2025台灣消化系聯合學術演講年會

New Frontier and Future Challenges in Digestive Diseases and Science

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論文摘要

台灣消化系醫學會(第五十五屆)學術演講年會
台灣消化系內視鏡醫學會(第三十四次)學術演講年會

TAIPEI

會長演講（台灣消化系醫學會）

From Bench to Bedside: Reflections on Digestive Research, Health Care, and the Wholeness of a Compassionate Life

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This presentation explores the comprehensive development of the medical field from four perspectives. First, in digestive research, our team has devoted many years to fundamental studies on gastrointestinal cancers. We successfully established two gastric cancer cell lines and, using differential display PCR, identified a tumor-suppressive gene—RIG1 (Retinoid Inducible Gene 1)—whose expression is upregulated by retinoic acid. In comparison with the related gene TIG1 (Tazarotene Inducible Gene 1) reported in the literature, both RIG1 and TIG1 expressions have been found to correlate positively with the differentiation of various gastrointestinal tumor tissues. In vitro studies confirmed that RIG1 can activate phospholipase A2 (PLA2), thereby altering the intracellular localization of RAS proteins and reducing RAS signaling activation to inhibit cancer cell growth; PLA2 activation also promotes the production of PGD2, which further facilitates cell differentiation. Our findings further indicate that TIG1, via proteins such as Vac14, DNAJC8, and SPINK2, suppresses cell proliferation and migration while promoting apoptosis. Although 30 years of basic research have demonstrated the potential of retinoids, their clinical efficacy in treating various digestive cancers remains suboptimal, and considerable challenges persist in translating these findings into clinical practice.

Second, in health care, obesity and related metabolic disorders have emerged as major challenges in modern society. We emphasize the importance of lifestyle modifications by promoting a high-fruit-and-vegetable, low-calorie diet combined with moderate exercise. These measures not only achieve significant weight reduction (with observed decreases of over 10%) but also improve gut microbiota and reduce blood levels of trimethylamine N-oxide (TMAO), thereby delaying the progression of chronic kidney disease. This approach offers an effective strategy for the prevention and control of chronic illnesses.

Third, regarding compassionate medical practice, we actively promote a vegetarian diet, believing that it not only benefits health and respects life but also aligns with sustainable development goals. Clinical data indicate that vegetarians incur, on average, 25% lower medical expenses compared to omnivores. Moreover, by integrating the efforts of our medical team and community volunteers, we successfully assisted a 280-kg patient to reduce his weight to 91 kg over five years, enabling him to resume a normal life and work. This case exemplifies the power of holistic care.

Finally, the fulfillment of a medical career depends not only on technical advancement but also on the transmission of medical ethics and expertise. Over the years, we have consistently upheld a spirit of teamwork and mutual support, dedicating ourselves to nurturing the next generation of healthcare professionals while achieving a harmonious integration of our professional, personal, and vocational pursuits. This holistic care philosophy, which focuses on both disease treatment and the overall well-being of patients and healthcare providers, provides a solid foundation for the future development of medical practice.

會長演講（台灣消化系內視鏡醫學會）

Adventure of Neurogastroenterology and Motility: A Lifelong Journey

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Neurogastroenterology and motility encompass gastrointestinal physiology, digestive motility, while deal with GERD, functional GI disorders or disordered gut brain axis. The career through my study and journey into neurogastroenterology and motility started on March, 2000 when there was an opportunity to do clinical research under the guidance of *Professor William C Orr* in Oklahoma City, US. Beside basic training on clinical research, the work was focused on the application of electrogastrography to explore gastric physiology and motility disorders, and interaction between GERD and sleep by using esophageal manometry, ambulatory pH monitoring, and polysomnography. On 2002, there was an important opportunity in my career to start a new work to set up a GI motility laboratory in Tzu Chi Hospital, Hualien where numerous motility works were continuously and successfully published. Subsequently, research experience has been further advanced by pursuing a PhD in medicine in UNSW, Sydney directed by *Professor Ian Cook* in 2006 with the thesis work investigating esophageal peristalsis, bolus clearance, sensory neural processing, and perception of esophageal stimuli in human esophagus, and their implications in patients with several dysphagia syndromes. From then, my research interest is predominantly focused on esophageal physiology and motility, secondary peristalsis, GERD. One novel aspect of my work is that I have applied combined intraluminal impedance and manometry and recently high-resolution manometry (HRM) to elucidate physiological mechanisms of distension-induced secondary peristalsis in human esophagus under different *in vivo* conditions using pharmacological/chemical stimuli and experiments. The other parts of my work are divided into the following major sections: *1)* the application of esophageal manometry/HRM to study esophageal motility in GERD and infective esophageal motility; *2)* the advances in our understanding of peristaltic characteristics, esophageal bolus clearance and symptom perception in different esophageal obstructive/perceive syndromes; *3)* exploring pathophysiology and diagnostic challenges in GERD using esophageal manometry and impedance, HRM, and ambulatory pH with and without impedance; *4)* providing the evidence for the expression of transient receptor potential vanilloid subfamily member-1 receptors (TRPV-1 receptors) and other novel nociceptors, mucosal ultra-structures, and neuropeptides as their roles in the pathogenesis of visceral hypersensitivity and symptom perception of GERD.

