a major global health challenge due to its increasing incidence and limited therapeutic options, especially in the case of unresectable tumors. Recent advancements in immunotherapy, particularly the use of Atezolizumab plus Bevacizumab (A+B) and other immune checkpoint inhibitors (ICIs), have opened new horizons for the management of unresectable HCC.

Aims: This study aims to present real-world experiences utilizing immunotherapy-based first-line systemic therapy for the treatment of unresectable HCC in a single medical center.

Methods: We retrospectively reviewed the medical records of patients with unresectable HCC in MacKay Memorial Hospital from Jan. 1st, 2020, to Jul. 31st, 2023. The patients who received immunotherapy-based first-line systemic therapy were enrolled. Mann-Whitney U test and Fisher exact test were applied for the analysis of potential risk factors between patients received the immunotherapy-based first-line therapy with atezolizumab plus bevacizumab (A+B group) and non atezolizumab plus bevacizumab (Non A+B group). According to the Kaplan-Meier method, overall survival (OS) and progression-free survival (PFS) curves were used to compare the difference between two groups.

Results: A total of 28 patients with unresectable HCC were enrolled and comprised of two groups; the A+B group (n = 15) and the Non A+B group (n = 13). 66.6% of patients were male and the mean age was 61.6±13.6 years. There were no differences between A+B and Non A+B groups in age, sex, Child - Pugh class, ALBI grade, BCLC stage, liver cirrhosis, total-bilirubin level, and extra-hepatic spread number. However, there were significant differences in infiltrative HCC ($p<0.05$). There was no significant difference in overall survival and progression-free survival curves between the A+B and the Non A+B groups ($p =0.77$ and 0.175). The median PFS of the A+B group and the Non A+B group was 8.3 months and 3.5 months, respectively. The median OS in the A+B group and Non A+B group was16.7 months and 14.4 months, respectively.

Conclusions: Although there is no significant difference in our real-world data, the patients with unresectable HCC receiving atezolizumab plus bevacizumab as immunotherapy-based first-line systemic therapy have a trend of longer median OS and PFS. Further prospective studies are necessary to draw a definitive conclusion.

P.032

PIVKA-II 用於預測胎兒蛋白正常之肝癌病患的預後
THE ROLE OF SERUM PIVKA-II LEVELS IN PREDICTING THE OUTCOMES OF PATIENTS WITH HEPATOCELLULAR CARCINOMA AND WITH NORMAL SERUM ALPHA FETOPROTEIN LEVELS

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Background: Alpha-fetoprotein (AFP) is a widely applied tumor marker for diagnosis and prognosis of hepatocellular carcinoma (HCC). Clinically, a substantial proportion of patients with HCC have normal serum AFP levels even in advanced tumor stages. Protein induced by vitamin K absence or antagonist-II (PIVKA-II) is a new tumor marker for HCC.
Aims: We aimed to investigate the role of PIVKA-II in predicting the outcomes of patients with HCC and with normal serum AFP levels.
Methods: We retrospectively reviewed 278 HCC patients with normal serum AFP levels (≤ 7 ng/mL), who were diagnosed in Taipei Veterans General Hospital from 2020 to 2023. Overall survival (OS) rates were calculated by the Kaplan–Meier method and compared by the log-rank test. The area under receiver operating characteristic curves (AUROC) was calculated to evaluate the predicted probability of survival by serum PIVKA-II.
Results: Among the enrolled patients, 143 (51.4%) patients had high serum level of PIVKA-II (> 100 mAU/L). Patients with high serum PIVKA-II levels had more tumor burden (including tumor number and tumor size), more macrovascular invasion and extrahepatic metastasis compared to those in the low PIVKA-II group. However, the grades of liver functional reserves, including serum albumin, bilirubin levels, platelet counts, and Child-Pugh class, were not significantly different between high and low PIVKA-II groups. A significantly worse OS was noted in patients with high PIVKA-II compared to the counterpart ($p < 0.001$). According to the AUROC, the performance of PIVKA-II was superior to the albumin-bilirubin grade, AST to platelet ratio index (APRI), fibrosis-4 score and the MELD score in predicting OS.
Conclusions: In HCC patients with normal serum AFP levels, the serum PIVKA-II level was associated with OS.

P.033

對侵犯性肝癌或不適合以動脈栓塞治療之 INTERMEDIATE STAGE HCC 接受動脈化學治療或免疫治療後接受根除性治療的預後探討
PROGNOSTIC EVALUATION OF CURATIVE TREATMENT FOLLOWING ARTERIAL CHEMOTHERAPY OR IMMUNOTHERAPY IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA OR INTERMEDIATE-STAGE HCC UNSUITABLE FOR ARTERIAL EMBOLIZATION

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Background: Treatment options for advanced hepatocellular carcinoma (HCC) or intermediate-stage HCC unsuitable for Transarterial Chemoembolization (TACE) are limited, with a generally poor prognosis. Sorafenib, a traditional treatment, extends survival but often fails to sufficiently induce tumor necrosis or a satisfactory disease control rate (DCR). Emerging evidence suggests that both arterial chemotherapy and immunotherapy can achieve significant tumor necrosis and improve survival. However, the role of curative treatment following successful tumor shrinkage in enhancing prognosis remains underexplored.
Aims: This study hypothesizes that liver cancer patients who undergo curative treatment after tumor shrinkage from complete cycles of arterial chemotherapy or immunotherapy will exhibit improved prognoses compared to those who do not receive such treatment.
Methods: A retrospective analysis was conducted on 97 patients with advanced or intermediate-stage HCC unsuitable for TACE, treated between 2016 and 2023. Demographic data were collected, and statistical significance for continuous and categorical variables was established using t-tests and chi-square tests, respectively. Subsequent survival analysis and multivariate analysis were performed.
Results: Among the 97 patients, nine underwent successful curative therapy (seven through curative surgery and two via Radiofrequency Ablation) following arterial chemotherapy or immunotherapy. These patients demonstrated a superior prognosis compared to those who did not receive curative treatment. Subgroup analyses

further highlighted better outcomes in comparison to the CR/PR group.

Conclusions: The study indicates that in the selected liver cancer cohort, patients with advanced or intermediate-stage HCC, unsuitable for TACE, who received curative treatments post-therapy, experienced significantly improved prognoses. This finding emphasizes the potential benefits of integrating curative interventions in the treatment regimen for such HCC patients.

P.034

病理定義 T1B 之大顆肝細胞癌患者接受切除手術後影響其存活率的特徵及預後因子
CHARACTERISTICS AND PREDICTOR OF SURVIVAL OUTCOME IN PATIENTS WITH LARGE PATHOLOGY-DEFINED T1B HEPATOCELLULAR CARCINOMA UNDERGOING RESECTION

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Background: As tumor size increase, the risk of microscopic vascular invasion (MVI) increase in patients with hepatocellular carcinoma (HCC). However, large T1b HCC (i.e., >5.0 cm without MVI) was noted in a small proportion of patients with HCC undergoing liver resection (LR).

Aims: We aim to clarify characteristics and predictor of survival outcome in this special population.

Methods: We enrolled 126 patients with HCC of pathological stage T1bN0M0 of the 8th edition of American Joint Committee on Cancer staging and tumor size > 5.0 cm who underwent LR between 2007 and 2021 at our institution. To identify prognostic factors, a multivariate regression analysis was performed using the Cox proportional hazards model with $p<0.05$ in univariate analysis.

Results: Cirrhosis was noted in 27 (21.4%) patients, poor tumor differentiation was noted in 3(2.4%) patients. the 5-year overall survival (OS) is 79 %; the 5-year recurrence-free survival (RFS) is 60%. univariate analysis showed that poor tumor differentiation was the only factor associated 5-year OS (HR=14.687; 95%CI=4.096-52.670; $p<0.001$). multivariate analysis showed that poor tumor differentiation was the only factor associated 5-year RFS (HR=6.711; 95%CI=1.989-22.644; $p=0.002$).

Conclusions: The survival outcome of this special population was good. Around 80% of these patients were non-cirrhotic. Poor tumor differentiation was the only factor associated with survival outcome.

P.035

注射吸毒者之病毒性肝炎感染的預防：系統性文獻回顧與統合性分析
PREVENTION OF VIRAL HEPATITIS INFECTION AMONG PEOPLE WHO INJECT DRUGS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: People who inject drugs (PWID) and engage in associated risk behaviors have become a significant public health concern, especially given the rapid spread of the human immunodeficiency virus (HIV) and hepatitis C virus (HCV). With similar modes of transmission for HIV-1, hepatitis B virus (HBV), and HCV—primarily through contact with infected blood—administering combination drug therapy to patients co-infected with both HIV/HBV and HIV/HCV could potentially compromise effectiveness due to the emergence of drug resistance. Additionally, prolonged use of such treatments may have adverse effects on liver function.

Aims: This study aims to explore various intervention approaches aimed at reducing the incidence of blood-borne infectious diseases and to review existing evidence for preventing viral hepatitis and HIV infections within this specific population. The research includes a comprehensive meta-analysis and a thorough literature review. In response to the World Health Organization's goal of eliminating viral hepatitis by 2030, this study aims to explore current evidence on preventing blood-borne virus infections among PWIDs.

Methods: We conducted a comprehensive search across three databases (PubMed, Embase, Cochrane Library) for relevant articles published in English between 2014 and 2023. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, assessed the paper's quality using the revised Cochrane Risk of Bias Tool (ROB 2), and conducted a meta-analysis using Review Manager Software version 5.3 (RevMan 5.3).

Results: Completion of the harm reduction program (HRP) and receiving all three vaccine doses resulted in a 28% reduction in the risk of HBV infection (OR = 0.72, 95% CI = 0.37–1.42, p-value = 0.34). Multiple interventions, such as peer outreach, mobile health, financial incentives, onsite HCV care, and vertically integrated HCV testing, significantly enhanced the willingness of PWIDs in the intervention group to undergo HCV treatment (OR: 5.91, 95% CI: 2.46 – 14.24, $p < 0.0001$). These interventions also promoted treatment adherence (OR: 15.04, 95% CI: 2.80 – 80.61, $p = 0.0002$) and increased the likelihood of achieving an HCV cure (OR: 1.53, 95% CI: 0.81 – 2.89, $p = 0.19$) compared to the control group.

Conclusions: While this study provided a comprehensive assessment of blood-borne infection prevention strategies tailored to PWIDs, it is important to recognize that their impact may be limited when drug resistance is a factor.

P.036

台灣自體免疫性肝炎病人的完全生化反應與肝硬化風險相關
COMPLETE BIOCHEMICAL RESPONSE ASSOCIATED WITH REDUCED CIRRHOSIS RISK IN TAIWANESE PATIENTS WITH AUTOIMMUNE HEPATITIS

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Background: Autoimmune hepatitis (AIH) is a rare disease and may advance to cirrhosis. Rapid treatment response has been shown to be associated with favorable outcomes, while delayed response may indicate patients who need an alternative therapy.
Aims: This study aimed to evaluate the relationship of treatment response and long-term outcomes in Taiwanese patients with AIH.
Methods: This retrospective cohort study included 37 histologically confirmed AIH patients undergoing prednisolone treatment at National Taiwan University Hospital. Patients were categorized into complete biochemical response (CBR), insufficient response (IR), and non-response (NR) groups based on the International Autoimmune Hepatitis Group (IAIHG) response endpoints proposed in 2022. The primary endpoint was cirrhosis development.
Results: Of the diagnosed AIH patients, 9 patients had cirrhosis and 28 patients did not. Nearly half of cirrhotic patients were noted in the NR group (NR vs non-NR:57.1% vs 16.7%, $p<0.05$). Over a median follow-up period of 53 months, 5 non-cirrhotic patients progressed to cirrhosis, and 2 patients developed HCC. The cirrhosis progression rate was lower in the CBR group compared with the IR and NR groups (5.6% vs. 28.6% vs. 66.7%, $p<0.05$). None of the CBR patients developed HCC.
Conclusions: Cirrhotic patients at the time of AIH diagnosis tended to be have poor treatment response. A rapid treatment response was associated with a lower risk of cirrhosis.

P.037

褪黑激素對肝硬化大鼠臟器血流動力學及門脈系統側枝循環之影響
MELATONIN ALLEVIATED SPLANCHNIC HYPERDYNAMIC CIRCULATION AND PORTOSYSTEMIC COLLATERALS IN CIRRHOTIC RATS.

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Background: Chronic liver damages may end up with cirrhosis and portal hypertension, featured by splanchnic hyperdynamic circulation, angiogenesis and collaterals formation. Melatonin is used to improve sleep quality, which exerts anti-inflammatory, anti-angiogenesis and vascular actions without significant side effects. However, the relevant impacts on aforementioned derangements are unclear.
Aims: To investigate the relationship between Melatonin and splanchnic hyperdynamic circulation and portosystemic collaterals in cirrhotic rats.
Methods: Liver cirrhosis was induced by bile duct ligation in Sprague-Dawley rats. The rats received melatonin (40 mg/kg/day, i.p.) or vehicle for 28 days. Experiments were performed on the 28 th day when cirrhosis developed.
Results: In cirrhotic rats, melatonin treatment significantly increased superior mesenteric artery resistance and reduced the blood flow. Melatonin enhanced the portosystemic collateral responsiveness to arginine vasopressin, reduced mesenteric vascular area, shunting degree and down-regulated mesenteric MMP-2 protein expression.
Conclusions: Melatonin improved the splanchnic hyperdynamic circulation, portosystemic collateral shunting and mesenteric angiogenesis in cirrhotic rats. These beneficial effects make melatonin potentially feasible in clinical setting, but further investigation is required.

P.038

新冠病毒感染與超音波量測脾腫大相關性之回溯性研究
CORRELATION OF SONOGRAPHIC SPLEEN SIZE AND SARS-COV-2 INFECTION. A RETROSPECTIVE STUDY.

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Background: The SARS-CoV-2(COVID-19) infection is not just a disease of the respiratory system. Documented reports have shown that the notorious global pandemic disease could affect the gastrointestinal tract, liver, gallbladder and splenomegaly. A recent study indicated that spleen size increased moderately in the first stages of the infection, and that this increase is correlated with the severity of the COVID-19 pneumonia. However, the study relied on CT scan. There is no study on correlation between spleen size and COVID infection using sonography as approach.

Aims: The objective of this study is to determine the significance of changes in splenic diameters after COVID-19 infection compared with the control group, utilizing sonography as the diagnostic tool.

Methods: Between October 1, 2022, and February 28, 2023, we enrolled 201 patients with regular sonography follow-up for our study. Among these patients, we obtained data on the date of COVID infection and demographic information. All enrolled patients were categorized into either the COVID or non-COVID group. Spleen size changes before and after COVID infection in the COVID group were analyzed and compared with the data from a similar time period in the non-COVID group.

Results: A total of 201 patients (104 males, 51%) were included in the study, comprising 92 COVID-infected patients (COVID group) and 109 patients naïve to COVID (non-COVID group). The mean time between COVID infection and abdominal echo date was 131.0 days. Patients in the COVID group had a significantly higher mean splenic diameter difference percentage (S%) of 2.64±3.85 compared to the S% of the non-COVID group (0.88±3.55) (p=0.02, 95% CI). The liver diameter difference percentage (L%) was higher in the COVID group but statistically insignificant (p=0.27). Subgroup analysis within the COVID group revealed no additional risk factors that increased the splenic diameter difference percentage (S%), including hepatitis B, hepatitis C, thalassemia, BMI, and other notable compounding factors.

Conclusions: Our data support the notion that spleen size increases in COVID-infected patients compared with non-COVID-infected patients, while the increase in liver diameter remained statistically insignificant.

P.039

肺血管通透性指數和血管外肺水指數在肝硬化患者合併敗血性休克的角色
PULMONARY VASCULAR PERMEABILITY AND EXTRAVASCULAR LUNG WATER INDEX IN PATIENTS WITH LIVER CIRRHOSIS AND SEPTIC SHOCK

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Background: Patients with cirrhosis are susceptible to bacterial infection, which may result in sepsis, septic shock, multiple organ failure, and a decreased survival rate. Cirrhotic patients also have increased capillary permeability and are prone to develop volume overload. Patients with septic shock may develop acute lung injury, characterized by enhanced pulmonary vascular permeability index (PVPI) and extravascular lung water index (EVLWI), both of which are associated with an unfavorable prognosis. It is plausible that pre-existing increased capillary permeability may further deteriorate when cirrhotic patients develop sepsis and septic shock. However, it remains unknown whether PVPI and EVLWI can predict the prognosis of cirrhotic patients with septic shock. Transpulmonary thermodilution (TPTD) is an established tool to monitor the hemodynamics in critically ill patients, which enables clinicians to calculate PVPI and EVLWI.

Aims: We conducted this retrospective study to investigate the prognostic significance of PVPI and EVLWI in cirrhotic patients with septic shock using TPTD (PiCCO, Pulsion Medical Systems, Germany).

Methods: In this retrospective study, we included 83 patients with liver cirrhosis and septic shock, in whom PiCCO was used to monitor hemodynamics. EVLW indexed to actual body weight (aEVLWI), EVLW indexed to predicted body weight (pEVLWI), PVPI, disease severity scores, and other biomarkers of septic shock were analyzed. We collected the data of aEVLWI, pEVLWI, and PVPI on the first 2 days.

Results: The overall 28-day mortality was 43.3 %. The non-survivors had higher disease severity scores, and lactate levels. PVPI on day 1 was significantly higher in no-survivors, while both aEVLWI, and pEVLWI on day 1 were not significantly different between survivors and non-survivors. The values of PVPI, aEVLWI, and pEVLWI on day 2 were significantly higher in non-survivors. The discriminating power of PVPI and EVLWI on day 2 to predict 28-day mortality was tested using the area under a ROC curve. The areas under ROC curves (mean ± SEM) were 0.713 ± 0.061, 0.660 ± 0.063 and 0.650 ± 0.063 for PVPI, aEVLWI, and pEVLWI on day 2 respectively. When stratified according to PVPI on day 2 (PVPI D2), those patients with higher PVPI D2 (>2.65) had higher levels of CRP (89.89 vs. 56.50 mg/L, p=0.016) and higher rates of 28-day mortality (82.6 % vs. 28.3 % p<0.001). In multivariate analysis, PVPI D2, MELD score and lactate were independent factors to predict 28-day mortality.

Conclusions: Higher levels of PVPI D2 are associated with a more pronounced inflammatory state and higher 28-day mortality rates.

第二部分：消化道及膽胰疾病

P.040

氫離子幫浦抑制劑對於肝癌合併中大型食道靜脈曲張病患之影響
EFFECT OF PROTON PUMP INHIBITOR IN HEPATOCELLULAR CARCINOMA PATIENTS WITH MEDIUM/LARGE ESOPHAGEAL VARICES

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Background: Proton pump inhibitor (PPI) are frequently used for gastrointestinal disease. In patients with liver cirrhosis, prolong using PPI may have negative effects and there was controversial evidence in patients with HCC. However, there is limited evidence of the effect of using PPI in HCC patients with esophgeal varices (EVs), especially in patients with medium/large EVs.
Aims: This study aimed to assess the impact of PPIs on adverse events in HCC patients with medium/large EVs.
Methods: We retrospectively enrolled HCC patients who received an esophagogastroduodenoscopy at the time of HCC diagnosis in Taipei Veterans General Hospital. Among them, 64 patients had large EV (F2 and/or F3) included. Thirty-nine patients received PPI and 25 patients didn't.
Results: During a median follow-up of 6.4 months (IQR 2.2-20.9 months), 59 patient dead and the remaining 5 patients alive at their last visit. In patients receiving PPI the median duration of therapy is 0.5 months (IQR 0-3.0 months). Cumulative overall survival between patients with PPI therapy or without were comparable (p=107). There were also similar cumulative variceal bleeding between two groups (p=0.222).
Conclusions: PPI use may not be associated with survival and variceal bleeding in cirrhotic patients with HCC and medium/large esophageal varices. However, further large prospective study is warranted.

P.041

比較內視鏡靜脈曲張結紮術與 PROPRANOLOL 對預防肝癌患者併發食道靜脈曲張首次出血：一個開放、雙中心、隨機對照試驗
ENDOSCOPIC VARICEAL LIGATION VERSUS PROPRANOLOL FOR THE PRIMARY PREVENTION OF ESOPHAGEAL VARICEAL BLEEDING IN PATIENTS WITH HEPATOCELLULAR CARCINOMA: AN OPEN-LABEL, TWO-CENTER, RANDOMIZED CONTROLLED TRIAL

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Background: According to the Baveno VII consensus, treatment with non-selective beta-blockers (NSBBs) should be used to prevent decompensation in patients with clinically significant portal hypertension. Endoscopic variceal ligation (EVL) is recommended for compensated patients with high-risk esophageal varices (EVs) who have contraindications or an intolerance to NSBBs. However, no randomized trials have directly compared the efficacy of EVL and NSBBs in the primary prevention of esophageal variceal bleeding (EVB) in patients with hepatocellular carcinoma (HCC).
Aims: This randomized trial aimed to address whether EVL or propranolol (PPL) is more effective at preventing initial EVB in patients with HCC.
Methods: Patients with HCC and medium-to-large EVs but without previous EVB were randomized to receive EVL (every 3-4 weeks until variceal eradication) or PPL (up to 320 mg daily) at a 1:1 ratio. Long-term follow-up data on EVB, other upper gastrointestinal bleeding (UGIB), nonbleeding liver decompensation, overall survival (OS), and adverse events (AEs) were analyzed using competing risk regression.