外賓演講（1）

Current Status of EUS-Guided Biliary and Pancreatic Interventions

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1. Introduction

For a long time, trans papillary approaches are standard in the access for bile and pancreatic duct. Recently, interventional EUS (I-EUS) using transmural routes are possible, and is going to spread rapidly in the world.[1] This advance depends on the developing of dedicated devices. With an effective device, I-EUS spreading may be very speedy, but very slow and limited in expert without such dedicated devices. In addition, there are some differences in the procedure for bile and pancreatic ducts because of the difficulty. I will try to explain the current situations in I-EUS procedures in biliary and pancreatic diseases.

2. Classification and terminology of Interventional EUS

There had been no definition of classification and glossary of terms in I-EUS.[2] Recently, the "Subcommittee of terminology of I-EUS" in Japanese gastroenterological endoscopy society (JGES) had classified I-EUS procedures into 5 categories; 1. EUS-guided sampling, 2. EUS-guided through-the-needle examination, 3. EUS-guided drainage/anastomosis (EUS-D/A), 4. trans-endosonographically/EUS-guided created route (ESCR) procedures, and 5. EUS-guided delivery.

EUS-D/A included 3 categories: D/A for organs (biliary, pancreatic and gallbladder), drainage of acquired fluid collections (Pseudocyst, WON and abscess) and anastomosis of digestive tract. EUS-guided biliary and pancreatic interventions are classified as EUS-D/A and Trans-ESCR procedures. In addition, trans-luminal D/A stent (T-DAS) was defined as the stents using for EUS-D/A. The aim of conventional stents is keeping the luminal patency by placing at the papilla or stricture, but T-DAS is keeping the ESCR. ESCR is a general term of the route created by EUS-guided procedures. For EUS-D/A, we should use the "anastomosis" and "tract" but fistula which is accidentally developed inconveniently. "Tract" is available for the ESCR in liver/pancreatic parenchyma and ESCR of EUS-guided drainage of acquired fluid collection. Endoscopic necrosectomy after EUS-guided drainage of Walled-off necrosis is the representative of trans-ESCR procedure.[3]

3. EUS-BD/A

a. Indications

Basically, EUS-BD/A was a salvage procedure when the conventional ERCP related procedures are difficult/failed.[4] There are 2 factors of indications; required biliary drainage and creation of the biliary access route and difficulties of biliary access. The cases with duodenal stricture, surgically altered anatomy are good indications. Recently, there are some challenges to extend the indications of EUS-BD/A, primary drainage, preoperative drainage, child cases and massive ascites cases.[5–7] These expanded indications are limited to the high-volume center with I-EUS expert.

b. Intrahepatic bile duct approach

Puncture the intrahepatic bile duct (IHBD) for EUS-D/A. According to the kinds of digestive trat, EUS-guided hepaticogastrostomy (EUS-HGS), EUS-guided hepaticoduodenostomy (EUS-HDS) and EUS-guided hepaticojejunostomy (EUS-HJS) are performing. There are some difficult steps in EUS-BD/A for IHBD, guidewire insertion and advancing, dilation of the puncture tract in liver parenchyma and insertion of the T-DAS.

c. Extrahepatic bile duct approach

EUS-guided choledochoduodenostomy (EUS-CDS) is categorized. Main indication of EUS-CDS is failed cannulation. Then, the chance of performance of EUS-CDS was not many in salvage indication. However, some centers are performing EUS-CDS as primary drainage methods because of no pancreatitis.[8] Recently, a small size Axios stent with hot delivery system was introduced for EUS-CDS and it is reported as safe and effective procedure with short procedure time.[9] The disadvantage is the occurrence of sump-syndrome by reflux of food contents. This equipment is not available for EUS-BD/A in Japan.