Results: Between June 2011 and April 2021, 144 patients were randomized to receive EVL (n=72) or PPL (n=72). In the EVL group, 7 patients experienced EVB, and 30 died; in the PPL group, 19 patients had EVB, and 40 died. The EVL group had a lower cumulative incidence of EVB (Gray's test, p=0.009) than its counterpart, with no mortality difference (Gray's test, p=0.085). For patients with Barcelona Clinic Liver Cancer (BCLC) stage A/B, EVL was better than PPL in reducing EVB (p<0.001) and mortality (p=0.003). For patients beyond BCLC stage B, between-group outcomes were similar. Other UGIB, nonbleeding liver decompensation, and AEs did not differ between groups. A competing risk regression model confirmed the prognostic value of EVL.
Conclusions: EVL is superior to PPL in preventing initial EVB in patients with HCC. The benefits of EVL on EVB and OS may be limited to patients with BCLC stage A/B and not to those with BCLC stage C/D.

P.042

冷套圈瘜肉切除術在胃瘜肉的臨床實用 - 單一醫學中心經驗
THE CLINICAL UTILITY OF COLD SNARE POLYPECTOMY FOR THE GASTRIC POLYPS - A SINGLE MEDICAL CENTER EXPERIENCE

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Background: Cold snare polypectomy(CSP), a safe removal technique, may still lead to adverse events like delayed bleeding and perforation. Factors such as large size, anticoagulant use, thick-stalked pedunculated lesions, and patient comorbidities elevate the risk of post-polypectomy bleeding. Histological analyses indicate that cold snare polypectomy is less damaging to submucosal blood vessels, resulting in a lower incidence of hemorrhage compared to conventional hot snare polypectomy(HSP). Our study aims to compare the rates of complication, including delayed post-polypectomy bleeding(DPPB) and perforation, associated with cold snare polypectomy and conventional hot snare polypectomy.
Aims: To assess the situation of complications associated with esophagogastroduodenoscopy (EGD) following snare polypectomy, encompassing both hot and cold snare techniques, in patients diagnosed with gastric polyps.
Methods: The medical records of patients with upper GI tract polyp in Taipei branch of MacKay Memorial Hospital from Jan. 1st, 2020 to Oct. 31th, 2023 were reviewed retrospectively. Patients with appropriate indications for polypectomy and histologically confirmed polyps were enrolled in the study. The Chi-square test and t-test were utilized to analyze the clinical background differences and associated complications between patients receiving cold snare polypectomy and conventional hot snare polypectomy.
Results: During the study period, 184 patients diagnosed with gastric polyps underwent treatment either through CSP or HSP. Of these, 20 patients were excluded from the analysis; this exclusion was attributed to either having undergone both HSP and CSP (n = 3) or having additional polypectomy procedures for esophageal or duodenal polyps simultaneously (n = 17). Post-procedural adverse events encompass clinically significant bleeding, referred

to as delayed post-polypectomy bleeding(DPPB), which was defined as the need to visit the emergency department or receiving intervention (such as repeat endoscopy, angiography, or surgery) within one day. Additionally, delayed perforation within 30 days following the procedure was also considered as another adverse event. The HSP group consisted of 10 men and 42 women, with a mean age of 55.4±16.0 years. In contrast, the CSP group included 30 men and 72 women, with a mean age of 55.0±13.0 years. The prevalence of the histological type depicted in Picture 1. The characteristics of size, location and histology type of polyps are also shown in Table 1. The count of polypectomies performed via CSP and HSP were presented in Table 2. The characteristics of resected polyps were similar between the two techniques except histology type. The mean polyp size was 0.98cm in the HSP group and 0.84cm in the CSP group(P = 0.032). Cases of patients with HSP were more likely to have a more frequent use of prophylactic clip (43.8% vs 75%, P<0.001) than those with CSP. During the resection of multiple polyps (more than 2), there was a higher observed incidence of CSP compared to HSP (p=0.002).

Conclusions: A prior study suggested that patients who underwent HSP experienced a higher rate of DPPB and perforation attributed to thermal injury. Our analysis revealed that patients undergoing conventional HSP, as opposed to those undergoing CSP, did not exhibit a significant occurrence of complication, including DPPB and perforation. This is likely due to the routine use of prophylactic clip placement to prevent them.

P.043

樣貌多變且高致死率的胃黑色素瘤
VARIABLE PRESENTATION AND HIGH MORTALITY OF GASTRIC MELANOMA

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Background: Melanoma, originating from melanocytes, represents a cutaneous malignancy with the BRAF oncogene frequently implicated in its genetic mutations. Notably, primary gastric melanoma is an exceedingly rare occurrence, as the majority of gastric melanomas are secondary to metastasis.

Aims: In this study, we aim to present a case series sourced from a medical center in central Taiwan, encompassing clinical symptoms, endoscopic findings, and outcomes.

Methods: In this retrospective study, we meticulously gathered data covering the period from 2003 to 2021. Those patients were unequivocally diagnosed with gastric melanoma, a determination supported by concrete pathological evidence.

Results: A total of 10 patients were enrolled, one was primary gastric melanoma the others were metastatic melanoma originating from various sites, including skin (6/9), buccal mucosa (1/9), esophagus (1/9), and conjunctiva (1/9). The prevalent clinical presentation among these cases was gastrointestinal bleeding (7/10) and epigastric discomfort (3/10). The endoscopic findings of metastatic gastric melanoma revealed a main submucosa tumor (usually 1 cm, the maximal size was 2.5 cm) characterized by central ulceration with black pigmented base, occasionally accompanied by small nodules. The number of submucosal masses varied, with most cases having 2-4 nodules (6/9), while a single nodule (1/9) and multiple nodules (>5 nodules, 2/9) were also observed. One case presented as amelanotic melanoma. The endoscopic finding of the primary gastric melanoma presented as black pigmented ulcerative mass (2.0 cm). The distribution of gastric melanoma was mostly observed in the body and cardia, with instances in the antrum and fundus. It's noteworthy that the majority of patients with metastatic melanoma succumbed within one year of diagnosis.

Conclusions: Gastric melanoma is uncommon in Taiwan people. In this case series, we could see that the gastric melanoma presented as submucosa tumor with black pigmented base ulcer but it could be amelanotic. Gastric melanoma demonstrates a poor outcome, as indicated by our study, wherein all cases of metastatic gastric melanoma succumbed within one year. Notably, primary gastric melanoma cases showed survival for more than one year, possibly attributed to the benefits of immunotherapy, which has shown promise in extending survival times.

P.044

在難治型胃食道逆流病人接受抗逆流黏膜灼燒手術後能停止使用氫離子幫浦阻斷劑的決定因子

DETERMINING FACTORS FOR DISCONTINUATION OF PPIS IN REFRACTORY GERD PATIENTS AFTER ANTI-REFLUX MUCOSAL ABLATION (ARMA)

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Background: The prevalence of proton pump inhibitor (PPI)-refractory gastroesophageal reflux disease (GERD) has been increasing recently. There's been a novel less invasive anti-reflux procedure in recent years. Anti-reflux mucosal ablation (ARMA), one of endoscopic anti-reflux procedures, represents an innovative and minimally invasive approach in managing GERD. The clinical outcomes in PPI-free patients after ARMA are scarcely reported.

Aims: This study aims to evaluate determining factors for discontinuation of proton pump inhibitors (PPIs) in refractory GERD patients after anti-reflux mucosal ablation (ARMA).

Methods: From September 2022 to August 2023, we conducted a prospective, single-center, single-arm interventional study on patients of PPI-refractory GERD with Hill's flap grade II/III. ARMA was carried out utilizing Hybrid Argon plasma coagulation (HybridAPC). Additionally, in patients diagnosed with Barrett's esophagus, Barrett's ablation was concurrently performed using HybridAPC during the same session. Esophagogastroduodenoscopy (EGD), high-resolution esophageal manometry, 24-hour pH impedance testing, and GERD questionnaires were evaluated before and three months after the ARMA procedure.

Results: A total of 13 patients (10 males, 3 females) underwent ARMA with a mean age 41.31 ± 14.9 years old, and five of the patients also received concurrent Barrett's ablation. A 100% technical success rate was attained among all patients, and subsequent follow-up EGD demonstrated the reduction of Hill's flap and the presence of a normal-appearing neo-squamocolumnar junction in each individual. The mean DeMeester score and acid exposure time based on pH monitoring also improved after the therapy, from 59.30 to 18.13 and from 18.2% to 3.1%, respectively. Notable reductions were observed in the post-ARMA GERD questionnaire scores, from 20.76 to 7.75 in FSSG, from 17 to 6.17 in RSI, and from 17 to 5 in GERD-HRQL. Among these 13 patients, 6 were refractory GERD, 2 were functional heartburn, 9 were abnormal esophageal motility, and the Hill grade from II to III were 4 and 9. There were 2 patients with Butterfly-shape ablation, and others 11 were U-shape ablation. 3 of 6 in refractory GERD (p=0.429), 8 of 13 with hiatal hernia(p=0.501), 1 of 2 in functional heartburn (p=0.715), 6 of 9 in abnormal esophageal motility (p=0.569), and 8 of 11 in U-shape (p=0.052) were PPI-free after ARMA. Two patients (15.3%) experienced transient epigastric pain, while vomiting was observed in two patients (15.3%). One patient (7.6%) encountered delayed bleeding (5 days after ARMA). Furthermore, there were no instances of perforation or stenosis observed among the patients.

Conclusions: Our experience has demonstrated that ARMA is a promising and safe endoscopic solution for PPI-refractory GERD. Moreover, it brings about improvements in both objective acid reflux indicators and GERD-related symptoms in terms of short-term outcomes. And it had a trend in patients with U-shape ablation were PPI-free after ARMA. It still needs further comprehensive study in the future.

P.045

無症狀胃部固有肌肉層之黏膜下腫瘤的預後和追蹤 - 醫學中心經驗
THE OUTCOME AND SURVEILLANCE OF ASYMPTOMATIC SMALL GASTRIC SUBEPITHELIAL LESIONS FROM MUSCULARIS PROPRIA - EXPERIENCE OF A MEDICAL CENTER

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Background: Gastric subepithelial lesions (SEL) are typically discovered incidentally during routine esophagogastroduodenoscopy (EGD). The lesions originated from the muscularis propria (MP) layer encompass a diverse range of tumors, from benign to potentially malignant. Histopathology decided the optimal management of asymptomatic gastric SEL, although invasive intervention is not recommended for lesion of small size (≤ 2cm). Currently, there is limited evidence regarding the natural course and surveillance strategy for these lesions.

Aims: We aim to elucidate the natural progression of small (≤ 2cm) gastric SEL originating from the MP layer and optimal surveillance interval in real-world clinical practice.

Methods: This retrospective study was conducted at Linkou Chang-Gung Memorial Hospital from January 2016 to December 2018. Enrolled cases included those undergoing first endoscopic ultrasound (EUS) workup within the period, with reported gastric subepithelial lesions (SELs) having diameter ≤ 2cm and originating from the muscularis propria (MP) layer. Size progression was defined as an increase of >20% in the largest diameter during EUS follow-up. Cases were categorized into two groups based on their initial size, <1cm and 1-2cm. Changes in tumor size, follow-up periods, clinical outcomes were analyzed.

Results: 180 cases of gastric subepithelial lesions (SEL) originating from the muscularis propria layer were analyzed, with a male-to-female ratio of 59:121 and a mean age of 57.7 years old. Among the cases, 51 cases did not undergo endoscopy follow-up, while 40 cases received follow-up for a minimum of 2 years (mean: 4.83 years) and 11 cases were lost. No reported mortality or adverse effects linked to the SELs during this observational period. 129 cases underwent either esophagogastroduodenoscopy (EGD) (n=17) or endoscopic ultrasound (EUS) (n=112). The EUS group was further categorized by size, with 69 cases measuring less than 1cm and 43 cases measuring 1-2cm. The mean follow-up period for EUS was 33.7 months. For lesions less than 1cm, the size change was noted to be 0.06mm per year, while lesions of 1-2cm reported a size change of 0.24mm per year. Notably, 24 cases (n=12 each in the <1cm and 1-2cm categories) demonstrated size progression during a follow-up period of 35.4 months. The growth rate for lesions less than 1cm was 0.7mm per year, compared to 2.7mm per year for lesions measuring 1-2cm, with a statistically significant difference ($P<0.05$). Six cases underwent surgical or endoscopic resection, one glomus tumor, one leiomyoma, and fourth gastrointestinal stromal tumors (very low risk) were reported.

Conclusions: Endoscopic ultrasound (EUS) could be applied as diagnostic modality for assessing the originating layer and size of asymptomatic small gastric subepithelial lesions (SEL). In cases of small gastric SEL originating from the muscularis propria (MP) layer, although a certain proportion (24 out of 112, 21.4% over 33.7 months) experienced size changes, no tumor-related symptoms or mortality were observed in the following period. As a result, the surveillance interval for EGD or EUS might be extended to 2-3 years following the initial EUS workup for lesions measuring less than 1cm.

P.046

早期黏膜下浸潤胃癌經內視鏡黏膜下剝除術後的預後和臨床結果：單一醫學中心的經驗
PROGNOSTIC AND CLINICAL OUTCOMES OF EARLY GASTRIC CANCER WITH SUBMUCOSAL INVASION FOLLOWING ENDOSCOPIC SUBMUCOSAL DISSECTION: INSIGHTS FROM A SINGLE-CENTER MEDICAL EXPERIENCE

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Background: Gastric cancer is a common cancer in the eastern countries. Early gastric cancer (EGC) is defined as carcinoma confined to the mucosa or submucosa, with or without lymph node metastasis (LNM). Intramucosal EGC(T1a) can be cured endoscopically by en bloc resection, such as endoscopic mucosal resection or endoscopic submucosal dissection. Gastric intramucosal early carcinoma(T1a) without lymph node metastatic (LNM) risk is an indication for endoscopic resection . In Japan Gastroenterological Endoscopy Society(JGES) guideline, the EGC patients with submucosal invasion(T1b) had higher LNM and needed extra gastric surgical resection and lymph node dissection for ensuring complete cancer clearance

Aims: However, some patients with T1b gastric cancer who received operation and lymph node dissection showed no LNM and they suffered from more postoperative complication without definite benefit. We present our hospital 10 years of EGC treatment experience and analyzed the clinical outcome.

Methods: We retrospectively reviewed database of Gastric cancer patients underwent endoscopic and/or surgical intervention from year 2011 till year 2022 in Kaohsiung Chang Gung Memorial Hospital. Institutional Review Board approval was obtained at Kaohsiung Chang Gung Memorial Hospital. The therapeutic criteria for endoscopic treatment are determined based on pathological biopsy reports and the depth of invasion observed under endoscopic ultrasonography(EUS). We excluded the gastrointestinal stroma tumor, neuroendocrine tumor or advanced gastric cancer. We analyze the treatment outcomes for early gastric cancer and the incidence of lymphatic metastasis at our hospital over the past decade

Results: There are 663 patients who underwent surgical treatment and 90 patients who underwent endoscopic submucosal dissection in our hospital. In surgical group, there are 37 patients as Tis(5.5%), 133 patients as T1a(21%), 124 patients as T1b(19.6%). The probabilities of LNM were 0%, 9%, and 20.1%, respectively. In endoscopic group, there are 25 patients as Tis(54%),18 patients asT1a(39%), 3 patients as T1b(6%). Among the 124 individual T1b surgical group, who had received gastrectomy combined with lymph node dissection , only 25 individuals exhibited LNM(20.1%). Among these 25 LNM patients, the majority demonstrated N1 involvement(defined as 1 to 2 nearby lymph nodes, 14/25, 56%). In endoscopic group, there are 3 patients as T1b and ESD pathological report showed margin free, who received extra surgical resection and lymph node dissection showed no LNM.

Conclusions: Based on the results from our hospital, the probability of lymph node metastasis in T1b early gastric cancer is approximately 20%, with the majority involving N1 metastasis. Endoscopic submucosal dissection (ESD) is performed according to the JGES guideline, and among patients with T1b pathology reports, there were no LNM after additional gastric and lymph node resection. Due to the T1b gastric cancer, there remains an approximate 20% lymph node metastasis rate. Therefore, in cases where the post-endoscopic submucosal dissection (ESD) pathological diagnosis indicates T1b, it is recommended to consider additional surgery or lymph node dissection to prevent potential metastasis.

P.047

內視鏡靜脈曲張結紮術與內視鏡氰基丙烯酸酯注射治療貴門至胃小彎急性靜脈曲張出血的比較

COMPARISON OF ENDOSCOPIC VARICEAL LIGATION AND ENDOSCOPIC CYANOACRYLATE INJECTION FOR THE TREATMENT OF ACUTE VARICEAL BLEEDING FROM THE CARDIA TO THE LESSER CURVATURE OF THE STOMACH

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Background: Practice guidelines endorse endoscopic variceal ligation (EVL) for the treatment of esophageal variceal bleeding and endoscopic cyanoacrylate injection (ECI) for the treatment of fundal variceal bleeding. However, the optimal treatment for acute variceal bleeding (AVB) from the cardia to the lesser curvature of the stomach is undefined.

Aims: This study aims to compare the efficacy of EVL and ECI for the treatment of AVB from the cardia to the lesser curvature of the stomach. Varices extending for 0 to 2 cm below the gastroesophageal (GE) junction are defined as cardiac varices (CVs), and varices extending for 2 to 5 cm below the GE junction along the lesser curvature of the stomach are defined as type 1 gastroesophageal varices (GOV1s).

Methods: Patients with bleeding from CVs or GOV1s who were treated by EVL or ECI at Taipei Veterans General Hospital were retrospectively evaluated. Clinical indicators, such as the presence of active spurting, active oozing, blood clots, or white nipple sign over CVs or GOV1s were documented carefully during endoscopy. Outcomes including the cumulative incidences of six-week rebleeding and probability of six-week survival were compared between the EVL group and the ECI group by Kaplan-Meier method and log-rank test. Cox proportional hazards regression analysis was used to determine the indicators of six-week rebleeding and mortality. Subgroup analyses based on the bleeding location were performed.

Results: Between February 2006 and August 2023, a total of 97 patients (mean age 59 years, 71.1% male) were evaluated. Fifty-two and 45 patients were treated with EVL and ECI, respectively. Baseline characteristic were similar between the two groups. Both groups achieved high hemostasis rates with no significant differences regarding to five-day treatment failure rates (p=0.246). No significant differences were noted between the two groups in terms of the cumulative incidences of six-week rebleeding (p=0.874) and probability of six-week survival (p=0.715). In multivariate analyses, ALT > 40 U/L was the only independent predictor of six-week rebleeding (HR 5.281, 95% CI 1.066-26.172, p=0.042), and Child-Pugh class C (HR 4.235, 95% CI 1.578-11.361, p=0.004) as well as creatinine > 1.3 mg/dL (HR 3.684, 95% CI 1.448-9.376, p=0.006) were the independent predictors of six-week mortality. In subgroup analyses, the cumulative incidences of six-week rebleeding were lower in the EVL group than in the ECI group for bleeding from CVs (p=0.031), but not for bleeding from GOV1s (p=0.840).

Conclusions: EVL and ECI offer similar efficacy for the treatment of AVB from the cardia to the lesser curvature of the stomach. Notably, EVL displays a lower six-week rebleeding rate then ECI for bleeding from CVs, but not for bleeding from GOV1s.

P.048

內視鏡橡皮圈結紮法和食道燒灼術治療難治型胃食道逆流症候群的臨床效果比較
COMPARISON OF CLINICAL EFFICACY OF ENDOSCOPIC BAND LIGATIONS AND ANTI-REFLUX ABLATION THERAPY FOR REFRACTORY GERD

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Background: GERD is a common gastrointestinal disorder, with about one-third of patients experiencing suboptimal responses to standard treatment with Proton pump inhibitors (PPIs). Due to the invasiveness and potential complications of antireflux surgery, minimally invasive endoscopic therapies have gained popularity.

Aims: The study aims to evaluate the safety and effectiveness of two endoscopic procedures: 1) banding using the Cook® 6 Shooter™ Saeed Multi-Band Ligator (EBL), and 2) antireflux ablation therapy (ARAT).

Methods: The study was prospectively, enrolling 10 patients with refractory GERD symptoms (defined as less than 50% improvement in symptom relief or GERDQLQ score ≧ 20 after 8 weeks of PPI treatment). All of them underwent esophageal manometry and 24 h pH monitoring with diagnosed as acid reflux disease or acid reflux hypersensitivity. Patients were randomly divided into two groups: the EBL group and the ARAT group, with 5 patients in each. In the EBL group, rubber bands were applied to three quadrants at the gastroesophageal junction (GEJ). Patients followed a soft diet and took dexilantprazole for 8 weeks. The ARAT group underwent a hybrid-APC with 270-degree ablation of the EGJ, a technique aimed at generating scar remodeling to reduce reflux. The followed by post-procedure care similar to the EBL group. The study assessed various metrics, including Chinese gastroesophageal reflux disease questionnaire (GERDQ), the gastroesophageal reflux disease–quality of life questionnaire (GERDQLQ), the reflux symptom index (RSI), the psychosomatic assessment (Beck Anxiety Inventory (BAI), the Beck Depression Inventory (BDI)). These were evaluated at baseline, and post-treatment at 3 months. Additionally, upper GI endoscopy was performed at 3 months to evaluate the Z line, and GEJ width.

Results: The ARAT group was significantly younger than the EBL group (37.0 ± 12.2 vs. 54.8±11.4, p=0.044). Gender distribution and BMI showed no significant differences between groups. The ARAT group had a higher prevalence of coffee and tea consumption (p=0.197 and p=0.038, respectively), but differences in smoking, alcohol, spicy food, and sweaty food consumption were not statistically significant. No significant differences in the prevalence of comorbidities like hypertension and insomnia were observed. The post-procedure herniation size was significantly reduced in the ARAT group compared to the EBL group (1.4±0.4 vs. 2.0±0.0, p=0.046). However, the change in herniation size (Δ herniation size) did not differ significantly between groups (0.0±0.6 vs. -0.3±0.3, p=0.268). Both groups showed improvement in GERDQ, GERDQLQ, RSI, BAI, BDI, and SSS-8 scores at 12 weeks, with no significant differences between the groups. The reduction in RSI and SSS-8 scores approached statistical significance (p=0.095 and p=0.053, respectively), suggesting a trend towards greater symptom improvement in the EBL group, although this did not reach conventional levels of statistical significance.

Conclusions: While both treatments resulted in improvements in GERD symptoms, quality of life, anxiety, depression, and somatic symptoms, there were no significant differences between the two groups in these outcomes. These findings highlight the potential of both EBL and ARAT as viable alternatives to traditional surgical approaches for refractory GERD, with each having unique advantages. Future studies with larger sample sizes and longer follow-up periods are warranted to further elucidate the differential impacts of these therapies on GERD outcomes.

P.049

比較經皮內視鏡胃造口術與傳統鼻胃管長期使用的安全性評估研究
COMPARATIVE SAFETY OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY VERSUS NASOGASTRIC TUBE FEEDING IN TAIWANESE PATIENTS: A POPULATION-BASED COHORT STUDY

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Background: Percutaneous endoscopic gastrostomy (PEG) has become an important intervention for providing long-term enteral nutrition support to patients with swallowing difficulties. However, studies comparing the effectiveness and safety of PEG feeding tubes versus nasogastric (NG) feeding tubes have shown inconsistent results.
Aims: We aimed to compare the incidence of complications and associated risk factors between PEG and NG tube feeding in a Taiwanese population.
Methods: This nationwide cohort study utilized Taiwan's National Health Insurance Research Database (NHIRD) to identify 743 patients undergoing PEG and 743 matched controls receiving NG tube feeding between 2002-2018. Propensity score matching (1:1 ratio) was carried out to balance confounding factors between groups. The primary outcomes were hospitalizations for peritonitis, peptic ulcer, gastrointestinal bleeding and aspiration pneumonia. Multivariate Cox proportional hazards regression analyses were conducted to determine adjusted hazard ratios (HRs).
Results: The PEG group had lower incidence rates of peritonitis (3.52 vs 4.53 per 1000 person-years), peptic ulcer (4.67 vs 8.62) and GI bleeding (7.65 vs 8.59), but higher aspiration pneumonia rate (15.4 vs 9.04) compared to NG group. Chronic kidney disease was an independent risk factor for aspiration pneumonia (adjusted HR 3.03, 95% CI 1.02-8.99). No significant differences in complication risks were found between PEG and NG using Kaplan-Meier analysis.
Conclusions: In this Taiwanese population, PEG was comparable to NG feeding regarding safety outcomes, making it a viable option for long-term enteral nutrition. Given the increased risk of aspiration pneumonia, it is advisable to exercise caution when using PEG in patients with chronic kidney disease.

P.050

萎縮性胃炎及腸上皮化生與胃部症狀之相關性：包括難治性疼痛、反覆性疼痛的一項病例回顧性群體研究
ASSOCIATIONS OF ATROPHIC GASTRITIS AND INTESTINAL METAPLASIA WITH GASTRIC SYMPTOMS: INCLUDING REFRACTORY PAIN AND RECURRENT PAIN - A RETROSPECTIVE COHORT STUDY

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Background: Gastric atrophy (GA) and gastric intestinal metaplasia (GIM) are significant risk factors for gastric cancer, assessed through the grading systems Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM). Existing studies have established a strong correlation between the severity of GA and GIM and an increased risk of developing gastric cancer. However, there has been limited research exploring how GA and GIM are linked to specific symptoms, especially refractory and recurrent pain.
Aims: The aim of this study is to explore the correlation between the objective severity grading of GA and GIM and the occurrence of symptoms, with a specific focus on refractory and recurrent epigastric pain.
Methods: A total of 431 consecutive individuals underwent endoscopy due to upper GI tract symptoms were retrospectively collected at the National Taiwan University Cancer Center from 2022/1/1 to 2023/12/31. The patient data collection included a clinical characteristics and symptoms, endoscopic findings, and pathology results. The included symptoms were GERD associated symptoms, refractory pain to acid suppressing medications (H2 blockers or PPIs), or recurrent pain post cessation of these medications, along with the patients' *H. pylori* infection history. The endoscopic findings consisted of observations related to gastritis, gastric ulcers, and duodenal ulcers. Biopsies were taken from antrum and body following the modified Sydney protocol. Furthermore, pathology results were gathered to assess intestinal metaplasia and atrophy, utilizing the OLGIM and OLGA grading systems. This study utilized Pearson's Chi-Square for categorical variables, and Kruskal-Wallis One-Way ANOVA for

categorical and numeric variables with a pre-defined P value of 0.05 for statistical significance.

Results: Within our cohort, the mean age was 62.6 years, with 48.3% being male patients. Epigastralgia was experienced in 59.2% of patients, of which 15.1% reported refractory abdominal pain to acid suppressing medications, and 6.2% had recurrent abdominal pain after discontinuing these medications. Furthermore, we observed that increased severity in GIM and GA was linked to older age. Age older than 50 years-old was linked to higher OLGIM and OLGA stages, with P-values of 0.0001 and 0.0010 respectively. Patients with GIM at OLGIM stage 1-4 reported significantly more symptoms than those without GIM, with a p-value of 0.0143. No statistically significant difference was observed for recurrent pain in this group. Interestingly, among those with GA at OLGA stage 1-4, compared to those without GA, a significant difference in recurrent pain was observed, with a P-value of 0.0208, while refractory pain exhibited no statistically significant difference. In sensitivity analyses, we also examined the influence of peptic ulcer disease or *H. pylori* infection, which could impact pain factors. The results remained consistent. Multivariable logistic regression showed that the presence GIM is associated with age (OR 1.10, P=0.0011) and past or present *H. pylori* infection (OR 7.15 , P=0.0013). GIM severity is associated with refractory pain (OR 16.11, P=0.0189). The presence of GA is also associated with recurrent pain (OR 4.32, P=0.0380).

Conclusions: Our study identified significant correlations between age and the stage of OLGIM, and OLGA. We also highlight that refractory pain to acid suppressing medications was associated with OLGIM stages, while recurrent pain showed a connection with OLGA stages. These findings emphasize the importance of considering gastric pathology in symptom evaluation. The study contributes valuable insights for early detection and treatment consideration in routine clinical practice.

P.051

解構與分析食道癌及胃癌的基因變異
DECIPHERING AND CHARACTERIZING THE GENOMIC CODE: INSIGHTS INTO ESOPHAGEAL AND GASTRIC CANCER GENETIC ALTERATIONS

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Background: Esophageal cancer (EC) and gastric cancer (GC) are major global health concerns, with the highest incidence and mortality rates found in Asia, especially in eastern Asia. In Taiwan, EC is the sixth leading cause of cancer in males and ranks fifth in mortality, while GC is the seventh in incidence and eighth in mortality. Despite medical advancements, the prognosis for both EC and GC remains poor, with five-year survival rates ranging from 15-25% for EC and 25-35% for GC. In EC, we focused on esophageal squamous cell carcinomas (ESCC) in this study owing to 93.15 % of EC cases in male are squamous cell cancer. This alarming statistic underscores the need for a comprehensive study on the genomic abnormalities in ESCC and GC, aiming to develop a specialized database for eastern Asian populations and formulate effective treatments.

Aims: This study aims to uncover genomic abnormalities in ESCC and GC, thereby contributing to the development of potential therapeutic strategies.

Methods: We analyzed whole genome sequencing (WGS) and targeted deep sequencing data from public databases, focusing on the top 10 single nucleotide variations (SNVs), copy number variations (CNVs), and tumor mutation burdens (TMB) in ESCC and GC. Additionally, genomic DNA sequencing was performed using ACT Onco+ on 74 ESCC and 17 GC tumor tissue samples obtained from KMU Hospital. This approach was undertaken to identify genetic alterations and assess their overlap with known mutations.

Results: Our findings in ESCC revealed significant genetic alterations, including SNVs in TP53, MUC16, and SYNE1, and CNVs in CDKN2A/B, CCND1, and BRCA2. In GC, notable genetic changes were identified as SNVs in TP53 and CNVs in CCNE1. Analysis of public datasets for ESCC highlighted overlapping SNVs (TP53, NOTCH1, KMT2D, PIK3CA) and CNVs (CDKN2A, CDKN2B, CRLF2, FGF3, FGF4, CCND1, FGF19, TP63). Similarly, for GC, overlapping SNVs (TP53, ARID1A, KMT2C, LRP1B) and CNVs (CDKN2A, CDKN2B, PTEN, MYC, ERBB2,

CCNE1, KRAS) were detected.
Conclusions: This study successfully reviewed public datasets and identified key genomic alterations in ESCC and GC within the Taiwanese population. The next phase involves integrating our findings with public data to discern mutually exclusive and co-occurring genetic variants. This integrated analysis is crucial for discovering novel synthetic lethal targets, offering new avenues for the treatment of ESCC and GC.

P.052

運用高解析食道功能儀探討食道無效性收縮之患者其橫紋肌收縮之表現
IMPACT OF INEFFECTIVE ESOPHAGEAL MOTILITY ON STRIATED ESOPHAGEAL MUSCLE CONTRACTION IN PATIENTS WITH: STUDIES USING HIGH-RESOLUTION MANOMETRY

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Background: Striated esophageal muscle contraction (SEC) is important for pharyngeal swallowing and deglutition augmentation against aspiration. Its clinical relevance is unclear in patients with ineffective esophageal motility (IEM).
Aims: In this study, we aimed to characterize and compare SEC in consecutive patients with and without IEM and also correlated SEC to primary and secondary peristalsis.
Methods: All eligible patients were evaluated for SEC, primary and secondary peristalsis using high-resolution manometry (HRM) with one mid-esophageal injection port. Primary peristalsis was assessed with ten 5-mL liquid swallows and multiple rapid swallows (MRS), while secondary peristalsis was performed with rapid air injections of 20 mL. The frequency of primary and secondary peristalsis as well as relevant motility parameters were measured, whereas SEC and its contractile (SECI) were evaluated in the esophageal contractile isocontour region between the distal UES margin and the nadir of the esophageal transition zone. IEM was defined using Chicago IV criteria.
Results: 140 patients (59.3% women, mean age 46.1± 13.1 years) were included. There was no difference in SECI between patients with and without IEM ($p = 0.91$). SECI was also similar between patients with and without secondary peristalsis for patients with IEM ($p = 0.63$) or normal motility ($p = 0.80$). No difference in SECI was seen between patients with and without MRS for patients with IEM ($p = 0.55$) and normal motility ($p = 0.88$). SECI was significantly higher in male patients than female patients in IEM patients ($p = 0.01$) but not in patients with normal motility group ($p = 0.93$). SECI significantly correlated with age in patients with normal motility ($r = -0.31$, $p = 0.01$), but not seen in patients with IEM ($r = -0.14$, $p = 0.24$).
Conclusions: Aging may have a negative impact on striated esophageal muscle contraction only in patients with normal motility but not in IEM patients. Male IEM patients have higher SECI than female IEM patients. Neither secondary peristalsis nor MRS is associated with striated esophageal muscle contraction in all patients.

P.053

食道麟狀上皮乳突瘤在不同食道位置的內視鏡和組織學特徵：單一中心的經驗
ENDOSCOPIC AND HISTOLOGICAL CHARACTERISTICS OF ESOPHAGEAL SQUAMOUS PAPILLOMA ACROSS ESOPHAGEAL SEGMENTS: A SINGLE-CENTER EXPERIENCE

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Background: Esophageal squamous papilloma (ESP) is a rare and benign lesion in the esophagus, characterized by white, wart-like projections observable during endoscopy. Its prevalence in esophagogastroduodenoscopy (EGD) examinations is reported to be between 0.01% and 0.45%, indicating that while rare, it holds clinical significance.
Aims: The aim of this study is to explore the clinical importance of the location of ESP, as determined through EGD and histological analysis.
Methods: In our cohort, we enrolled 63 patients with pathologically confirmed ESP from January 2019 to August 2022. The esophagus was divided into three segments: the upper esophagus (20-24 cm from the incisors), the middle esophagus (25-29 cm from the incisors), and the lower esophagus (30-40 cm from the incisors). Patients were categorized based on the location of the ESP within these defined segments. For each group, we recorded demographic and clinical variables, including sex, age, and the size of the lesions. We utilized analysis of variance (ANOVA) to compare continuous variables and the chi-squared test to analyze categorical variables across the three groups.
Results: Of the 63 patients with ESP, histological examination revealed that none of the ESP cases revealed dysplasia. The location of ESP distribution was 15 in the upper esophagus, 20 in the middle, and 28 in the lower segment. The mean age was 60.8 years, and 49.2% of patients were female. The mean lesion size was 5.1 mm. ESP across different esophageal segments was similar, with measurements of 4.9 mm, 3.8 mm, and 6.0 mm for the upper, middle, and lower esophagus respectively (P=0.157). No significant differences in age or sex were observed among the different esophageal segments ($P > 0.05$).
Conclusions: In conclusion, our study indicates that ESP is predominantly a benign lesion of the esophagus, and we observed no significant variations in age, gender, or lesion size across the different esophageal segments.

P.054

胃癌細胞移植粒線體之代謝體學研究
THE METABOLOMIC PROFILE OF GASTRIC CANCER AFTER MITOCHONDRIAL TRANSPLANTATION

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Background: Gastric cancer (GC) is a serious cancer in the modern society. Mitochondria are essential for ATP production that deeply affect the metabolism of cancer cells. Transferring mitochondria to reduce the malignancy of cancer cells was recently reported. Currently, the gastric cancer cell AGS transplanted with gastric epithelial cell GES-1 that exhibited a lower mitochondrial membrane potential (MMP) showed a reduced malignancy.
Aims: To further understand metabolomic regulation of reduced cancer malignancy, the AGS transplanted with GES-1 mitochondria was subjected to metabolomic analysis.
Methods: Over 16 metabolites with 1.5 fold higher or 0.7 fold lower than the control treatment were identified. These metabolites were involved in energy, TCA cycle, Pentose-phosphate pathway (PPP) and glycolysis.
Results: In the TCA cycle, an accumulated isocitrate coupled with the decreased malate was observed indicating the mitochondrial function of AGS was impaired by the transplanted GES-1 mitochondria. Further elucidate the levels of glucose and lactate revealed that extracellular lactate was decreased while the glucose remained a sustained level. Lower expression of lactate transporter MCT1 implies that lactate was restricted in the AGS cells.
Conclusions: Concluded above result, the key enzymes involved in lactate transportation and the conversion of TCA cycle are essential for transplanted GES-1 mitochondria to reduce the malignancy of gastric cancer AGS cells.

P.055

脂肪間質幹細胞在調節胃癌進展的機轉探討
INVESTIGATING THE MECHANISM BY WHICH ADIPOSE MESENCHYMAL STEM CELLS REGULATE THE PROGRESSION OF GASTRIC CANCER

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Background: Gastric cancer is a very common digestive tract cancer in Asian countries, and the death rate caused by gastric cancer ranks third in the world. Adipose mesenchymal stem cells (ADSCs) may be involved in the development of cancer. Altered energy metabolism contributes to more ATP source, and the growth and metastasis of cancer through up-regulating the uptake of energy-rich metabolites such as lactate, ketone bodies and glutamate et al.
Aims: In this study, we will investigate the regulation of ADSCs on the energy metabolism of gastric cancer cells.
Methods: We explored the effect of ADSCs on regulation of energy metabolism proteins MCT1, SLC6A14, OXCT1 and OXCT2 of gastric cancer cells, using RT and q-PCR assays. We measured the levels of lactate, ketone bodies, glutamate and ATP in human gastric cancer cells, using ELISA.
Results: ADSCs significantly induced higher expressions of MCT-1, SCL6A14, OXCT-1/2 and ACAT-1 in human AGS gastric cancer cells. The levels of lactate, glutamate, ketone body and ATP were then measured in human AGS gastric cancer cells co-cultured with ADSCs. We observed that ADSCs significantly upregulate lactate, glutamate, ketone body and ATP levels in human AGS gastric cancer cells.
Conclusions: These results suggest that ADSCs may be involved in the development of gastric cancer through regulating energy metabolism.

P.056

抗氧化藥物透過 NRF2-TP53 路徑控制人類胃癌類器官進展的異質效應
HETEROGENEOUS EFFECTS OF ANTIOXIDATION DRUGS ON CONTROLLING THE PROGRESSION OF HUMAN GASTRIC CANCER ORGANOIDS VIA NRF2-TP53 PATHWAYS

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Background: Gastric cancer (GC) organoids are frequently used to examine the tumorigenic ability of human GC. GC organoids can be used in the identification of novel antioxidant drugs to prevent the progression of GC.
Aims: GC organoids were used to examine cell proliferation and death as well as cancer development. Invasion/migration assay, xenotransplantation, and reactive oxygen species (ROS) production were used to examine the effects of antioxidant drugs, including perillaldehyde (PEA), cinnamaldehyde (CA), and sulforaphane (SFN), on GC.
Methods: Through using site-directed mutagenesis (SDM) on AhR reporter we established, we identify the critical cis-element of activating phase I and phase II response. The enzyme system was further studied through Jdp2 knock out mouse embryonic fibroblast (MEF) compared with WT-MEF, in order to establish the complex shift between phase I and phase II response. Last, we used 2545 pancreatic carcinoma to confirm the critical role of phase I and phase II enzyme system to the ROS insensitive cancers.
Results: PEA and CA repressed the proliferation of human GC organoids, whereas SFN enhanced it. Caspase 3/7 activities were repressed on treatment with PEA and CA. In addition, the tumor formation and invasive activities were repressed on treatment with PEA and CA, whereas they were enhanced on treatment with SFN. ROS production and the expression of p53, nuclear factor erythroid 2-related factor (Nrf2), and Jun dimerization protein 2 were also downregulated on treatment with PEA and CA, but not SFN. Nrf2 knockdown reversed the effects of these antioxidant drugs on the invasive activities of the three-dimensional GC organoids.
Conclusions: The novel antioxidant drugs PEA and CA

inhibited the development and invasive activity of human GC, which were evaluated using GC organoids. By contrast, SFN increased tumorigenesis. Moreover, ROS production was also inhibited by treatment with PEA and CA but not SFN. Nrf2 plays a key role in the differential effects of these antioxidant drugs on cancer invasion. PEA and CA can potentially be new antitumorigenic therapeutics for GC.

P.057

OMEGA-3 脂肪酸透過 GRP78 調控胃癌幹細胞化與抗藥性
OMEGA-3, POLYUNSATURATED FATTY ACID, MODULATES GRP78-MEDIATED GASTRIC CANCER STEMNESS AND CHEMORESISTANCE

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Background: Chemotherapy is the treatment of choice for gastric cancer, but the currently available therapeutic drugs for the treatment have limited efficacy. GRP78 was found highly expressed in gastric cancer tissue, and play an important role in cancer stemness and drug resistance of chemotherapy by gain-of function of antioxidant properties. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) are essential nutrients, because they cannot be made endogenously.

Aims: They recognized as essential components of the human diet, have exhibited considerable promise in targeting malignant cells, and have reported to inhibit gastric cancer cell proliferation through NF-kB/Akt pathway. However, the mechanisms of omega-3 in the regulation of gastric cancer stemness and chemoresistance are not clear.

Methods: After treatment of n-3 PUFAs, the GRP78 mediated cancer stemness-related protein expressions and cellular oxidative stress in human gastric cancer cells, AGS, were evaluated by western blotting and flow cytometry. The chemoresistance of these cells was evaluated by Cell Counting Kit-8 (CCK8) following co-treatment with 5-fluorouracil (5-FU) and n-3 PUFAs.

Results: In the present study, n-3 PUFAs was demonstrated to inhibit human gastric cancer stemness-related protein, CD44 and CD24, expressions by GRP78-mediated pathway. Moreover, n-3 PUFA also induced human gastric cancer cell oxidative stress and suppressed the chemoresistance.

Conclusions: Omega-3 fatty acids reduced GRP78-mediated cancer stemness and chemoresistance. Therefore, the results suggested that supplementation with omega-3 fatty acids may benefit for patients with undergoing chemotherapy.