4. EUS-PDD/A

a. Indications

Basic concept is same as EUS-BD/A. The cases with stricture of pancreatojejunostomy, failed cannulation and passage of the stricture are main indications.[10] Advanced chronic pancreatitis or pancreatic ductal cancer with pancreatitis or pancreatic leakage at the tail portion are indicated.

b. Details of the EUS-PDD/A

EUS-PDD/A is considered the most difficult I-EUS procedure currently. Very hard pancreatic parenchyma, tortuous pancreatic duct, difficult to keep the scope position and difficult to puncture in good directions were main hurdle of EUS-PDD/A. EUS-guided pancreatogastrostomy (EUS-PGS), EUS-guided pancreatoduodenostomy (EUS-PDS) and EUS-guided pancreatojejunostomy (EUS-PJS) are performing. Most difficult steo in EUS-PDD/A was dilation of puncture tract, but after introduction of drill-dilator (Tornus, Olympus medical systems, Tokyo, Japan), this step became easier.

5. Trans-ESCR procedures

We can perform most of the trans-papillary procedures by trans-ESCR procedure. Stone, stricture management, insertion of the baby scope are currently available through the ESCR.[11] However, some procedures require maturation of the ESCR and increasing the procedure times. In this lecture, I will try to introduce some trans-ESCR procedure for both biliary and pancreatic disorders.

6. Conclusions

EUS-D/A for biliary and pancreatic disorders are effective procedures but have many issues for establishment. The author believes that EUS-BD/A can become a primary procedure because of avoidance of post procedural pancreatitis and feasible for performance. EUS-PDD/A required breakthrough with dedicated effective devices for the establishment. Trans-ESCR procedures are available but required dedicated devices.

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外賓演講（2）

The Evidence and Practice of MASLD in Japan

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Since the new nomenclature for steatotic liver disease was defined, several clinical studies have been conducted and evidence is accumulating. The concordance rate between MASLD and NAFLD in 3,709 patients at our institute was 96%. The prevalence of MASLD in the Japanese general population, based on an analysis of 71,254 citizens, was 25.8%, of whom 1.7% had advanced fibrosis. Among first-degree relatives with fibrosis-advanced MASLD, 15.1% had fibrosis-advanced MASLD, with an odds ratio of 11.8 compared with non-MASLD.

When screening for MASLD with fibrosis, FIB-4 >1.3 had a PPV of 55% for advanced fibrosis. The problem with FIB-4 is that its diagnostic accuracy decreases with age. However, by using M2BPGi, a single reference value can be used to identify advanced fibrosis regardless of age. In an analysis of 2,645 patients who underwent a health check at our hospital, 1.1% had an M2BPGi >1.5 and 71.4% of these patients had moderate or advanced fibrosis.

The next step after screening is to assess liver fibrosis, as this is the most important indicator of prognosis in MASLD. In 428 patients whose liver stiffness was assessed by MR elastography, liver-related events and the development of HCC increased in parallel with fibrosis progression, while the risk of cardiovascular events was highest in moderate liver fibrosis, with a reduced risk in cirrhosis.

In a study using a large Japanese database, liver-related events were more frequent in lean MASLD than in overweight MASLD, whereas cardiovascular events were more frequent in overweight MASLD. When comparing MASLD, Met-ALD and ALD, the risk of cardiovascular events was highest in MASLD, followed by Met-ALD and ALD, whereas the risk of liver-related events was highest in ALD, followed by Met-ALD and MASLD. These data indicate the value of subclassifying steatotic liver disease according to BMI or alcohol consumption.