P.058

甘露醣受體透過脂質代謝重編途徑促進胃癌的腫瘤侵襲及進程
MANNOSE RECEPTOR PROMOTES TUMOR AGGRESSIVENESS OF GASTRIC CANCER VIA LIPID METABOLIC REWIRING PATHWAY

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Background: Metastatic gastric cancer (GC) further hampered the efficacy of therapeutic treatments and worsened the prognosis of patients. Growing evidence indicated that Mannose Receptor C Type 2 (MRC2) is overexpressed in multiple types of human cancers and involved in extracellular collagen remodeling process of cancer cells, potentially facilitating tumorigenesis and aggressive metastasis.
Aims: We explored whether MRC2 modulates tumor metastasis via a lipogenesis-related pathway, which further affects the disseminating progression of gastric cancer.
Methods: We analyzed the stomach tumor tissues of patients, compared with the adjacent normal gastric epithelial tissue. checked mice pyloric tissues of wildtype and Mrc2 knock-out mice. In vitro study, we use MRC2 overexpression and MRC2 knockdown in human gastric cancer cell line. We checked the migration and invasion ability of gastric cancer cells and elevated the expressions of epithelial, mesenchymal, and EMT regulators.
Results: In our clinical data, we demonstrated that MRC2 expression level increases in GC tissue and lead to poor prognosis. In vitro study, manipulations of MRC2 positively regulated the functions of migration and invasion in the GC cell lines as compared to control cells. MRC2 was demonstrated to significantly promote the EMT process via the modulation of Stearoyl-CoA desaturase-1 (SCD1), a vital enzyme in fatty acid metabolism, through enhancing the levels of PPAR gamma, an upstream regulator of SCD-1. Consistent with our in vitro study, we verified that MRC2 knockdown suppressed the tumor development of GC in animal models.
Conclusions: Conclusively, we innovatively demonstrated that MRC2 play a critical role in the metabolic reprogramming process of lipogenesis, further promoting oncogenic developments of tumor cells.

P.059

自噬相關之訊號路徑調控幽門桿菌感染胃癌細胞的癌化現象
AUTOPHAGY-RELATED SIGNALING PATHWAYS REGULATE TUMORIGENESIS OF *HELICOBACTER PYLORI* INFECTED GASTRIC CANCER CELLS

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Background: Gastric cancer is the third leading cause of cancer death globally. Cancer cells may regulate their proliferation, survival, motility and carcinogenic processes by degradation-related mechanisms. The canonical autophagy utilizes degradation system to suppress the carcinogenic factors to prevent cancer development. The pathogenesis of gastric cancer is closely related to the formation of an autophagosome-mediated downstream signaling pathway by *H. pylori* infection-induced cells.
Aims: In this report, we reported the possible autophagy-related signaling pathways involved in *H. pylori* infection caused gastric cancer tumorigenesis.
Methods: The effect of autophagy-related signaling pathways in AGS gastric cancer cells under *H. pylori* infection was determined with or without genetic knockout of Atg5 gene. Autophagy-related signaling pathways in cells (AGS and AGS-CRISPR/Cas9-knockout -ATG5-gene cell lines) was determined by RNA-Seq and Western blotting.
Results: To elaborate the autophagy-related signaling pathways in *H. pylori* infected gastric cancer cells, we generated the AGS-CR-ATG5-R1 cell line using CRISPR/Cas9 knockout system as inhibiting autophagy model accompanied with the parental control cells (AGS). KEGG Pathway Analysis revealed that knockout of Atg5 gene remarkably affected many signaling pathways in this cancer cell line. We further used immunoblotting to verify that only the JNK signaling pathway is related to autophagy.
Conclusions: The JNK pathway is regulated by autophagy in *Helicobacter pylori*-infected gastric cancer cells toward increasing tumorigenesis.

P.060

幽門螺旋桿菌感染的人類胃癌 3D 類器官中癌症進展和侵襲的信號異質性
SIGNALING HETEROGENEITY OF CANCER PROGRESSION AND INVASION IN HUMAN GASTRIC CANCER 3D-ORGANOIDS INFECTED BY *HELICOBACTER PYLORI*

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Background: The gastric cancer- and normal-organoids from the cancerous parts and iPS cells were established several years ago. Owing to the remarkable degree to which they recreate the cellular diversity observed in the human stomachs, they have attracted significant interest as a novel model system for precision medicine.
Aims: However, many questions remain regarding the extent to which these cultures recapitulate gastro-development and mechanism of cancer progression infected by *Helicobacter pylori (H.p.)*.
Methods: We prepared three-dimensional (3-D) organoids of human stomach cancers and examined the correlation between the tumorigenicity and cytotoxicity of *H. pylori*. In addition, the effects of hepatoma derived growth factor (HDGF) and tumor necrosis factor (TNFα) on the growth and invasion activity of *H. pylori*-infected gastric cancer organoids were examined (TH Chu et al., Oncogene, 38, 646106477, 2019). Green fluorescence protein-labeled *H. pylori* was used to trace the infection in gastric organoids. The cytotoxicity of Cag toxins from different species of *H. pylori* did not affect the proliferation of each *H. pylori*-infected cancer organoid. To clarify the role of HDGF and TNFα secreted from *H. pylori*, we prepared recombinant HDGF and TNF and measured the cytotoxicity and invasion of gastric cancer organoids
Results: HDGF controlled the growth of each organoid in a species-specific manner of *H. pylori*, but TNFα decreased the cell viability in all *H. pylori*-infected cancer organoids. Furthermore, HDGF did not change the invasion activity of *H. pylori*-infected cancer organoid, however, TNFα decreased the invasion activities of these organoids. We found different signaling of cancer progression and invasion of human gastric organoids in response to HDGF and TNFα during infection by *H. pylori*. Recombinant HDGF and TNFα inhibited the development and invasion of *H. pylori*-infected gastric cancer differently.
Conclusions: Thus, we conclude that HDGF and TNFα are independent signals for development of *H. pylori*-infected gastric cancer. The signaling of growth factors in 3-D organoid culture systems is different from those in two-dimensional cancer cells.

P.061

術中冷凍切片無法導引上消化道肌肉層黏膜下腫瘤的治療方向的決定：一個前瞻性研究
INTRA PROCEDURAL FROZEN BIOPSY RARELY GUIDE THE DECISION OF ENDOSCOPIC RESECTION OF UPPER GASTROINTESTINAL SUBEPITHELIAL TUMORS WITH MUSCLE LAYER INVOLVEMENT: A PROSPECTIVE STUDY

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Background: Subepithelial lesions (SEL) of the gastrointestinal tract represent a mass or mass-like structure project into the lumen and rise from non-mucosal layer within wall. It is the mix of benign and potentially malignant entities including tumors, cysts, or extraluminal structures causing extrinsic compression of the gastrointestinal wall. One meta-analysis reported reviewed the pooled complete resection rate was 91.4% (95% CI, 77.9 to 97) of the lesion that originated from the submucosal layer in 290 gastric subepithelial tumors (SETs) resected by ESD. We proposed a novel method to obtain frozen section of the SELs and cease the procedure if the pathologist proved non-malignant result to dramatically decrease the procedure time, complication such as perforation and bleeding, thus improve treatment algorithm for SELs.

Aims: To evaluate the efficacy of intra procedural frozen biopsy in guiding the decision of endoscopic resection of upper gastrointestinal subepithelial tumors with muscle layer involvement

Methods: We prospectively enrolled patients undergoing ESD for subepithelial lesion at esophagus and stomach from 2020 September 8 to 2022 March 8 at Ditmanson Medical Foundation Chia-Yi Christian Hospital.

Results: The average age is 50.5 (ranging from 35 to 70). The three most prominent comorbidity were diabetes (28.6%, N=4), hypertension (21.4%, N=3) and hepatitis C (7.1%, N=1) respectively. The constitution of the specimen from the esophagus and stomach were 53%(N=8) and 40%, (N = 6) respectively. (Table 1) The prediction of pre-resection origin was 100% compatible with the final layers of ESD with both muscle layer involvement versus submucosal layer involvement about 85.7%(n=12) versus 14.3%(n=2). The final diagnosis with leiomyomas as majority (n=11, 78.6%) and GIST, gastritis cystic profunda, ectopic pancreas consisting 7.1%(n=1) each. Of the 14 frozen biopsy specimens, the final diagnosis of 13 specimens were leiomyoma(n=11), GIST(n=1) and gastritis cystic profunda(n=1) which were all diagnosed as spindle cell tumor in the intra-procedure frozen biopsy which provides no guidance for further decision making.

Conclusions: The pathological finding of a frozen section cannot predict the final pathologic diagnosis, especially for GIST and leiomyoma. Therefore, it should not be suggested for use in the ESD of subepithelial lesions in the future.

P.062

利用基因工程小鼠模型來探討 LKB1 和 PTEN 缺陷在胃癌發病機制中的作用
DEVELOPMENT OF A GENETICALLY ENGINEERED MOUSE MODEL RECAPITULATING LKB1 AND PTEN DEFICIENCY IN GASTRIC CANCER PATHOGENESIS

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Background: Gastric cancer (G.C.) is a lethal human malignancy, boasting the highest mortality rate among all cancers. Recent advances in molecular pathology have unveiled a comprehensive genetic profile associated with the initiation and progression of G.C. These encompass the activation of KRAS, along with the inactivation or loss of E-cadherin, PTEN and P53, forming the corner-stone for delving into the genetic and molecular underpinnings of this malignancy.

Aims: This study is set to leverage the H+/K+ ATPase Cre transgene strain to target Cre recombinase expression at parietal cells within the stomach precisely.

Methods: This strategic maneuver seeks to selec-tively nullify the functions of both LKB1 and PTEN in a manner specific to the stomach, thereby instigating the development of G.C. in a fashion akin to human gastric adenocarcinoma. More-over, the study endeavors to dissect the intricate ways these alterations contribute to the histopathologic advancement of gastric tumors, their potential for invasiveness and metastasis, angiogenesis, and the evolving tumor stromal microenvironment.

Results: Our results show that conditional deletion of PTEN and LKB1 provides an ideal cancer microenvironment for G.C. tumorigenesis by promoting cancer cell proliferation, angiogenesis, and metastasis.

Conclusions: The conditional abolition of LKB1 and PTEN genes leads to a cascade of events that disrupt stomach homeostasis. This disruption includes the induction of tumorigenesis, promotion of Epithelial-Mesenchymal Transition (EMT), upregulation of cancer stemness, and the creation of a pro-inflammatory microenvironment conducive to carcinogenesis. Ultimately, the loss of PTEN and LKB1 in mouse stomach tissues drives carcinogenesis, facilitates tumor invasion, and promotes angiogenesis. These collective processes culmi-nate in the development of gastric intestinal type adenocarcinoma in mice. These findings provide valuable insights into the molecular mechanisms underlying gastric cancer de-velopment and suggest potential targets for therapeutic interventions in the future.

P.063

針對食道癌病人合併吞嚥困難、食道氣管瘻管接受全包覆可伸展食道金屬支架位移的預測因子回溯性研究
RISK FACTORS OF STENT MIGRATION IN ESOPHAGEAL CANCER PATIENTS UNDERWENT FULLY-COVERED SELF-EXPANDING METAL STENTS FOR MALIGNANT DYSPHAGIA OR TRACHEOESOPHAGEAL FISTULA

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Background: More than 50% of esophageal cancer patients are diagnosed in advanced diseases and commonly experience dysphagia, some of whom even had tracheoesophageal fistula. Self-expandable metal stent (SEMS) is one of the recommended palliative methods. However, complications such as chest pain and stent migration are not uncommon.
Aims: The aim of this study was to examine the predictors of stent migration in esophageal cancer patients undergoing SEMS placement for dysphagia or fistula.
Methods: We conducted a retrospective cohort study to include patients with esophageal cancer and dysphagia/tracheoesophageal fistula. Clinicopathological information, stent characteristics and patients' outcome were collected for analysis. Side effects of SEMS were recorded, potential predictors were examined and patients' nutritional outcome was compared in the migration and non-migration groups.
Results: A total of 54 patients with esophageal cancer who received fully covered SEMS between 2013 and 2022 were included. We found tumor across the esophagogastric junction (adjusted odds ratio (OR)=32.64, P = 0.01) and sex female (adjusted OR=12.5, P = 0.02) were significant predictors for stent migration. There was a decreasing tendency in body mass index/body weight in the migration and non-migration groups, but the former had a steeper downslope.
Conclusions: Fully covered SEMS is a safe and effective strategy to palliate dysphagia or fistula. Tumor across esophagogastric junction and female sex were at higher risk predictors of stent migration. A careful patient selection would optimize the effect of SEMS placement, especially in those with short expected lifespan.

P.064

揭示 ELAFIN 在食道鱗狀細胞癌預後中角色：從 3D 影像與基因分析之洞察
DECIPHERING ELAFIN'S ROLE IN ESCC PROGNOSIS: INSIGHTS FROM 3D IMAGING AND GENOMIC ANALYSIS

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Background: Esophageal cancers rank as the sixth deadliest malignancy globally, presenting limited curative options. Among the various biomarkers studied, the role of elafin, a molecule produced by epithelial cells, is notable in esophageal squamous cell carcinoma (ESCC). While the association of high serum elafin levels with increased ESCC risk is established, the relationship between elafin levels and ESCC prognosis remains to be fully understood.
Aims: This study investigates the relationship between serum elafin levels and ESCC prognosis, focusing on the spatial distribution of elafin in locoregional ESCC tissues and the identification of elafin-related pathways influencing ESCC progression.
Methods: The study employs a comprehensive approach, beginning with three-dimensional confocal imaging to model elafin distribution in locoregional ESCC tissues. This is followed by an analysis of whole genome microarrays from ESCC cell lines and their more invasive sublines. Finally, in-vitro experiments using RNA-sequencing are conducted to pinpoint potential pathways related to elafin.
Results: Imaging results show elafin distributed as an interweaved-like fibrous structure in the stroma of high-serum-elafin patients with poorer prognoses, contrasting with its confinement around the tumor nest in patients with lower serum levels and better outcomes. Analysis of the TCGA dataset reveals a correlation between higher elafin mRNA levels in stage I-IIIA ESCC patients and shorter survival. The in-vitro studies indicate that elafin promotes ESCC cell proliferation, migration, and invasion, likely through the epithelial-mesenchymal transition pathway.
Conclusions: The study highlights elafin's significant role in ESCC progression, with higher levels linked to poorer patient prognoses. Inhibiting elafin could, therefore, offer a new therapeutic approach to enhance survival in patients with locoregional ESCC.

P.065

成人腸套疊：著重在病患於腹部電腦斷層檢查前大腸鏡影像
ADULT INTUSSUSCEPTION: EMPHASIS ON COLONOSCOPIC IMAGES OF SUSPECTED COLONIC INTUSSUSCEPTION BEFORE ABDOMINAL CT EXAMINATION

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Background: Adult intussusception is rare, and represents 5% of all cases of intussusception, [World J Gastroenterol. (2009) 15(4):407–11. Ann Surg. (1997) 226(2):134–8.] with an estimated incidence of be 2 cases/1,000,000 population/ year [World J Gastroenterol . 2007; 13: 3641-4 Postgrad Med J 2005;81:174-7] Intussusception in adults is entirely different from the pediatric form, regarding clinical, and pathological aspects. [Ann Surg. 1997 Aug; 226(2): 134–8 Eur Surg. 2013 Jan; 45(5): 239–44.) Adult intussusception can have acute, subacute, and chronic symptoms. They often present with non-specific symptoms such as intermittent chronic abdominal pain, nausea and vomiting, making diagnosis difficult [Visc Med 2021;37:120–127]. Most adult intussusceptions have underlying secondary causes. Commonly used diagnostic modalities for intussusception include abdominal ultrasound, and CT scan. Abdominal CT scan is the most sensitive test for adult intussusception. However, in clinical practice, abdominal CT scan as the initial examination for chronic abdominal pain with lower gastrointestinal symptoms in out-patient department is not always feasible, so recognizing the colonoscopic pictures can raise the awareness for adult intussusception.

Aims: To report our clinical experience with adult intussusception in the last 5 years, with emphasis on colonoscopic images of highly suspicious colonic intussusception before abdominal CT scan examination.

Methods: From Jan. 2018 to Oct. 2023, a total of 10 cases with discharge diagnosis of adult intussusception were analyzed for clinical presentations, diagnostic methods, causes, and colonoscopic pictures. The inclusion criteria were 1:) patients above 18 years old, 2;) diagnosis made by abdominal ultrasound, abdominal CT scan, or surgery. Intussusceptions in children were excluded. Acute symptoms were defined as less than four days, subacute symptoms (4-14 days), and chronic symptoms as more than 14 days.[International Journal of Surgery 2011;9:297-301].

Results: There were 6 male and 4 female patients with the mean age of 68 years (20-99 years). Two presented with acute abdominal pain, 1 acute vomiting, 1 chest pain (the chief problem was angina, and transient intussusception found incidentally on CT), and 6 patients with chronic abdominal pain. One adult intussusception was diagnosed by abdominal ultrasound, and 9 cases by CT scan. Five patients had colonoscopy performed. Five cases were ileocolic, 3 enteric, and 2 colonic intussusceptions. Three enteric intussusceptions were caused by fibroma (ileum), inflammatory fibroid polyp (jejunum), and 1 efferent loop (intussusception into remnant of stomach due to adhesion). One ileocolic intussusception was caused by colon cancer, and 2 ileocolic intussusceptions were idiopathic ileocolic intussusceptions after surgery. With the other 2 ileocolic intussusceptions, one was transient (incidental finding on CT, and the other one was intermittent intussusception with normal colonoscopy later). In two colonic intussusceptions, one was hepatic flexure colon cancer, and the other one diagnosed by ultrasound without tissue proof. Six patients underwent surgery (3 enteric type, and 3 ileocolic type), and one had colonoscopic biopsy. Secondary causes could be found in 71.4% (5/7) of adult intussusception excluding those without tissue proof and surgery. In 5 cases of adult intussusception, 3 had pre-CT colonoscopic examinations. In 2 pre-CT colonoscopic examinations, the symptoms were chronic abdominal pain, bloody stool, and the colonoscopic findings of mass with exudate, clear cut relatively normal mucosa, and a coil-spring pattern at the base of the mass led to the suspicion of intussusceptions. On review of another pre-CT colonoscopy performed by another gastroenterologist, a relatively normal bulging mucosa was seen at the base of colon cancer, which should raise the suspicion of intussusception retrospectively. In 2 post CT colonoscopic examinations, one was normal colonoscopy (intermittent intussusception), and the other colonoscopic report was hepatic flexure colon cancer only.

Conclusions: Adult intussusceptions are rare, and most cases are secondary. Chronic abdominal pain and lower gastrointestinal symptoms, colonoscopic pictures of mass with exudate, clear cut relatively normal mucosa, and coil-spring pattern at the base of the mass should lead to the suspicion of intussusception

P.066

換水大腸鏡插入過程中嚴重疼痛的預測因子
PREDICTIVE FACTORS FOR SEVERE INSERTION PAIN DURING WATER EXCHANGE COLONOSCOPY

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Background: Water exchange (WE) colonoscopy is known for being less painful, yet a subset of patients experience severe abdominal pain during the insertion phase. This study aimed to identify predictive factors for severe insertion pain during WE colonoscopy.
Aims: This study aimed to identify predictive factors for severe insertion pain during WE colonoscopy.
Methods: A retrospective analysis was conducted on patients who underwent WE colonoscopy at Dalin Tzu Chi Hospital. Logistic regression analyses were used to isolate independent factors associated with severe insertion pain (defined as a pain score > 5).
Results: The study included 462 patients, comprising 291 men and 171 women, with a median age of 57 years (IQR: 49–64 years). The median maximum pain score during the insertion phase was 0, and 50.2% of patients reported experiencing no pain. However, 9.3% of patients reported severe pain. Multivariate logistic regression analysis revealed that being female (OR = 2.724, P = 0.002) and having a body mass index (BMI) below 25 kg/m² (OR = 2.402, P = 0.010) were significantly associated with severe pain. Notably, female patients with a BMI less than 25 kg/m² experienced the highest incidence of severe pain (16.8%), in contrast to male patients with a BMI of 25 or higher, who had a much lower incidence (3.7%).
Conclusions: This study identified female gender and a BMI under 25 kg/m² as key factors associated with severe insertion pain during WE colonoscopy. These findings can assist clinicians in identifying patients who might be better suited for WE colonoscopy without sedation, thereby improving patient care and procedural planning.

P.067

代謝因素對大腸腺瘤復發的影響
INFLUENCE OF METABOLIC FACTORS ON THE RECURRENCE OF COLORECTAL ADENOMAS

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Background: Metabolic disturbances are significant risk factors for colorectal neoplasm, yet their impact on metachronous colorectal neoplasms is not well understood.
Aims: This study aims to identify the risk factors for adenoma recurrence, focusing on metabolic factors and initial colonoscopy findings.
Methods: Study Design: A cross-sectional, retrospective hospital-based study.
Participants: Individuals who underwent complete colonoscopies between January 2014 and February 2020 were retrospectively analyzed. The study focused on those with two colonoscopies, where adenomas were identified during the first colonoscopy.
Grouping: Participants were categorized into Group A (no adenoma at follow-up colonoscopy) and Group B (adenoma present at follow-up colonoscopy).
Comparative Analysis: The study compared age, gender, findings from the initial colonoscopy, and baseline metabolic profiles between the two groups.
Statistical Methods: The analysis involved t-tests for continuous variables, chi-square tests for categorical variables, and logistic regression for assessing the relationship between variables and the presence of adenomas at follow-up.
Results: From 33,073 colonoscopies, 2013 individuals were selected (Group A: 1024; Group B: 989).
The median ages were 51.9 years (95% CI, 51.3-52.5) for Group A and 53.5 years (95% CI, 53.5-54.6) for Group B ($p < 0.05$). The male proportion was 67.97% in Group A and 80.18%% in Group B ($p < 0.05$). The interval between colonoscopies was not significantly different between groups.
Findings at the first colonoscopy, such as larger adenoma size, multiple (>3) adenomas and the presence of villous histology or severe dysplasia were significant more common in Group B.
Group B exhibited a significantly higher prevalence of metabolic derangements such as hypertriglyceridemia, glucose intolerance, overweight, obesity and fatty liver, which were associated with the recurrence of adenomas (p

< 0.05).

Conclusions: The findings highlight the significance of initial colonoscopy results in predicting the risk of metachronous colorectal adenoma. Metabolic factors such as hypertriglyceridemia, glucose intolerance, and overweight are strongly associated with adenoma recurrence. These insights are crucial for developing targeted surveillance strategies in patients with a history of colorectal adenomas, emphasizing the need for personalized patient management based on initial colonoscopy findings and metabolic profiles.

P.068

COVID-19 疫情時期大腸癌趨勢的雙重面貌：發生率下降與晚期癌比率上升
THE TWO FACES OF COLORECTAL CANCER TREND IN THE ERA OF COVID-19 PANDEMIC: DECLINING INCIDENCE AND THE RISE OF ADVANCED STAGES

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Background: In Taiwan, Colorectal Cancer (CRC) is highly prevalent. The COVID-19 pandemic has disrupted CRC screening and diagnosis, leading to potential changes in disease incidence and stage at diagnosis. This study aims to clarify these impacts using real-world data.

Aims: To investigate the effects of the COVID-19 pandemic on CRC incidence and staging in Taiwan.

Methods: We analyzed CRC data from the Taiwan Cancer Registry Database (2015-2021). The pre-pandemic period (2015-2019) was compared with the pandemic period (2020-2021). Incidence rates were calculated per 100,000 individuals, and cases were categorized into non-advanced (stages 0, I, II) and advanced stages (III, IV). Annual incidence changes and stage distribution were assessed, using the Chi-square test for statistical significance ($p<0.05$).

Results: The incidence of CRC decreased from 43.92 per 100,000 in 2015 to 38.42 per 100,000 in 2021, with an annual reduction rate of 2.35%. Pre-pandemic, 57.1% of cases were non-advanced, and 41.1% were advanced. During 2020-2021 pandemic, non-advanced cases fell to 52.9%, while advanced cases rose to 44.4%. During the pandemic period, there was a significant increase in the risk for advanced-stage CRC, with a risk ratio of 1.09 (95% CI: 1.08-1.11, $p<0.001$).

Conclusions: Our study reveals a dual trend in CRC in Taiwan during the COVID-19 era: a decline in overall incidence but an increase in advanced-stage diagnoses, underscoring the extensive impact of pandemic-related lockdowns on cancer care. This trend suggests a heightened need for colorectal screenings and advanced CRC treatments post-lockdown. These insights underscore the importance of a healthcare system capable of providing uninterrupted cancer care during health crises and highlight the critical role of real-world data in shaping effective health policies.

P.069

胃腸道之子宮內膜異位症之系列報告
ENDOMETRIOSIS INVOLVING THE GASTROINTESTINAL TRACT: A CASE SERIES REPORT

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彰化基督教醫院胃腸肝膽科

Background: Endometriosis is a chronic, estrogen-dependent inflammatory condition characterized by the presence of endometrial-like glands and stroma outside the uterine cavity. It impacts around 10% of reproductive-aged women, with 35%-50% of those experiencing pelvic pain, infertility, and/or organ dysfunction. Among the affected areas is the gastrointestinal tract, involved in 3.8%-37% of cases, with the rectosigmoid colon being the most common site, followed by the rectum, ileum, appendix, and cecum. While many patients exhibit mild symptoms, severe complications like gastrointestinal bleeding, bowel obstruction, and perforation can arise. In this retrospective review, we examine 18 cases from 17 patients with gastrointestinal tract-involved endometriosis, encompassing seven biopsies and eleven resections, analyzing clinical characteristics and outcomes.

Aims: To evaluate the distribution and clinical presentation of endometriosis of gastrointestinal tract

Methods: This research accessed the pathology database for intestinal endometriosis, including biopsy and resection records. We retrieved 18 cases (17 patients) from the ASUS Lumos v3.3 Electronic Medical Record database at CHANGHUA CHRISTIAN HOSPITAL (Jan. 2012 to Dec. 2022). Clinical presentation, gross findings, and image analysis were collected and examined.

Results: We summarizes the clinical characteristics and macroscopic findings of the 18 cases. Patient ages ranged from 20 to 59 years (mean 48 years). Symptoms included lower gastrointestinal bleeding (n=6, 33%), abdominal pain (n=4, 22%), constipation (n=2, 11%), change in bowel habits (n=1, 5%), rectal pain (n=1, 5%), diarrhea (n=1, 5%), and abdominal bloating (n=1, 5%). Some cases were asymptomatic (n=3, 16%). Intestinal endometriosis locations included rectum (n=9, 50%), sigmoid colon (n=3, 16%), appendix (n=3, 16%), cecum (n=2, 11%), and ileum (n=2, 11%). Colonoscopy reports were available for 13 cases, with 6 cases of biopsy and one case of polypectomy outcomes revealing ulcer, polyps, and tumors. Resections (n=11) had image study reports, commonly indicating wall thickening or tumor lesions in Computed Tomography. One patient had endometriosis in both terminal ileum and sigmoid colon, mimicking terminal ileum tumor in colonoscopy and a soft tissue mass around the sigmoid mesocolon in Computed Tomography.

Conclusions: Intestinal endometriosis is a rare disorder primarily presenting as lower gastrointestinal bleeding or abdominal pain, often mimicking symptoms of intestinal malignancy. Predominantly located in the rectum, with some cases in the sigmoid colon and appendix, and rarely in the cecum or ileum, clinicians treating premenopausal female patients should consider the potential for endometriosis.

P.070

內視鏡醫師徒手壓病人肚子可以在換水大腸鏡時減少迴路產生
ABDOMINAL COMPRESSION ADMINISTERED BY THE PERFORMING ENDOSCOPIST IS EFFECTIVE IN REDUCING LOOPING DURING WATER EXCHANGE COLONOSCOPY

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Background: Loop formation is the most frequent cause of cecal intubation failure during colonoscopy. The formation of loops also results in patient discomfort. To reduce loop formation, external abdominal pressure is usually used manually provided by an assistant. Water exchange (WE) can reduce abdominal pain and loop formation during insertion of colonoscopy, but loop formation still can be encountered.

Aims: To evaluated whether abdominal compression performed by the endoscopist during colonoscopy could reduce loop formation.

Methods: Patients undergoing WE colonoscopy were randomized to receive colonoscopist-administered (colonoscopist group) or assistant-administered abdominal pressure (assistant group) when the tip of the colonoscope could not advance after straightening the scope by withdrawal. In the colonoscopist group, the endoscopist himself applied the manual pressure when loops formed. If failed, an assistant took over and applied the abdominal pressure instead. In the assistant group, an endoscopic assistant applied abdominal pressure when looping was noted. The cecal intubation time, need for abdominal pressure by the assistant and other procedure data were recorded.

Results: A total of 120 patients were enrolled (n=60 in each group). The baseline characteristics of the patients were similar between the two groups. The cecal intubation time were similar between the two groups (13.7 ± 4.6 min and 14.2 ± 5.0 min for colonoscopist and assistant group, respectively, P = 0.485), The proportion of patients in need of abdominal pressure administered by the assistant were lower in the colonoscopist group than the assistant group (21.7% vs. 45.0%, P = 0.011). Other procedural data were similar between the two groups.

Conclusions: During WE colonoscopy, abdominal pressure administered by the endoscopist when loops formed did not reduce the cecal intubation time, but could reduce the need for the help by the assistant with applying abdominal pressure. Whether endoscopist administered abdominal pressure could help during traditional air insufflation colonoscopy warrants further study.

P.071

自動化電腦輔助系統應用於在訓練階段前之大腸息肉的標記和分類
AUTOMATED COMPUTER-ASSISTED SYSTEM FOR COLON POLYPS LABELING AND CLASSIFICATION IN PRE-TRAINING STAGE

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Background: In the first stage of developing a computer-assisted detection and classification system (CADe/CADx), it is crucial to not only collect images from collaborated hospitals but also to engage numerous endoscopists in the task of labeling and classifying colon polyps, which is vital in the pre-training phase. The labeling process demands considerable time and workforce commitment. The manual labeling is susceptible to external factors such as fatigue and human errors, which impacts the accuracy of dataset annotation and classification. We highlight the need to establish an automated system for polyp image labeling that facilitates the training phase of the model development. This study focuses on training an automated labeling models using the state-of-the-art YOLO (You Only Look Once) algorithm series, with an emphasis on comparing their accuracy in labeling and classification. The best-performing model among these was applied to enhance the colorectal polyp labeling system and to replace repetitive tasks, providing high-quality and a large volume of labeling images while reducing labor expenses and ensuring consistent classification accuracy.

Aims: This study focuses on training an automated labeling models using the state-of-the-art YOLO (You Only Look Once) algorithm series, with an emphasis on comparing their accuracy in labeling and classification.

Methods: This study was conducted in Dalin Tzu-Chi Hospital (IRB Number: B11101011) to obtain still images and videos of colorectal polyps. For the videos, the frames were initially segmented and polyp images were extracted. These polyp images were obtained from white light and narrow-band imaging (NBI) endoscopy. Subsequently, the annotation tool Labelimg was used for polyp category labeling and classification. The study classified polyps into three categories: SSA, TA, and HP, with 700 images for each category. The dataset was divided into three parts using ten-fold cross-validation: Train (600 images), Validation (50 images), and Test (50 images). This study pre-evaluated the YOLO series of algorithms, including YOLOv4, YOLOv5, YOLOv6, YOLOv7, YOLOX, and YOLOR. The parameter settings for these algorithms included setting max_batches to 6000 for YOLOv4, while the epochs for all others were set to 300. Image dimensions were set to 608. Due to limited GPU memory, the batch size was set to 4. All other parameters followed the original papers of each algorithm. The training was conducted using an NVIDIA GeForce RTX 2070 graphics processor (Figure 1.). The model performance was evaluated with confusion matrix. In the confusion matrix, there are four values: True Positive (TP), False Positive (FP), True Negative (TN), and False Negative (FN). Through these values, we calculate metrics such as Accuracy, Precision, Recall, F1 Score (Figure 2.). The trained model performance was assessed with mean Average Precision (mAP). The mAP is the average of the average precision (AP) for all classes, where AP is a value between 0 and 1 that measures the model's performance for each class.

Results: Among all the YOLO series tested in this study, YOLOv7 shows the best performance with a mAP of 74.93% and a precision of 0.77, followed by YOLOv5 and YOLOR, as shown in Tables 1 and 2. Therefore, YOLOv7 is chosen as the labeling model to provide better accuracy and efficiency. We selected 100 images of polyps for test. Manually labeling and classifying these images took approximately 213 seconds, whereas using the NVIDIA GeForce RTX 2070 graphics processor, the same task was completed in 18 seconds. This demonstrates a significantly faster labeling and classification speed compared to manual method (Figure 3.). By using the "classes.txt" and ".pt" weight files, the model is applicable to the automatic object recognition algorithms across diverse areas, especially in fields where image labeling technology is not as advanced, thereby reducing the hurdles associated with adopting automated labeling techniques. This approach reduces potential data security concerns and decreases the cost related to cloud storage.

Conclusions: This study found that among the YOLO series algorithms compared, YOLOv7 performed the best for automated labeling and classification system. This study focuses on labeling and classifying colon polyps and introduces a more efficient and cost-effective method that minimizes human error and expense. It tackles the challenges involved in labeling images before training and extends the use of the assistive labeling system to areas with less advanced object recognition technologies, particularly in sensitive medical imaging. The goal is to decrease the time required for model development while enhancing the accuracy of labeling and classification.

P.072

利用即時電腦輔助系統在換水和空氣大腸鏡下之腺瘤和大腸鏡查檢次腺瘤偵測率的比較 - 一項隨機對照研究

A COMPARISON OF ADENOMA DETECTION AND ADENOMA PER COLONOSCOPY RATES USING REAL-TIME COMPUTER-AIDED SYSTEM IN WATER EXCHANGE AND AIR INSUFFLATION - A RANDOMIZED CONTROLLED STUDY

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Background: In a retrospective video analysis, we proved that the strengths of water exchange (WE) and computer-aided detection (CADe) complemented the weaknesses of each other. CADe increased WE polyp and adenoma detection rate and WE reduced false positive of CADe compared with the air insufflation. In current study, we adapted adenomas per colonoscopy (APC) as an improved quality indicator. The APC, defined as the total number of adenomas resected divided by the total number of colonoscopies, higher rate decreases the incidence of post-colonoscopy colon cancer within 3 years of index examination. We applied the CADe model to conduct a randomized controlled real-time study to compare the ADR and APC between the WE and air insufflation method.

Aims: We applied the CADe model to conduct a randomized controlled real-time study to compare the ADR and APC between the WE and air insufflation method.

Methods: By mimicking the methods established to identify diseases in plants, we developed a CADe model using convolutional neural network (CNN) with transfer learning approach (YOLOv4) to detect colon polyps. The CADe algorithm achieved a mean average precision of 94.0% and the area under receiver operating characteristic curve of 0.98. The sensitivity and specificity were set to 0.96 and 0.97, respectively. The positive predictive value was 0.98 and negative predictive value was 0.93. The algorithm was validated by a video analysis study. To assess the real-time application, 228 eligible patients were prospectively recruited to undergo real-time CADe colonoscopies inserted with either WE or air insufflation method. The resected polyps were evaluated by a blinded pathologist.

Results: The real time CADe colonoscopies included patients inserted with either WE (n=114) or air insufflation (n=114) methods. Table 1. shows that the WE group had significantly higher adenoma detection rate (ADR), 60.5% versus 47.4%, P=0.046. The number of adenomas is higher in WE (n=174) compared with the air insufflation (n=125). The APC showed significantly higher in WE group compared with the air insufflation group (1.53 versus 1.10, P=0.043), respectively.

Conclusions: This first real-time CADe comparison revealed ADR was significantly higher in WE than the air insufflation. The APC was significantly lower in the air insufflation group. The CADe algorithms proved our hypothesis of higher ADR and APC in the WE group in the randomized controlled real-time colonoscopy.

P.073

傳統腺瘤和鋸齒狀息肉切除後大腸直腸癌發生率和相關死亡的長期風險：系統性回顧和網絡統合分析

LONG-TERM RISK OF COLORECTAL CANCERAND RELATED DEATH AFTER REMOVAL OF CONVENTIONAL ADENOMA AND SERRATED POLYPS : A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Background: Long-term risk of colorectal cancer (CRC) and CRC-related mortality after baseline conventional adenomas and serrated polyps (SPs) removal remains unclear.

Aims: We aimed to evaluate the risk of CRC and CRC-related mortality in individuals with different subtypes of polyps (including low-risk adenomas (LRAs), high-risk adenomas (HRAs), SPs alone (further stratification with small SPs and large SPs) and synchronous SPs withconventional adenoma (SPs with A)) and those with no adenoma through a systematic review and component network meta-analysis (CNMA).

Methods: A comprehensive literature search was performed to select studies reporting CRC and/or CRC-related mortality with polyp characteristics afterindex colonoscopy. Electronic databases, including PubMed, EMBASE, and the Cochrane Library, were searched for articles published before August 2023. Primary outcome were CRC incidence and CRC-related mortality, calculated as incidence rate ratio (IRR) with 95% confidence interval (CI, unadjusted analysis) and hazard ratio (HR) with 95% CI (adjusted analysis, where reported).

Results: Twenty one studies with 7,396,136 person-years were included in our final analysis. On unadjusted NMA, the highest two risks of CRC were patients with large SPs (IRR, 2.99; 95% CI, 2.01-4.44) and HRAs (IRR, 2.93; 95% CI, 2.47-3.48). Patients with HRAs had highest CRC-related mortality (IRR, 3.40; 95% CI, 2.77-4.16). When using available adjusted data, patients with large SPs (HR, 3.48; 95% CI, 1.71-7.10) and HRAs (HR, 2.80; 95% CI, 2.42-3.23) still had highest two risks of CRC. And patients with HRAs had highest CRC-related mortality (HR, 2.40; 95% CI, 2.03-2.84).For component NMA, the risk of CRC could be categorized as low risk (small SPs and LRAs), intermediate risk (SPs with A) and high risk (large SPs and HRAs).

Conclusions: Current systematic review and CNMA demonstrate the risk of CRC and CRC-related mortality is significantly higher for patients with HRAs or large SPs, and the risk is only marginally higher in patients with small SPs or LRAs. Patients with HRAs or large SPs at baseline colonoscopy may need more intensive surveillance.

P.074

分析大腸息肉病人唾液與糞便中的牙齦紫質單孢菌
ANALYSIS OF PORPHYROMONAS GINGIVALIS IN SALIVA AND FECES OF COLON POLYP PATIENTS

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Background: Periodontal disease, accompanied by oral inflammation and pathological changes in the microbiome, induces gut dysbiosis. Porphyromonas gingivalis (Pg) is a common periodontal pathogen that acts synergistically to promote oral carcinogenesis. Previous studies have reported the presence of Pg in the feces and tumor tissue of colorectal cancer patients. However, limited data exist on the association between the oral/periodontal microbiome and colon polyps.
Aims: This study aimed to examine the prevalence and quantity of Pg in the saliva and feces of patients with and without colon polyps.
Methods: Patients who underwent lower gastrointestinal endoscopy for routine inspections were included in the study. Saliva and feces samples were collected before endoscopy using sterilized specimen bottles. 1 mL of saliva and 20g of feces were collected from each study participant. Samples were immediately transferred to the laboratory using ice packs and stored frozen at -20℃ until PCR analysis.
Results: The study included 30 patients with colon polyps and 23 without polyps. Among them, 29 (54.7%) were female, and 24 (45.3%) were male. The median age of the patients was 64.81±8.43 years old. Saliva samples from patients with colon polyp showed higher amounts of Pg compared to controls (7326.83±1240.68 vs 16266.82±3130.36, respectively; p = 0.01). The Pearson correlation coefficient between feces and saliva Pg was 0.50 (P < .001).
Conclusions: This study revealed higher amounts of Pg in the saliva of patients with colon polyps. These findings suggest potential applications in identifying high-risk groups for colon polyps through saliva microbiome analysis, as well as in exploring the relationship between oral health, particularly mouth and gingival conditions, and preventing colon polyps.

P.075

原發性小腸淋巴瘤的臨床病理學研究：中台灣一醫學中心之經驗
CLINICOPATHOLOGICAL STUDY OF PRIMARY SMALL INTESTINAL LYMPHOMA: A SINGLE INSTITUTE EXPERIENCE IN TAIWAN

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Background: Lymphoma is a cancer that origin from cells of lymphatic system, the lymphatic system includes spleen, lymph nodes, bone marrow and thymus gland. Because lymph tissues are exist in many parts of the body, lymphoma can start almost anywhere. The gastrointestinal (GI) tract is the common site of extranodal non-Hodgkin's lymphoma, accounting for 30-45% of all cases. Primary small intestinal lymphoma (PSIL) occurs infrequently, accounting for 20% to 30% of primary gastrointestinal (GI) lymphomas. Primary small bowel lymphoma are difficult to diagnose preoperatively because of endoscopic inaccessibility
Aims: The aim of the study was to investigate the clinicopathological features of primary small bowel lymphoma in a single institute experience in Taiwan.
Methods: From January 2013 to December 2021, we retrospectively reviewed the medical charts at China Medical University Hospital. Patients who were diagnosed as primary small bowel lymphoma (PSIL) via double balloon enteroscopy (DBE) were included into this study. Patients who were diagnosed as primary small bowel lymphoma (PSIL) with method of DBE were included into this study. Clinical data were obtained from the medical records and from the physicians responsible for patient care. Clinical data abstracted included age, gender, symptoms, tumor location, co-mobidity, treatment methods, and outcomes.
Results: A total of 10 patients with primary small bowel lymphoma (PSIL) were enrolled into this study. There were 4 females and 6 males, with a male-to-female ratio of 1.5:1. The mean age was 67.6 years (range, 58-75years). In our present study, as regards clinical symptoms, all 10 patients were symptomatic. They most commonly presented with GI bleeding (8 patients, 80%). Followed by abdominal pain in seven, fever in five, and diarrhea in four, and weight loss in two patient. In terms of co-

morbidities, 8 of 10patients (80%) had hypertensive disease and cardiovascular disease, 6 (60%) had diabetes mellitus, 2 (20%) had chronic liver disease with or without liver cirrhosis, and one (10%) had prostate cancer. Primary small bowel lymphoma involved the jejunum in 6 (60%) of 10 patient, the ileum in 3 (30%) of 10 patients, and the 4th portion of duodenum in 1 (10%) of 10 patient. The pathology type of lymphoma, including 6 case(6/10, 60%) with diffuse large B cell lymphoma(DLBCL), 2 case(2/10, 20%) with Burkitt's lymphoma, 1 case(1/10, 10%) with peripheral T-cell lymphoma, 1 case(1/10, 10%) with low grade B-cell lymphoma, 1 case(1/10, 10%) with follicular lymphoma. One patient was diagnosed as diffuse large B cell lymphoma, GC type in distal jejunum and combined with follicular lymphoma in middle jejunum. Three patients receive surgical operation. Another seven patient receive systemic chemotherapy. Four patients died of disease progression, one of these four cases receive surgical operation and one patient receive operation died of infection. Another five patient still alive and regular follow up now.