The impact of cardiometabolic risk factors on prognosis is another important issue. The number of cardiometabolic risk factors showed a strong association with cardiovascular events, but not with liver-related events. Reducing the number of cardiometabolic risk factors within one year was associated with a reduced risk of cardiovascular events, but not with liver-related events. Analysis of the association between HbA1c levels and prognosis in 63,3279 patients showed that the risk of both liver-related and cardiovascular events increased with increasing HbA1c.

In conclusion, it is important to assess the risk of both cardiovascular and liver-related events in MASLD, taking into account liver stiffness, obesity, alcohol consumption, number of cardiometabolic risk factors and diabetes control status.

外賓演講（3）

The Future of Esophageal Diagnostics: Advancements in Technology and Artificial Intelligence

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The landscape of esophageal diagnostics is undergoing a significant transformation with the advent of advanced imaging, functional assessment techniques, and artificial intelligence (AI). This presentation will explore the latest innovations in esophageal evaluation, focusing on how technology is enhancing diagnostic precision, improving patient outcomes, and streamlining clinical workflows.

Traditional methods such as endoscopic visualization remain essential for assessing dysphagia, reflux, and chest pain. The Los Angeles Classification System for esophagitis and the flap valve concept for esophagogastric junction (EGJ) disruption are critical in evaluating mucosal and structural integrity. Additionally, esophageal function testing has evolved, incorporating Lyon 2.0 reflux criteria and Chicago Classification 4.0 high-resolution manometry (HRM) to better characterize motility disorders.

A major focus of this talk will be the integration of artificial intelligence (AI) into endoscopic and manometric diagnostics. The groundbreaking GULLET AI system, developed using 1,000 endoscopy videos linked to HRM data, has demonstrated an achalasia detection accuracy of 91.1%, showcasing its potential to revolutionize endoscopic interpretation. Additionally, the ELIA (Endoscopic Lesion Image Analyzer) system, powered by the ARIES platform, provides an automated, AI-driven approach to generating endoscopic reports, reducing clinician workload and enhancing diagnostic consistency.

Beyond AI, novel technologies such as 4D high-resolution manometry (HRM) are redefining esophageal function assessment. By integrating pressure-volume metrics, bolus retention analysis, and esophageal distensibility measurements, 4D HRM allows for a more dynamic and precise evaluation of esophageal motility disorders. New methodologies also include functional lumen imaging probe (FLIP) panometry for assessing EGJ compliance and peristaltic strength in real time.

Another exciting development is the vEsophagus™ in-silico model, a simulation-based platform that mimics esophageal function under varying physiological and pathological conditions. This model allows researchers to test therapeutic interventions virtually before applying them in clinical practice, bridging the gap between research and patient care.

This session will provide a comprehensive overview of how machine learning, AI-driven diagnostic tools, and advanced motility metrics are shaping the future of esophageal disease evaluation. By combining traditional diagnostic techniques with big data analytics, deep learning models, and real-time functional imaging, we are paving the way for more accurate, personalized, and efficient approaches to diagnosing and managing esophageal disorders.

Attendees will gain insight into emerging technologies that will transform esophageal diagnostics, with a focus on improving disease detection, classification, and therapeutic decision-making in both clinical and research settings.

外賓演講（4）

Current Topics in Endoscopic Tissue Acquisition and Genomic Medicine

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Pancreatic cancer (PC) is a highly lethal malignancy and ranks as the fourth most common cause of cancer-related death worldwide. EUS-FNA is now play an important role in diagnose of PC. Especially, current EUS-FNB technique allows tissue acquisition which made it possible not only histological assessment but also genetic analysis. Although tissue obtained by EUS-FNA has been used for the genetic analysis, it has been hampered by low tissue quantities due to fibrotic nature of the PC. However, there are a number of new techniques to optimize molecular analyses which help clinical decision-making to guide the selection of therapy. At present, chemotherapy remains the standard of care for the management of advanced PC although only a minority of patients can benefit from anticancer drugs. However, the identification of known molecular targets allows for treatment with currently available therapeutics such as BRCA mutation tumors with platinum and PARP inhibitor or HER2-amplified tumors with anti-HER2 therapies such as trastuzumab or KRAS G12C mutation tumors with Sotorasib and mismatch repair deficits carrying tumor with immune checkpoint inhibitors (ICI). Here advancement of genetic analysis using tissue obtained by EUS-FNA will be reviewed and discussed for future precision medicine for PC.