Conclusions: In conclusion, the results of our present study showed primary small intestine lymphoma are rare in Taiwan and their diagnosis are usually needs deep small bowel enteroscopy. These patients who suffered from primaly small intestine lymphoma usually old age and have co-mobidity disease. Compared with those reported in other countries, primary small intestine lymphoma in Taiwan have the same clinicopathologic feature

P.076

對比增強諧波內視鏡超音波於區分壺腹腺瘤和腺癌的應用—前瞻性隊列研究
UTILITY OF CONTRAST ENHANCED HARMONIC ENDOSCOPIC ULTRASOUND (CEH-EUS) FOR DIFFERENTIATING AMPULLARY ADENOMA AND ADENOCARCINOMA – A PROSPECTIVE COHORT STUDY

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Background: The differential diagnosis between ampullary adenoma and adenocarcinoma before performing endoscopic papillectomy is essential. However, it is often challenging only depending on endoscopic biopsy, especially for large or nonexposed protruded-type ampullary neoplasm. The potentially additional diagnostic value of contrast enhanced harmonic endoscopic ultrasound (CEH-EUS) has never been investigated.

Aims: The aim of this study was to prospectively evaluate the diagnostic performance of CEH-EUS for differentiating ampullary adenocarcinoma from adenoma.

Methods: Patients with suspicious ampullary neoplasm larger than 1cm were prospectively enrolled from April 2019 through July 2023 at National Taiwan University Hospital and followed up for at least 6 months. All included patients underwent CEH-EUS with Sonazoid for evaluation of microvasculature. Two blinded reviewers classified the perfusion images into two categories: iso-hyperenhancement or hypoenhancement. The perfusion pattern was further categorized as homogenous or heterogenous pattern, depending on any perfusion defect noted. The vessel images were categorized as having a regular spotty vessel or an irregular vessel.

Results: A total of 58 patients were screened in this study, and finally 44 patients were included. Among the 44 patients, 24 (54.6%)were diagnosed with benign lesions (including 16 cases of low-grade dysplasia and 8 cases of high-grade dysplasia), while the remaining 20 patients (45.4%) were diagnosed with malignancy. The perfusion of hypo-enhancement determined by CEH-EUS in the diagnosis of malignancy with a sensitivity and specificity of 35% and 91.7%, respectively. The presence of perfusion defects (heterogenous pattern) was calculated to diagnose malignancy with a sensitivity and specificity of 95% and 70.8%, respectively. The presence of irregular vessels predicted the diagnosis of ampullary malignancy, achieving

a sensitivity of 28.57% and a specificity of 87.5%. Based on the definite diagnosis, the pattern of CEH-EUS of the ampullary neoplasm with hypoenhancement, heterogeneous or the presence of irregular vessels were observed statistically significance in malignancy group comparing with low-grade adenoma (P-value < 0.05). In 11 cases (25%), final diagnosis changed after CEH-EUS.

Conclusions: The presence of hypo-enhancement, perfusion defect, or irregular vessels in ampullary neoplasms seen on CEH-EUS may be accurate predictors of malignant ampullary lesions. CEH-EUS also offers slightly improved diagnostic accuracy compare with conventional EUS combined with endoscopic biopsy.

P.077

手術前內視鏡膽道引流對於接受胰十二指腸切除術治療胰腺癌患者的影響。

IMPACT OF PREOPERATIVE ENDOSCOPIC BILIARY DRAINAGE IN PATIENTS UNDERGOING PANCREATICODUODENECTOMY FOR PANCREATIC CANCER.

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Background: The impact of preoperative endoscopic biliary drainage (EBD) on the incidence of post-pancreaticoduodenectomy complications and patient survival is unclear.

Aims: The aim of this study was to assess the survival outcomes and safety of preoperative EBD in patients undergoing pancreatoduodenectomy for pancreatic cancer.

Methods: We performed a comprehensive and retrospective collaborative network analysis using TriNetX data from December 24, 2018, to December 24, 2023. Patients were identified from databases using the International Classification of Diseases, Tenth Revision, Clinical Modification codes, along with procedure codes, who had a diagnosis of pancreatic adenocarcinoma and underwent pancreatoduodenectomy, as well as received endoscopic biliary drainage in the drainage group. For the upfront surgery group, we enrolled individuals who did not undergo drainage in the entirety leading up to their operation. Using propensity score matching (PSM), we established matched groups in a 1:1 ratio. Odds Ratio(OR) with 95% confidence intervals (95% CI) were computed to evaluate safety outcomes and pertinent complications, while the Kaplan-Meier method was employed to assess survival probabilities.

Results: The study included 143 patients who underwent preoperative biliary drainage and 438 patients who received upfront surgery for pancreatic adenocarcinoma. After performing PSM (1:1), both groups were comprised of a well-matched 113 patients each. When compared to the upfront surgery group, the preoperative EBD group exhibited a higher risk of complications, such as bile leakage (OR: 1.308, 95% CI: 0.665-2.571) and pancreatic fistula (OR: 1.565, 95% CI: 0.892-2.746). However, the risk was similar for duodenal anastomosis

stricture (OR: 1, 95% CI: 0.399-2.505), intra-abdominal abscess/hematomas (OR: 1, 95% CI: 0.399-2.505), and wound dehiscence (OR: 1, 95% CI: 0.399-2.505). Regarding overall survival, patients who underwent preoperative EBD demonstrated similar 1-month (98.198% vs. 98.173%, P = 0.9981), 90-day (96.204% vs. 95.295%, P = 0.7391), and 1-year (82.013% vs. 82.137%, P = 0.9733) survival rates compared to those who had upfront surgery. In subgroup analysis, the preoperative EBD group has better 1-year overall survival rates in patients with preoperative total bilirubin level at 10-15 mg/dL (57.273% vs. 46.753%, P = 0.6552), and <65 years old.

Conclusions: In the TriNetX matched cohort study on resectable pancreatic adenocarcinoma, preoperative EBD was linked to comparable outcomes in short-term and 1-year survival, but increased the risks of postoperative bile leakage and pancreatic fistula.

P.078

合併嚴重急性膽囊炎和膽管炎的八十歲病患在接受介入性內視鏡逆行性胰膽管造影和膽囊切除術的預後

OUTCOME OF CHOLECYSTECTOMY IN OCTOGENARIANS WITH CONCURRENT ACUTE CHOLECYSTITIS AND CHOLANGITIS RECEIVING PERCUTANEOUS TRANSHEPATIC GALLBLADDER DRAINAGE AND INTERVENTIVE ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Background: Acute cholecystitis (AC) with concurrent cholangitis is a life-threatening disease in elder patients

Aims: We aimed to investigate the outcome of receiving cholecystectomy in patients aged ≥ 80 years with moderate to severe AC who had received percutaneous transhepatic gallbladder drainage (PTGBD) and subsequent interventive endoscopic retrograde cholangiopancreatography (ERCP).

Methods: From January 2008 to February 2021, we retrospectively enrolled 174 patients receiving PTGBD and subsequent ERCP in Taipei Veterans General Hospital. Patient were divided into cholecystectomy or non-cholecystectomy groups after discharge. Clinical outcomes including overall survival rate, recurrent rate of biliary tract events, and complications of ERCP and cholecystectomy were analyzed. Kaplan-Meier model was used to interpret the overall survival.

Results: There were 34 patients receiving cholecystectomy (cholecystectomy group) and 98 patients receiving conservative treatment (non-cholecystectomy group) after receiving PTGBD and subsequent interventive ERCP. The overall mortality rate and biliary tract event related mortality were not different between the cholecystectomy group and the non-cholecystectomy group (20.5% vs. 35.7%, p=0.082; 0% vs. 3%, P=0.083, respectively). The 1-year recurrent rate, 3-year recurrent rate and 5-year recurrent rate of biliary tract events were significantly lower in the cholecystectomy group (2.9% vs. 18.4%, P=0.002；5.9% vs. 20.4%, P=0.014；8.8% vs. 24.5%, P=0.02, respectively). There was no difference in terms of 1-year recurrent rate of cholangitis (2,9% vs. 5.1%, p=0.605), and pancreatitis (0% vs. 0%). The overall ERCP-related complication rate was low (4%) in this elderly

population. The overall surgical complication was 11.8% in the cholecystectomy group.
Conclusions: Cholecystectomy had lower recurrent rate of biliary tract events than conservative treatment in octogenarians with moderate-to-severe cholecystitis and concurrent cholangitis receiving subsequent interventive ERCP.

P.079

膽管結石病患於逆行性膽管胰管攝影術後的脂肪酶及澱粉酶數值升高相關因素分析
FACTORS ASSOCIATED WITH HIGH LIPASE/AMYLASE LEVELS IN COMMON BILE DUCT STONE PATIENTS POST ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PROCEDURE

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Background: Asymptomatic hyperamylasemia was up to 18.3% in endoscopic retrograde cholangiopancreatography (ERCP) procedures in the previous studies report. According to ESGE guidelines (European Society of Gastrointestinal Endoscopy), the incidence rate of ERCP-related pancreatitis (PEP) varies from 3.5% to 9.7%. However, not every high level of lipase or amylase would progress to PEP in real world practice.
Aims: Aim of the study was to evaluate factors associated with high lipase or amylase levels in common bile duct (CBD) stone patients post ERCP procedure.
Methods: We conducted a retrospective study focused on 165 CBD stones patients with naïve papilla accepted ERCP procedures from January 1, 2020, to December 31, 2022 in Liouying Chi Mei hospital. 32 patients with high lipase or amylase level or pre-ERCP pancreatitis were excluded initially. Total 133 CBD stone patients were divided into groups A (83pt), B(29pt), C(19pt) and D (2pt) according to post-ERCP clinical results(amylase /lipase level). Group A with normal amylase/lipase level post ERCP procedure, group B with asymptomatic hyperlipasemia or hyperamylasemia lower than 3 times of normal upper limit post ERCP procedure, group C with asymptomatic hyperlipasemia or hyperamylasemia upper than 3 times of normal upper limit after ERCP and group D with post-ERCP pancreatitis. Factors contributing ERCP pancreatitis in pre, during and post procedure were evaluated among each group with a standard statistical method.
Results: In this study, group A without elevated Amylase / lipase level was 62.4% (83/133), group B less than three times amylase /lipase level was 21.8% (29/133) and group C greater than three times amylase /lipase level was14.2 % (19/133) and the post ERCP pancreatitis rate was 1.5 % (2/133) (group D). Significant statistic difference between group A and C in univariant analysis were pre-ERCP Hb

level (P=0.036), pre-ERCP AST level (P=0.041), pre-ERCP ALT level (P=0.013), Female gender (P=0.024), alcohol use (P=0.025), usage double wire cannulation (P=0.002), P-duct stent drainage (ERPD) (P=0.034). Further Logistic regression analysis showed usage double wire cannulation (OR: 11.574; CI 1.28~104.611) was proven to be the significant risk factors correlation between group A and C. There was no obvious factor found statistic difference between group A and B in univariant analysis.

Conclusions: 1. Double wire cannulation had significantly increased the risk causing asymptomatic high amylase and lipase level over upper limit three times in CBD stone patient accepting ERCP procedure 2. Post ERCP -Patients with asymptomatic high amylase / lipase level less than 3 times of upper limits share similar risks in patients with normal amylase and lipase level.

P.080

年輕型遺傳性胰臟炎與其基因分析 - 一個醫學中心的案例分析
JUVENILE HEREDITARY PANCREATITIS AND GENETIC MUTATION ANALYSIS- A CASE SERIES FROM A TERTIARY MEDICAL CENTER

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Background: Hereditary pancreatitis is a rare cause of acute, acute recurrent and chronic pancreatitis in the pediatric and adolescent population. Common associated gene mutations include PRSS1, SPINK1, CFTR, CTRC, CASR, CLDN2. Patients with hereditary pancreatitis usually suffer from recurrent acute pancreatitis, develop chronic pancreatitis eventually, and require frequent endoscopic interventions.

Aims: In this study, clinical information of 4 patients with hereditary pancreatitis followed up at National Cheng Kung University Hospital (NCKUH) is presented. All of the 4 patients received endoscopic interventions, one patient failed endoscopic treatment and received surgical intervention for biliary drainage; 3 patients had resolution of pancreatic pseudocyst after endoscopic interventions.

Methods: All the 4 patiens presented as symptomatic chronic pancreatitis when they were in childhood to teenager age. Despetc treat the symptosm of the chronic pancreatitis by endosocpic methods, We performed whole exone sequence from the blood, and found all of them has different genetic mutation which related to hereditary pancreaitits and one of the patient has a strong family history.

Results: 4 Taiwanese patients with hereditary pancreatitis followed up in the NCKUH are presented. The characteristics of 4 patients is summarized in Table 1. Patient 1 and Patient 2 are sisters in the same family with PRSS1 gene mutation; Figure 1 is their family tree. Patient 3 and Patient 4 are from different family, but both patients are male and diagnosed with SPINK1 gene mutation. The onset age of initial symptoms was before 10 years in 3 patients (Patient 1, 3, 4) and 13 years in Patient 2, which was similar to previous report, 10 years for PRSS1 R122H mutation and 14 years patients for PRSS1 N29I mutation.4 3 patients (Patient1, 2, 4) presented with acute or subacute recurrent pancreatitis with acute epigastric pain and vomiting; Patient 3 had chronic intermittent epigastric pain

and abdominal distention for 6 months initially. 3 patients (Patient 1, 2, 3) were found pancreatic pseudocyst at initial presentation. Patient 2 developed pancreatic pseudocyst with internal hemorrhage and Patient 3 had a huge pancreatic pseudocyst, size 11 cm. Chronic pancreatitis at initial medical visit was presented in 3 of 4 patients (Patient 1, 2, 3); Patient 4 also developed chronic pancreatitis 6 years after onset of symptoms.

Conclusions: In this case series, 4 young patients with hereditary pancreatitis were presented. Our study showed successful experience of endoscopic intervention in managing hereditary pancreatitis and pancreatic pseudocyst in 3 of 4 patients. Further larger studies to evaluate the efficacy of endoscopic interventions and possible risk factors of treatment failure are necessary.

P.081

以內視鏡超聲引導的細針穿刺相關的醫源性胰臟炎的評估

THE ASSESSMENT OF IATROGENIC PANCREATITIS RELATED TO ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY

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Background: Pancreatitis is one of the complications of endoscopic ultrasonography guided fine needle biopsy. Reported iatrogenic acute pancreatitis following EUS-FNB of pancreatic lesions were rates ranging from 0.19% to 2.0%.

Aims: The aim of our study was to evaluate the frequency and the possibility risk factors of acute pancreatitis after EUS-FNA of pancreatic cysts and solid lesions.

Methods: We conducted a retrospective analysis of 406 patients who underwent Endoscopic Ultrasound (EUS) for pancreatic mass lesions from January 2018 to December 2023. As a diagnostic tool for iatrogenic pancreatitis, we utilized serum lipase levels exceeding three times the normal amount. Serum lipase was assessed only if symptoms attacked and related to pancreatitis, such as abdominal pain or persistent abdominal fullness, manifested after the procedure, rather than through routine examination. We excluded cases with a diagnostic EUS and those experiencing an acute pancreatitis episode just before the EUS-fine needle biopsy.Among the cases, 28 developed pancreatitis after EUS-Fine Needle Biopsy (FNB). After ruling out the possibility of ERCP-related or other procedure-related pancreatitis, only 15 cases were identified as having iatrogenic pancreatitis following EUS-FNB.

Results: All patients underwent FNB using the Boston 22G-Acquired needle with the Rapid On-Site Evaluation (ROSE) method. Of the 15 cases, 8 were female and 7 were male. Two patients had a history of alcoholism, 2 had diabetes mellitus, and 7 had hypertension. The mean age was 60.7±11.3 years. The median size of the pancreatic lesions was 31.2 mm (ranging from 13 to 54 mm). The majority of patients were diagnosed with adenocarcinoma (13 adenocarcinoma, 1 well-differentiated Neuroendocrine Tumor (NET), and 1 inflammatory pseudotumor). Among the cases, 7 had a cystic component, and 8 presented as solid masses. Nine cases exhibited well-

defined margins, while 6 had blurred or infiltrative margins. All masses were hypoechoic, with 8 lesions displaying heterogeneous components. Seven cases exhibited common bile duct (CBD) dilation, and 13 cases had pancreatic duct (P duct) dilation. Eight cases received an echo-contrast agent (Sonazoid, GE Healthcare, Oslo, Norway) before FNB. Nine lesions were in the pancreatic head, 4 in the uncinate process, and 2 in the neck. Needle punctures were performed from the duodenal second portion (6 cases) and the bulb (11 cases) as the FNB puncture sites.

Conclusions: Within our dataset, pancreatic duct (P duct) dilatation emerged as a potential risk factor, regardless of whether it resulted from tumor compression or involvement with Intraductal Papillary Mucinous Neoplasm (IPMN). The earlier study indicated that pancreatic cysts exhibited a statistically higher incidence of developing pancreatitis following EUS-FNA in comparison to cases with solid lesions. Nevertheless, in our dataset, the presence of a cystic component did not demonstrate statistical significance regarding iatrogenic pancreatitis after FNB.

P.082

高齡膽管結石患者於逆行性膽管胰管攝影術後相關危險因子分析一回溯性研究
RISK FACTORS ASSOCIATED WITH ELDER PATIENTS WITH COMMON BILE DUCT STONES POST ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PROCEDURE , RETROSPECTIVE STUDY

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Background: Aging is often categorized as a high-risk factor and high mortality rate for Endoscopic retrograde cholangiopancreatography (ERCP) in previous studies. However, ERCP procedure has become more popularly applied in elderly patients due to the aging society In Tainan countryside.

Aims: The study retrospectively investigated the risks associated with ERCP examination in elderly populations residing in areas with high prevalence of gallstones disease.

Methods: We conducted a retrospective study focused on 165 CBD stones who underewent ERCP procedures from January 1, 2020, to December 31, 2022 in Liouying Chi Mei hospital. The patients were categorized to two group: the elderly group (age ≥ 80) and the younger group (age < 80). Factors contribute to ERCP in pre, during and post procedure were investigated with standard statistic method.

Results: The younger group included 128 people (77.6%), while the elderly group had 37 individuals (22.4%). Regarding preoperative biliary pancreatitis proportions, the elderly group (5/37) and the younger group (25/128) were 13.5% and 19.5% respectively ($p>0.05$). In univariate analysis, the elderly group showed significantly less difficult with cannulation to orifice of papilla ($p=0.05$) but had a higher utilization of balloon dilation ($p<0.05$) . Additionally, in two-sample t-test analysis, the elderly group had a significantly longer hospital stay; the mean hospital stay for the older and younger groups was 13 ± 8.7 days and 9.5 ± 6.7 days, respectively ($p=0.0095$). There was no significant statistical difference between the two groups in terms of post-ERCP complications (perforation, bleeding, pancreatitis and infection)

Conclusions: Elderly patients have a longer hospitalization period, but a lower rate of difficult cannulation and no obvious association with biliary pancreatitis as compared to younger patients. Further research will be needed to explore the correlation between hospital stay and age.

P.083

JDP2 調控 ROS 平衡與細胞擴張與侵入性，於胰臟癌細胞消退經由 AHR-NRF2 基因電池

JDP2 CONTROLS THE ROS BALANCE AND CELL SPREADING, INVASION, AND PANCREATIC CANCER REGRESSION THROUGH AHR-NRF2 GENE BATTERY

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Background: The crosstalk between aryl hydrocarbon receptor (AhR) and nuclear factor (erythroid-derived 2)-like 2 (Nrf2) signaling is called the "AhR–Nrf2 gene battery", works synergistically in detoxification to support cell survival. Nrf2-dependent phase II gene promoters are controlled by coordinated recruitment of the AhR to adjacent dioxin responsive element (DRE) and Nrf2 recruitment to the antioxidative response element (ARE).
Aims: The molecular interaction between AhR and Nrf2 members including phase I and II gene complexes, and their mediators are poorly understood.
Methods: Through using site-directed mutagenesis (SDM) on AhR reporter we established, we identify the critical cis-element of activating phase I and phase II response. The enzyme system was further studied through Jdp2 knock out mouse embryonic fibroblast (MEF) compared with WT-MEF, in order to establish the complex shift between phase I and phase II response. Last, we used 2545 pancreatic carcinoma to confirm the critical role of phase I and phase II enzyme system to the ROS insensitive cancers.
Results: Here we demonstrated that AhR promoter was activated by phase I ligands such as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) through the AhR–Jdp2–Nrf2 axis in a time- and special transcription-dependent manner. Jdp2 was a bifunctional activator of phase I enzyme ligand- and phase II enzyme ligand-mediated transcription in response to TCDD. After TCDD exposure, Jdp2 activated the AhR promoter at the DRE and then moved to the ARE where it activated the promoter to increase reactive oxygen species (ROS)-mediated functions such as cell spreading and invasion in normal cells, and cancer regression in mutant kRAS–p53-driven pancreatic tumor cells. We conclude that Jdp2 plays a critical role in AhR promoter activation through the AhR–Jdp2–Nrf2 axis in a spatiotemporal manner. The AhR functions to maintain ROS balance and cell spreading, invasion, and cancer regression in a mouse model of mutant kRAS–p53 pancreatic cancer. These findings provide new insights into the roles of Jdp2 in the homeostatic regulation of oxidative stress and in the antioxidation response in detoxification, inflammation, and cancer progression.
Conclusions: In this study, the evidence suggests that Jdp2 is crucial for linking both AhR-Nrf2 battery for AhR promoter activation and ROS homeostasis. Our results also suggested the phase I and phase II detoxification response can be triggered through the same protein complex including AhR, Jdp2, and Nrf2. This complex is crucial for modulating the balance of ROS, and controls the shifting of phase I to phase II detoxification response. Activation of phase I detoxification enzymes by AhR-Jdp2-Nrf2 complex binding on DRE cis-elements will result in signification increase of ROS. When ROS accumulates to a point that triggers the AhR-Jdp2-Nrf2 complex, the complex will bind to ARE cis-elements in order to maintain the homeostasis of oxidative stress.

P.084

年輕發病膽管癌的臨床特徵與預後：某醫療中心的回顧性研究
CLINICAL CHARACTERISTICS AND PROGNOSIS OF YOUNG-ONSET CHOLANGIOCARCINOMA: A RETROSPECTIVE STUDY IN ONE MEDICAL CENTER

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Background: Cholangiocarcinoma (CCA), a cancer of the bile ducts, is typically diagnosed in older adults, and the median onset years is between 67 and 72 years. Nevertheless, a limited understanding of early-onset diseases remains, underscoring the necessity for dedicated research. According to previous studies, the patients who are diagnosed with young-onset CCA have characteristics such as having a greater proportion of intrahepatic CCA, primary sclerosing cholangitis, and more likely to have gene mutations. To our knowledge, the condition of young-onset CCA is still unknown in Taiwan.

Aims: The study aimed to analyze the clinical characteristics, treatment results, and survival rates between young-onset CCA patients and their older counterparts.

Methods: We retrospectively reviewed the medical records of patients with CCA in MacKay Memorial Hospital from Jan. 1st 2015, to Dec. 31st 2021. The patients with histologically proven CCA were enrolled. We compared clinical characteristics and outcomes between patients with young-onset cholangiocarcinoma, diagnosed between the ages of 18 and 50 years, and patients with typical-onset cholangiocarcinoma, diagnosed at the age greater than 50 years. Chi-square test and t-test were applied for the analysis of clinical features of patients who are diagnosed with young-onset CCA and those with typical-onset CCA. Utilizing the Kaplan-Meier method, survival curves were compared between the two groups.

Results: A total of 152 patients with histologically proven CCA were enrolled and comprised of two groups; the young-onset group (n = 15) and the typical-onset group (n = 137). The young-onset CCA was comprised of nine males (60 %), and the typical-onset CCA, was comprised of 64 males (46.7%)(p=0.418). The mean age of the young group was 43.9 years old, and the mean age of the typical group was 67.6 years old. There were no differences between young-onset and typical-onset groups in tumor sizes, tumor numbers, smoking, alcoholism, diabetes, gallstones, intrahepatic duct (IHD) stone, post-cholecystectomy, NASH/NAFLD, viral hepatitis, and liver cirrhosis. The young group had a greater proportion of intrahepatic CCA subtype (86.7% vs. 56.7%, p=0.048) than the typical-onset group. While there was no significant difference in the survival curve between the two groups, the young group had a more prolonged median survival than the typical group (25 months vs.13 months, p=0.269).

Conclusions: According to our analysis, more young-onset patients had intrahepatic type CCA than typical-onset patients. The median survival of the young onset group was longer than the typical-onset group, but there was no significant difference. More sample size and subgroup analysis are needed for further research.

P.085

內視鏡超音波導引下組織取得是否適用於懷疑淋巴癌病灶的診斷？
IS ENDOSCOPIC ULTRASOUND GUIDED TISSUE ACQUISITION (EUS TA) FEASIBLE FOR LESIONS SUSPECTED LYMPHOMA?

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Background: he preferred method for obtaining the tissue from lesions suspected lymphoma is incisional biopsy especially for subtyping. For intra-abdominal and mediastinal suspected lymphoma lesions some patients are not feasible or not willing for surgical incisional biopsy. Nowadays endoscopic ultrasound guided tissue acquisition (EUS TA) is a procedure to obtain the cells/tissue from intra-abdominal and mediastinal lesions.
Aims: We analyzed our data to elucidate the feasibility of EUS TA for lesions suspected of lymphoma.
Methods: From Aug. 2016 to Oct. 2023 there were twelve patients with suspected lymphoma lesions enrolled for the analysis. We collected the characteristics of the demography and the lesions. We also recorded the type and size of the needle, the puncture route, cytological and histological diagnosis and subtypes of lymphoma.
Results: The average age of twelve patients was 62 +- 17 years old and male gender was predominant (male : female = 7 : 5). The average size of suspected lymphoma lesions was 45 mm(standard deviation +- 18mm). The most common site of lesions was intraperitoneal (n=7) followed by pancreatic (n=4) and mediastinal (n=1)(Table 1). There were three kinds of needle used for tissue acquisition (fine needle biopsy needle(FNB) 22G was n= 9, fine needle aspiration needle(FNA) 19G was n=2, FNA 22G was n=1). About the puncture route the number of trans-gastric route was seven, trans-duodenal was four and trans-esophageal was one. As for the cytological diagnoses positive for malignant cells were eight , suspicious was one(FNB 22G needle), atypia was one(FNB 22G needle) and negative for malignant cells were two(FNA needle(1), FNB needle(1)). By means of histology ten patients were confirmed as lymphoma, one was crushed tissue immunoreactive for CD20 and one was atypical lymphoid cell proliferation. About the subtypes of lymphoma, diffuse large B cell lymphoma(DLBCL) was the most common and other two patients were Burkitt's lymphoma and follicular lymphoma(Table 2).
Conclusions: According to our preliminary data EUS guided tissue acquisition for diagnosis of lymphoma is feasible. We suggested using FNB needle with 22G at least or FNA needle with 19G which was expected to gain high probability of confirmed diagnosis.

P.086

評估內視鏡超音波穿刺檢體取得之效率及正確性：快速染色影像加強法對比巨觀現場評估法

A RAPID DYE-BASED ENHANCING METHOD VERSUS MACROSCOPIC ON-SITE EVALUATION (MACE) ON EFFICACY AND ACCURACY OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY (EUS-FNB)

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Background: Macroscopic on-site evaluation (MACE) increases the diagnostic yield of endoscopic ultrasound-guided fine needle biopsy (EUS-FNB), by ensuring the adequate acquisition of biopsy specimens with a minimal number of needle passes. However, MACE requires additional time for separating the specimen and may result in unnecessary tissue loss. Unexperienced pathologist also have the possibility to make mistake in pathology reports due to miss the tissue core.

Aims: The aim of the present study was to evaluate the efficacy and accuracy of a novel rapid dye-based enhancing method compared to the MACE technique during the EUS-FNB procedure. Moreover, the study evaluated whether the dye-based enhancing method could reduce the number of needle passes.

Methods: We analyzed consecutive patients performing EUS FNB for pancreatic, biliary and non-pancreaticobiliary solid lesions, evaluated by dye-based enhancing method group, which use hematoxylin to stain over tissue core immediately after FNB, and combined with open-cell foam thin filter application, in comparison with MOSE technique group, with 2-3 passes each. Samples were differentiated into core tissue ≤ 2 mm or only necrotic or haematic material, and core tissue > 2mm. We use door-knocking method to obtain specimen without negative-pressure syringe attached, then evaluated by the same pathologist. In both group, a 22 guage Franseen-tip needle (Acquire, Boston Scientific Co., Natick, MA, USA) was used. The study evaluated the specimen on-site handling time, the number of needle passes, and the diagnostic accuracy of two groups.

Results: The analysis was performed on 84 patients (40 dye-based enhancing method, 44 MOSE). The overall diagnostic accuracy was 86.9% (73/84). The diagnostic accuracy was higher in dye-based enhancing method group 90% (36/40 lesions), vs MOSE 84% (37/44 lesions), but not statistically significant, $p = 0.23$. But in dye-based enhancing method group, it had lesser specimen on-site handling time (25 seconds vs 3 minutes), $p < 0.01$, and lesser number of needle passes (2.1 times vs 2.8 times), $p < 0.01$. In samples with core tissue > 2 mm, there was no significantly different between two groups in diagnostic accuracy (28/29, 96.5% vs 30/32, 93.75%). But in samples with ≤ 2 mm or only necrotic or haematic material, the diagnostic accuracy was higher in dye-based enhancing method group , (8/12, 66.7% vs 7/12, 58.3%), $p = 0.06$

Conclusions: The dye-based enhancing method showed a comparable diagnostic accuracy to the MOSE technique, and even higher in sample with only little tissue core. Besides, it also had lesser specimen handling time, and may potentially reduce the number of passes.

P.087

利用膠囊內視鏡評估疑似小腸出血病人之檢查時機
TIMING OF CAPSULE ENDOSCOPY IN EVALUATION OF PATIENTS WITH SUSPECTED SMALL BOWEL BLEEDING

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Background: Capsule endoscopy (CE) is a valuable and safe examination for diagnosing small bowel diseases. In earlier models, the relatively short battery life led to a modest completion rate of about 83.5% in meta-analysis. The battery life of the new-generation VCE has increased to at least 12 hours and even up to 20 hours in real-world practice, enabling prolonged examinations. The impact of prolonged VCE examination time on VCE performance, including completion rate and diagnostic yield, remains inconclusive.

Aims: To evaluate completeness and diagnostic yield in patients undergoing prolonged CE examinations.

Methods: Since 2016, we have implemented an overnight protocol for VCE examinations at our hospital using the Olympus endocapsule 10 (EC-10; Olympus Corp., Japan). After ingesting 10 ml of simethicone, patients swallow the capsule endoscope. Doctors checked the capsule endoscopy 2-3 hours after CE ingestion for the confirmation of small bowel entry. Patients keep CE recording overnight and return to the clinic the following morning. For some inpatients with active bleeding, VCE is checked at least after 12 hours at midnight. VCE recording is halted earlier if colon arrival is confirmed. All CE procedures are reviewed by experienced endoscopists. We reviewed consecutive VCE examination records from January 2016 to December 2020. VCE completeness was defined as the capsule endoscopy reaching the cecum within the recording time. We subcategorized the VCE records into within 8 hours, within 12 hours, and the entire course, and compared VCE completion rates and diagnostic yields between these groups. Statistical analysis was performed using Cochran's Q test. P-values less than 0.05 were considered significant.

Results: During the study period, a total of 88 patients between the ages of 20 and 90 received VCE. Their median age was 72 years, with 49 patients (55.7%) being male. Among them, 69 patients (78.4%) were inpatients, and 84 patients (95.5%) were suspected of having small bowel bleeding. The median small bowel transit time was 361 minutes (range: 91-1134 minutes), with a total exam time ranging from 452 to 1273 minutes. Within 8 hours of capsule endoscope ingestion, 58% of patients completed the small bowel evaluation, which was significantly lower than the 79.5% completion rate within 12 hours ($p < 0.001$) and the 93.2% completion rate in the whole course of the overnight study ($p < 0.001$). The diagnostic yield within 8 hours was 71.6%, also significantly lower than the 81.8% yield within 12 hours ($p < 0.001$) and the 83% yield in the whole course of the overnight study ($p < 0.001$) (see Figure 1). No capsule retention was encountered in this study.

Conclusions: 1. Prolonged overnight VCE examination can improve completion rates and diagnostic yields using capsule endoscopes with a battery life of over 12 hours. 2. Prolonged overnight VCE examination should be considered routine practice, especially for inpatients.

P.088

腸道超音波在發炎性腸炎之臨床應用：一所醫學中心經驗
INTESTINAL ULTRASOUND IN THE CLINICAL PRACTICE OF INFLAMMATORY BOWEL DISEASE: A SINGLE HOSPITAL EXPERIENCE

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Background: The gold-standard approach for investigating inflammatory bowel disease (IBD) is ileocolonoscopy, yet it is invasive. Intestinal ultrasound (IUS), a noninvasive and reliable point-of-care tool for assessing bowel inflammation, is widely accepted in Europe but has only recently been employed for IBD evaluation in Taiwan.
Aims: This study aims to assess the daily practice of IUS in IBD, examining its timing, purpose, and association with other modalities.
Methods: Demographics of IBD patients receiving IUS at a single tertiary center between January 2022 and December 2023 were identified.
Results: Enrolling 22 IBD patients, 13 with ulcerative colitis (UC), and 77.3% male, the mean age was 44.9 ± 18.3 years, with a mean disease duration of 5.4 years at IUS. Conventional therapy was prescribed in 90.9% patients, and 59.1% patients received biologics. The most common disease locations were pancolitis and terminal ileum lesion in UC and Crohn's disease (CD) patients, respectively. The common IUS indications included disease complications (55.6%) and response to therapy (44.4%) in CD, and regular follow-up (53.8%) in UC. IUS correlated with ileocolonoscopy in UC and computed tomography in CD. Wall thickening was a common parameter of IUS (100% in UC, 92.3% in CD), and bowel wall stratification was more commonly used in CD than UC (55.6% vs. 15.4%, p=0.049).
Conclusions: As clinicians become more familiar with IUS in IBD, its usage is likely to increase. IUS has the potential to reduce the necessity of ileocolonoscopy, being considered reliable, objective, and well-accepted.

P.089

膽結石患者之糞便微菌叢與代謝物分析
THE FECAL MICROBIAL AND METABOLIC PROFILE IN GALLSTONE PATIENTS

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Background: Gallstone disease is a prevalent health concern leading to numerous cholecystectomies. Cholesterol stones (CS) and pigment stones (PS) are two primary types of gallstones. CS is associated with metabolic disorders and high biliary cholesterol, while PS is mainly related to calcium hydrogen bilirubinate. The exact role of gut microbiota in gallstone formation is still being studied.
Aims: We aim to explore the crosstalk between gut microbiota, gut metabolomic, and metabolic parameters in gallstone patients compared to controls.
Methods: From March 2019 to February 2021, we recruited gallstone and healthy participants. Fresh stool samples were collected before cholecystectomy (if needed) and frozen. 16s rRNA sequencing was performed, followed by differential abundance analyses. UHPLC-MS/MS was used for quantifying fecal short-chain fatty acids (SCFAs) and bile acids.
Results: 20 gallstone patients and 30 healthy subjects for control group were enrolled. A total of 777 Operational Taxonomic Units (OTUs) at 97% sequence identity. The control group manifested abundance of Faecalibacterium and Prevotella 9, whereas Desulfovibrionaceae and Bacteroides uniformis were notably present in CS group and more Escherichia-Shigella in PS group. In metabolite analysis, in 18 qualified participants, only n-butyric acid displayed significant higher level in controls than gallstones group ($p < 0.01$). Specific bile acids, including 3α-hydroxy-12 ketolithocholic acid, deoxycholic acid, and cholic acid showed no intergroup differences.
Conclusions: We identified certain bacterial taxa that are different between PS, CS and control group, n-butyric acid may serve as the biomarker for differentiate gallstones patients. However, future research is still needed to establish the correlation between the gut microbiota and the metabolites.

P.090

膠囊內視鏡用於兒童的臨床應用性與可行性於中台灣醫學中心
CLINICAL APPLICATION AND FEASIBILITY OF CAPSULE ENDOSCOPY IN CHILDREN AT A MEDICAL CENTER IN CENTRAL TAIWAN

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Background: Capsule endoscopy (CE) is a noninvasive examination for excellent visualization of small bowel mucosal lesions
Aims: To evaluate the clinical efficacy and safety of CE in pediatric patients
Methods: From April 2014 to December 2022, CE procedures performed in children younger than 18 years of age at Taichung Veteran General Hospital were analyzed retrospectively
Results: Among 136 procedures, the completion rate was 95.6% (n=129), with a median age of 14 years old. Suspicion or evaluation of inflammatory bowel diseases (IBD) (41%) was the most common indication for CE. Other common indications of CE were chronic unexplained abdominal pain (35%) and obscure gastrointestinal bleeding or iron deficiency anemia (22%). No procedure-related complications occurred. The completion rate of CE is 95.6%. The diagnosis of three patients with incomplete study were CD with small bowel stricture, graft-versus-host disease and duodenal ulcers. A total of 86 CE procedures showed positive findings, and the overall diagnostic yield rate was 63.2%. Small bowel ulcers (65.12%) were the most common findings. Overall, 26.5% of CE examinations resulted in a new diagnosis and 44.9% of CE exams led to a change in therapy. The findings of CE in IBD patients resulted in therapeutic changes in up to 48.1% of patients.
Conclusions: CE is a safe and feasible diagnostic method to study the small intestine in children, especially for IBD. Incomplete study could be an indicator of positive finding and can potentially be a guide to identify the site of possible strictures.

P.091

比較進階療法在發炎性腸道疾病治療中的持續性：一項醫學中心的回溯性世代研究
COMPARING THE PERSISTENCE OF ADVANCED THERAPIES IN INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE COHORT STUDY CONDUCTED AT A TERTIARY MEDICAL CENTER

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Background: The prevalence of inflammatory bowel disease (IBD) is swiftly on the rise in Asia, where advanced therapies have markedly transformed outcomes for the cases with moderate to severe disease activity. Among various factors, the persistence of treatment holds paramount importance in choosing appropriate treatment option. We present the first study in Asia that compares real-world persistence rates among advanced therapies in IBD patients in Taiwan.
Aims: To compare the persistence of advanced therapies in inflammatory bowel disease in Taiwan.
Methods: Conducted as a retrospective cohort study, we enrolled IBD patients who underwent treatment with five advanced therapies—infliximab (IFX), adalimumab (ADA), vedolizumab (VDZ), ustekinumab (UST), and tofacitinib (TOF)—at Linkou Chang Gung Memorial Hospital from October 2017 to September 2023. UST followed a standard maintenance dosing frequency of every 12 weeks, while TOF was exclusively allowed as a second-line treatment option for UC in Taiwan. The study compared baseline data and drug persistence rates within the initial 52 weeks for the overall group, biologic-naïve patients, and biologic-experienced patients.
Results: A total of 511 IBD patients were included, with 41.1% diagnosed with ulcerative colitis (UC) and 58.9% with Crohn's disease (CD). UST exhibited the highest escalation rate at 24.2%. Across all five drugs, secondary loss of response was the primary cause for discontinuation. Further baseline characteristics were presented in Table 1. In the Kaplan-Meier analysis, UST demonstrated the highest 52-week persistence rates in overall (88.31%, $p < 0.001$, Figure 1a), biologic-naïve patients (96.97%, $p < 0.001$, Figure 1b), and biologic-experienced CD patients (81.82%, p=0.023, Figure 1c). While statistically insignificant, UST also exhibited the highest 52-week persistence in overall (66.67%, p=0.083, Figure 1d),

biologic-naïve (80%, p=0.445, figure 1e), and biologic-experienced (57.14%, p=0.359, Figure 1f) UC patients.
Conclusions: UST showcased the superior 52-week persistence in among advanced therapies in CD patients. However, it's noteworthy that the rate of dose escalation in UST surpassed that of other therapies.

P.092

接受過安潰悠治療的克隆氏症患者，後續使用抗腫瘤因子和喜達諾的療效及安全性比較分析

COMPARISON OF EFFICACY AND SAFETY BETWEEN USTEKINUMAB AND ANTI-TNF IN VEDOLIZUMAB EXPERIENCED CROHN'S DISEASE PATIENTS

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Background: As biologic therapies become increasingly prevalent for managing moderate to severe inflammatory bowel disease (IBD), the optimal selection of treatment sequences has gained significance. This involves choosing the most appropriate biologic agent after prior exposure or non-responsiveness to a preceding regimen. Vedolizumab (VDZ), an α4β7-integrin inhibitor specific to the gut, is acknowledged for its efficacy in treating moderate to severe IBD. However, limited studies have explored the comparative effectiveness of alternative biologics, such as ustekinumab (UST) and anti-tumor necrosis factor agents (anti-TNF), following exposure to VDZ.
Aims: To compare the teatment persistence of anti-TNF and ustekinumab in IBD patients who were previously treated with vedolizumab.
Methods: In this retrospective study conducted at Chang Gung Memorial Hospital in Linkou, a prominent 3700-bed medical facility in Taiwan, we enrolled 110 IBD patients who underwent treatment with UST or anti-TNF agents (including adalimumab and infliximab) from May 2019 to September 2023. UST's standard maintenance dosing in Taiwan is every 12 weeks. We employed Kaplan-Meier analysis and Cox proportional hazards models to assess the 52-week treatment persistence of UST versus anti-TNF.
Results: Among the 110 participants, 40 were diagnosed with ulcerative colitis (UC), and 70 with Crohn's disease.

Demographic factors such as age, gender, and body mass index were comparable between the anti-TNF and UST groups. Secondary non-response was the primary reason for vedolizumab discontinuation in both groups. Anti-TNF group showed higher rate of IBD-related admission and opportunistic infection rate compared to UST group, although without statistical significance (Table 1). In the Cox proportional hazards models, UST demonstrated significantly higher 52-week retention in overall IBD (HR: 5.36, 95% CI: 1.84-15.62, P = 0.002) and in Crohn's disease patients (HR: 10.75, 95% CI: 1.34-86, P = 0.025) compared to anti-TNF. Kaplan-Meier analysis also showed statistically significance (Figure 1a-1b). Although UST also exhibited superior persistence at 52 weeks in UC patients, the difference was not statistically significant in both Cox proportional hazards models (HR: 2.25, 95% CI: 0.63-8, P = 0.211) and Kaplan-Meier analysis (Figure 1c). At the 52-week mark, 73.7% of the anti-TNF group and 81% of the UST group were not on steroids. Secondary non-response remained the predominant cause for discontinuation of the current biologic. Notably, UST required more frequent dose adjustments than anti-TNF. The safety profile of both treatments was comparable.

Conclusions: UST demonstrated superior treatment persistence compared to anti-TNF in Crohn's disease patients previously exposed to vedolizumab. However, UST required more frequent dosing adjustments.

P.093

糞便微生物移植對患有和不患有發炎性腸道疾病患者的艱難梭菌感染的比較療效：一項回顧性研究

COMPARATIVE EFFICACY OF FECAL MICROBIOTA TRANSPLANTATION FOR *CLOSTRIDIOIDES DIFFICILE* INFECTION IN PATIENTS WITH AND WITHOUT INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE COHORT STUDY

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Background: *Clostridioides difficile* infection (CDI) significantly exacerbates and worsens the prognosis of inflammatory bowel disease (IBD). While fecal microbiota transplantation (FMT) is recognized as a safe and efficacious therapy for patients battling recurrent or refractory CDI, but comparative studies focusing on the success rates in IBD and non-IBD patients remain scarce.

Aims: The primary aim of our study is to fill the current knowledge gap concerning the impact of FMT on patients with CDI, with a specific emphasis on comparing the success rates between patients with and without IBD.

Methods: In this retrospective cohort study conducted at Chang Gung Memorial Hospital between April 2019 and February 2023, patients undergoing FMT via colonoscopy for recurrent or refractory CDI were enrolled. Participants were categorized into IBD and non-IBD groups based on their underlying conditions. We compared baseline characteristics and clinical outcomes at one-month and one-year follow-up intervals. CDI diagnosis was confirmed through positive CD toxin A/B genes and associated clinical symptoms. Donor specimens were sourced from Chang Gung Microbiota Therapy Center's fecal bank.

Results: Our study included 88 patients who received FMT, comprising 30 in the IBD group and 58 in the non-IBD group. The indications were recurrent CDI in 31 patients, refractory CDI in 54, and both conditions in 3 patients. Among the IBD subgroup, 20 patients had ulcerative

colitis, and 10 had Crohn's disease. In the baseline comparison, the IBD group was significantly younger (mean±SD, 45.23±16.45 years vs. 61.90±24.40 years, P = 0.001) and had fewer comorbidities such as hypertension (10.0% vs. 55.2%, P < 0.001), diabetes mellitus (6.7% vs. 31.0%, P = 0.014), and cancer (3.3% vs. 31.0%, P = 0.012) than the non-IBD group. Additionally, the IBD group had less prior Fidaxomin use (6.9% vs. 26.3%, P = 0.021) and fewer HMG-CoA reductase inhibitor users (0.0% vs. 15.5%, P = 0.025). Post-FMT, IBD severity indices showed significant improvement at one month. The mean partial Mayo score in the IBD group decreased by 2.9 points, the endoscopic Mayo subscore decreased by 0.7 points, and the Crohn's Disease Activity Index decreased by 79.98 points. At this time, the IBD group showed a similar percentage of negative CDI toxin A/B tests (83.3% vs. 63.8%, P = 0.174) and comparable success rates of FMT (80.0% vs. 78.9%, P = 0.908). At the one-year follow-up, the eradication rate (94.4% vs. 73.9%, P = 0.112) and comparable success rates of FMT (70.0% vs. 67.6%, P = 0.857). No safety issues or adverse effects were reported in any of the patients.

Conclusions: FMT demonstrates safety and efficacy in treating recurrent or refractory CDI in both IBD and non-IBD patients, also aiding in mitigating IBD-associated inflammation.

P.094

高光譜成像技術模擬窄頻影像在磁控膠囊內視鏡之應用

NOVEL METHOD TO ENHANCE VISUALIZATION OF MUCOSA BY HYPERSPECTRAL IMAGING TO MIMIC NARROW BAND IMAGING IN MAGNETIC-ASSISTED CAPSULE ENDOSCOPY

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Background: Narrow band imaging (NBI) is more efficient in detecting early gastrointestinal cancer than white light imaging (WLI) does. NBI technology is available only in the conventional endoscopy, but unavailable in magnetic-assisted capsule endoscopy (MACE) system due to MACES's small size and obstales in image processing issues. MACE is an easy, safe and convenient tool for the both patients and physicians to avoid the disadvantages of conventional endoscopy. Enabling NBI technology in MACE is mandatory.

Aims: To develop a novel Spectrum Aided Vision Enhancer (SAVE) algorithm to enhance diagnosis by converting WLI to informative wavelengths in MACE system to mimic the NBI in conventional endoscopy.

Methods: Dataset

The WLI MACE images were captured using InsightEyes MACE System, while the conventional endoscope WLI images were captured using the Olympus CV-290. Images in both MACE and traditional endoscopy were obtained from 44 patients with gastroesophageal reflux symptoms (male= 29, mean age: 49.4 years). The NBI images in the peak wavelength of 540 nm were captured from the conventional endoscope.

Hyperspectral imaging (HSI) technology

Calibration of the spectrometer and the endoscopic camera were required to obtain the conversion matrix that transformed the RGB images from conventional endoscopy and MACE into a hyperspectral image. A regular 24-color checker referred to as the x-rite classic was utilized. The images were transformed to the CIE 1931 XYZ color space

and the 3 channels that corresponded to the values of the RGB color would be in a range from 0 to 255 before the conversion, which would be scaled down to a range of 0 -1 after the conversion.

Spectrum Aided Vision Enhancer (SAVE) for MACE

For conventional Olympus endoscope system, there is a reference NBI capture mode, which would serve as a reference in comparison with the SAVE-generated images. A color calibration was performed for both the Olympus endoscope and MACE. For this calibration, the standard 24 color checker was used and the enhanced SAVE image simulated from the HSI conversion algorithm was compared with the real NBI image capture by Olympus endoscope. Once the color was matched between the simulated enhanced SAVE image and the real NBI of the Olympus endoscope, the enhanced SAVE images for the MACE and conventional endoscopy were fine-tuned.

Parameters used for qualitative analysis of the SAVE Images

Three parameters were used to evaluate similarities of the images between the 2 endoscopy systems. The first parameter was structural similarity index metric (SSIM), which compared the WLI of the Olympus endoscope with the enhanced SAVE image from the HSI conversion algorithm developed in MACE. SSIM can be defined as the amount of similarities between the reproduced and the real image. The SSIM values range between 0% to 100%. Whereas 100% represents the images between 2 endoscopy systems are completely same, 0% represents completely different images between systems. The second parameters, entropy, represented the differences between the WLI images obtained from the Olympus endoscope and the enhanced SAVE images simulated from the HSI conversion algorithm from MACE. Entropy was used to classify textures. A low entropy denoted low disorder and low variance within the component, representing a better reproduction of the image. The third parameter, pixel to signal noise ratio (PSNR), was utilized in the context of image compression algorithms. PSNR served as a parameter for evaluating the quality of the reproduced image.

Results: SSIM

The Olympus images showed a higher SSIM value than that in the MACE images.(Olympus vs. MACE: 94.27% vs 90%). Nevertheless, the average SSIM for MACE was still around 90%. It can also be seen that the top three highest achieved SSIM value was from the MACE of 96%.

Entropy

The entropy difference in both the MACE and the Olympus endoscope displayed similar values. The average entropy difference in MACE was 1.17%, while the average difference in the Olympus endoscope was 0.37%. However, the majority difference in MACE was caused by only one image. If we removed that particular image, the entropy difference value in MACE system would decrease to just 0.03%, which result was better than that in Olympus endoscope.

PSNR

The PSNR of the MACE images came in at an average of 28.0216 db, while the PSNR of the Olympus images was 27.8819 db, which results demonstrated a better quality of the reproduced MACE images than Olympus images.

Detection of mucosal break in esophago-gastric junction (EGJ)

SAVE algorithm can clearly identify the mucosal break in the EGJ in the patients with gastroesophageal disorder (GERD) in MACE system, which evidences will be demonstrated in the meeting.

Conclusions: 1. A novel visual enhancing SAVE algorithm was successfully developed to convert the WLI images obtained from MACE camera into visually enhanced images. 2. SAVE-generated images from MACE were in close similarity to the NBI from in Olympus endoscopy. 3. Future use of the novel technology for real time application of MACE in GERD patients and in early detection of esophageal cancer is promising.

P.095

LACTICASEIBACILLUS PARACASEI PS23 在老化的 SAMP8 小鼠中有效地調節腸道微生物組成，並改善腸道功能
LACTICASEIBACILLUS PARACASEI PS23 EFFECTIVELY MODULATES GUT MICROBIOTA COMPOSITION AND IMPROVES GASTROINTESTINAL FUNCTION IN AGED SAMP8 MICE

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Background: Probiotics are reported to improve gastrointestinal (GI) function via regulating gut microbiota (GM). However, exactly how probiotics influence GM and GI function in elders is poorly characterized.
Aims: Therefore, in this study, we assessed the effect of the probiotic Lacticaseibacillus paracasei PS23 (LPPS23) on the GM and GI function of aged mice.
Methods: LPPS23 is a strain isolated from healthy human feces. There were four groups of senescenceaccelerated mouse prone-8 (SAMP8) mice (n = 4): a non-treated control group, a saline control group,a low dose LPPS23 and a high dose group. Non-treated mice were euthanized at 16 weeks old, and others were euthanized at 28 weeks old. Intestine, intestinal mucosa, and fecal samples were collected, and intestinal length was measured. Intestinal Permeability was measured on fluorescence plates. We also identified the microbial species that were enriched from the class to species level using LEfSe analysis.
Results: As age-related intestinal shortening and barrier dysfunction are associated with GM alterations, we measured intestinal length, intestinal permeability, and phagocytotic activity in 16-week-old untreated SAMP8 mice and 28-week-old SAMP8 mice. Significant age-related declines in intestinal function were observed in the mice including decreased length of the intestine (Figure A,B), increased intestinal permeability (Figure C), and decreased phagocytotic activity (Figure D) in the FA group compared to the FC group.. Bacteria belonging to the order Lactobacillales increased in the FPS23H mice. Moreover, both the high and low doses of LPPS23 enhanced bacteria belonging to the order Pseudomonadales, and the low dose of LPPS23 promoted bacteria from the class Saccharimonadia. The bacteria enriched in the FA group belonged to the class Acidimicrobiia, genus Lachnospiraceae_UCG_001, genus Ruminococcaceae_ UCG_009, and order Acetobacterales. Bacteria from the genus Prevotella and Klebsiella were enriched in the FC group (Figure E,F)
Conclusions: LPPS23 improved the GI function of aged mice due to the longer intestine length, and lower intestinal permeability, in LPPS23-treated mice.

P.096

本院歷年來幽門桿菌陽性率變化趨勢
THE CHANGING TREND OF *HELICOBACTER PYLORI* POSITIVITY RATE AT OUR INSTITUTION OVER THE YEARS

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Background: *Helicobacter pylori* infection is a significant public health concern as it may lead to peptic ulcers or even gastric cancer. However, given the advancements in public health and the widespread use of panendoscopic examinations, it's important to pay attention to the trend in the *Helicobacter pylori* positivity rate.
Aims: For the reasons mentioned above, it is valuable to understand the trends in the prevalence of *H. pylori* positivity.
Methods: We collected data from Dalin Tzu Chi Hospital over a 19-year period, from January 2003 to December 2021, during which 61,488 panendoscopy procedures were performed at our hospital's health examination center. We analyzed *Helicobacter pylori* positivity rate changes among these patients and also explored variations based on panendoscopy frequency in our secondary analysis.
Results: Over the past 19 years, the average *Helicobacter pylori* positivity rate declined significantly from 44.8% in 2003 to 12.6% in 2021 (P<0.001). Analysis of panendoscopic exams during health check-ups revealed a decreasing trend: initial exam - 34.1%, second exam - 18.5%, and third exam - 11.9% (P<0.001). Multivariate analysis identified factors influencing *Helicobacter pylori* positivity, including year (odds ratio, 0.95; 95% CI, 0.95-0.96; P<0.001), panendoscopy frequency (odds ratio, 0.61; 95% CI, 0.59-0.62; P<0.001), duodenal ulcers (odds ratio, 2.37; 95% CI, 2.23-2.53; P<0.001), age (odds ratio, 1.01; 95% CI, 1.01-1.01; P<0.001), and gastric ulcers (odds ratio, 1.25; 95% CI, 1.20-1.30; P<0.001).
Conclusions: The *Helicobacter pylori* positivity rate has been steadily declining, largely due to repeated panendoscopic examinations and the monitoring and treatment of the infection.

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胃幽門螺旋桿菌感染和治療與中心視網膜脈絡膜炎之相關性
THE ASSOCIATION OF *HELICOBACTER PYLORI* INFECTION AND TREATMENT WITH CENTRAL SEROUS CHORIORETINOPATHY

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Background: Studies had demonstrated several extra-gastrointestinal associations of *Helicobacter pylori* (*H. pylori*) infection including neurological, dermatological, hematologic, ocular, cardiovascular, metabolic, allergic, and hepatobiliary diseases. When it comes to ocular disease, several studies have demonstrated a positive association between *Helicobacter pylori* infection and Central serous chorioretinopathy (CSC). On the other hand, the effect of treatment of *H. pylori* infection on CSC had some inconsistence.
Aims: We aimed to investigate the association of *H. pylori* infection and treatment with the occurrence of CSC in Taiwanese population.
Methods: The study was conducted with National Health Insurance Research Database (NHIRD) in Taiwan. We collected patients over 18 years old with or without newly diagnosed peptic ulcer disease (PUD) or *H. pylori* between 2009 to 2015 and followed until 2018 for the incidence of CSC. We further divided the *H. pylori* infection subjects into treated and non-treated group. The distributions of risk factors were analyzed with Chi-Square test for the categorical variables and independent t test for continuous variables. Cox proportional hazards model analyses were performed to determine the hazard ratios (HR) of CSC among the matched groups. P-value < 0.05 was defined as statistically significant.
Results: A total of 1,012,973 subjects in the non- *H. pylori* group and 1,012,973 patients in the *H. pylori* group were

enrolled after propensity score matching. The incident rate ratio of CSC in *H. pylori* group compared to non- *H. pylori* group was 1.097 with 95% confidential interval (CI) of 1.094-1.100. According to cox proportional hazards model, the risk of CSC was also significant higher in *H. pylori* group compared to non- *H. pylori* group. The incident rate ratio of CSC in treated *H. pylori* group was higher compared to non-treated *H. pylori* group. (HR: 1.137, 95% CI:1.129-1.145). In cox proportional hazards model, the risk of CSC in non-treated *H. pylori* group was not significantly higher than non- *H. pylori* group while the risk of CSC incidence in treated *H. pylori* group compared to non- *H. pylori* group was significantly higher.

Conclusions: The results revealed that *H. pylori* infection increased the risk of CSC. However, of the *H. pylori* infection subjects, treatment of *H. pylori* had even higher risk to develop CSC. Our findings were in line with current studies that *H. pylori* infection is one of the risk factors of CSC. However, we found that treatment of *H. pylori* further increased the risk of CSC which was contrary to the results of most of the other research. Additional research with a sizable database is essential to substantiate our findings.

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「鉍劑 - 阿莫克西林 - 鉀離子競爭性酸阻斷劑三合療法」於台灣治療幽門螺旋桿菌感染之領航研究

PILOT STUDY OF BISMUTH/ AMOXICILLIN/POTASSIUM-COMPETITIVE ACID BLOCKER TRIPLE THERAPY FOR THE TREATMENT OF *HELICOBACTER PYLORI* INFECTION IN TAIWAN

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Background: A meta-analysis showed the pooled eradication rate of vonoprazan-amoxicillin dual therapy in the first-line treatment of *H. pylori* infection was only 85.0%. Bismuth salts possess a synergistic effect on antibiotics and have been used to increase eradication efficacy for *H. pylori* infection. Whether the addition of bismuth to high-dose vonoprazan dual therapy can reliably achieve an eradication rate > 90% remains unclear.

Aims: To assess the efficacy and safety of 14-day bismuth/ amoxicillin/ potassium-competitive acid blocker (PCAB) triple therapy for the treatment of *H. pylori* infection in Taiwan.

Methods: In the retrospective cohort study, adult patients with *H. pylori* infection in An Nan Hospital, Kaohsiung Veterans General Hospital, Kaohsiung Medical University Hospital and Ai-Ran Hospital who received bismuth/ amoxicillin/vonoprazan triple therapy between January 2021 and December 2023 were included. Patients were followed up according to a standard procedure. They returned at the second week to assess drug adherence and adverse events. Post-treatment *H. pylori* status was assessed by 13C-urea breath test at least 4 weeks after treatment. The rates of eradication and adverse events were assessed.

Results: In total, 36 *H. pylori*-infected patients were included in the study. The intention-to-treat eradication rate of bismuth/amoxicillin/vonoprazan triple therapy was 94.4% (34/36; 95% confidence interval [CI]: 86.9 to 101.2%). The modified intention-to-treat and per-protocol eradication rates were both 97.1% (34/35; 95% CI: 91.6 to 102.6%, and 33/34; 95% CI: 91.5 to 102.7%). Thirty five out of 36 patients (97.2%) had good drug adherence, and

the frequency of adverse events of bismuth/amoxicillin/vonoprazan triple therapy was only 8.3% (3/36).
Conclusions: The pilot study of bismuth/amoxicillin/vonoprazan triple therapy shows that this single-antibiotic anti-*H. pylori* therapy can achieve a very high eradication rate with good drug adherence and a low frequency of adverse events.

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高濃度氧氣水對於幽門桿菌 *HELICOBACTER PYLORI* 的抑制效果研究
STUDY ON THE INHIBITORY EFFECT OF OXYGEN WATER ON *HELICOBACTER PYLORI*

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Background: *Helicobacter pylori* is a Gram-negative, spiral-shaped, microaerophilic bacterium that causes gastritis, peptic ulcers, and gastric cancer. Gastric cancer is the second leading cause of cancer-related deaths worldwide, and the eradication of *H. pylori* may decrease the risk of gastric cancer. However, the prevalence of bacterial antibiotic resistance varies from region to region and appears to be increasing significantly over time in many countries. At the same time, global antimicrobial eradication rates for *H. pylori* have been declining. Hence, the method to enhance the eradication is a critical issue. Since *H. pylori* lives in an environment of low oxygen, low pH, and high carbon dioxide, theoretically, in a high-concentration oxygen environment, *H. pylori*, including drug-resistant strains, will be effectively inhibited.
Aims: The previous study demonstrates that the use of 0.2% H_2O_2 can effectively inhibit *H. pylori* in the animal model, but H2O2 is cytotoxic, and the use has been restricted in the human body. 0.2% of H_2O_2 has been tested to produce approximately 30-35ppm of dissolved oxygen in the solution, which is speculated to be the main reason for inhibiting *H. pylori*. The amount of dissolved oxygen in general drinking water is about 3-5ppm. If pressurized pure oxygen technology is used, the amount of dissolved oxygen in the water can be increased to 40ppm. In theory, it will have an inhibitory effect on *H. pylori* that likes low-oxygen environment, including drug-resistant *H. pylori*.
Methods: Using pure oxygen and pure water, in a closed high-pressure (70psi) container, an aqueous solution with a dissolved oxygen content of 40ppm can be produced. Soak the cultured general *H. pylori* and drug-resistant *H. pylori* strains in 40ppm oxygen water for 5 minutes, detect the number of residual bacteria, and compare the survival rate with the BHI solution of the control group. Use CDC plate solid-state culture in a microaerophilic

incubator to culture general *H. pylori* and drug-resistant *H. pylori* strains for 48 hours. The number of bacteria is cultured to about 10^8.

Results: In the first experiment, *H. pylori* was mixed with 40 ppm oxygen water for 5 minutes, and then cultured with CDC plate for 72 hours. Repeated experiments found that the number of *H. pylori* was reduced by 84.6±5.5%. Repeating the experiment using drug-resistant *H. pylori*, and using 40 ppm oxygen water also, reduced the number of bacteria by 93.9±5.0%. The first experiment confirmed that oxygen water can suppress *H. pylori*, but it cannot eliminate *H. pylori*. Re-cultivate the surviving *H. pylori* as the second generation, and then treat it with oxygen water to cultivate the surviving *H. pylori* into the third generation. By analogy, test 30 generations of normal and drug-resistant *H. pylori*, the inhibitory rate of oxygen water for both strains still reaches 80-99% .

Conclusions: High concentrations of oxygen can inhibit *H. pylori*. Experiments have shown that 40ppm oxygen water has an inhibition rate of more than 80% for general *H. pylori* and drug-resistant *H. pylori*. Although *H. pylori* cannot be eradicated, its numbers can be effectively suppressed. In addition, after 30 generations of continuous treatment with oxygen water, the bactericidal rates of general *H. pylori* and drug-resistant *H. pylori* did not change significantly, both were above 80%, indicating that general and drug-resistant *H. pylori* strains did not show resistance to oxygen water. Oxygen water is drinking water sold in shopping malls and has no side effects on the human body. This would be an effective adjuvant treatment, especially for patients infected with drug-resistant *H. pylori*.

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