外賓演講（5）

Rome Foundation and International Neurogastroenterology and Motility Societies Consensus on Idiopathic Gastroparesis

Jan Tack

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Over the last decades, the nature and definition of gastroparesis, the relevance of GE testing, and especially the separation of idiopathic gastroparesis from functional dyspepsia and other upper gastrointestinal disorders, have been topics of intense debate To establish consensus on the definition and management of idiopathic gastroparesis, international experts, selected by Neurogastroenterology and Motility societies and initiated by the Rome Foundation, devised 144 statements through a Delphi approach, with at least 80% agreement required. This consensus defined idiopathic gastroparesis as the presence of symptoms associated with delayed gastric emptying in the absence of mechanical obstruction. Nausea and vomiting were identified as cardinal symptoms. Frequently co-existing symptoms are early satiation and postprandial fullness. Diagnosis requires these symptoms alongside delayed gastric emptying, measured by a 4-hour scintigraphy or gastric emptying breath test of a mixed composition meal, in the absence of mechanical obstruction. Therapeutic options of proven efficacy were limited. Dietary adjustments, nutritional support per ESPEN guidelines for significant weight loss or intractable vomiting, and opioid cessation were recommended by consensus. Anti-emetic and prokinetic agents are considered potentially beneficial. The consensus offers a global perspective on idiopathic gastroparesis.

外賓演講（6）

Additional Treatment Plan Based on Metastatic & Recurrence Rate of Colorectal T1 Cancer

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The risk of lymph node metastasis (LNM) in colorectal T1 cancer is primarily assessed based on the guidelines of the Japanese Society for Cancer of the Colon and Rectum (JSCCR). These guidelines weakly recommend surgical resection when submucosal (SM) invasion exceeds 1000 μm, lymphovascular invasion (Ly/V) is present, budding grade is moderate to poor (BD G2/3), or when a poorly differentiated adenocarcinoma component is identified.

Recent meta-analyses have indicated that the risk of LNM is extremely low if factors other than SM invasion depth are negative. However, interobserver variability remains a concern in measuring SM invasion depth, and even with immunohistochemical staining, the diagnostic concordance rate for Ly/V assessment remains suboptimal.

A recent multicenter study by the JSCCR, analyzing more than 4000 cases of T1 colorectal cancer, identified additional risk factors for LNM, including SM invasion depth exceeding 2000 μm, tumor location (rectum/sigmoid colon), female sex, and moderately differentiated adenocarcinoma. Notably, rectal cancer is often treated less aggressively due to concerns about postoperative quality of life. However, rectal cancer has a higher metastatic recurrence rate compared to colon cancer.

Given these challenges, additional chemoradiotherapy (CRT) is currently being investigated as a potential treatment option in clinical trials, such as JCOG1612. This presentation will discuss the current status and limitations of endoscopic treatment for colorectal T1 cancer and highlight the necessity for additional therapeutic strategies.

外賓演講（7）

Evolving Challenges in HBV Reactivation

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Hepatitis B virus reactivation (HBVr) is a serious event which can result in liver failure and death, but it is preventable. HBVr occurs when immune response of patients with HBV infection is suppressed. It is more common in patients with chronic HBV infection (hepatitis B surface antigen positive [HBsAg+]), but it can also occur in those with past HBV infection regardless of the presence or absence of hepatitis B surface antibody (HBsAg negative, IgG hepatitis B core antibody positive [HBsAg-/anti-HBc+]) because of the persistent presence of HBV DNA in the liver even after serologic recovery. HBVr was first described in patients receiving chemotherapy for malignancies. It has since been reported to be associated with other immunosuppressive therapies including biologics used in a variety of non-malignant diseases as well as target therapies for malignancies. The incidence of HBVr reported to be associated with each class of immunosuppressants and immunomodulators is highly varied due to lack of consensus in the definition of HBVr, and variations in study design and patient selection. Current literature notes that B-cell depleting agents such as rituximab, are associated with the highest risk of HBVr.

Data on the risk of HBVr with new therapies are sparse. Several professional society guidelines have provided recommendations on prevention of HBVr associated with new classes of immunosuppressants and immunomodulators, but these guidelines focused on select therapies commonly prescribed for diseases within that specialty and most were not accompanied by systematic review of the published literature. Thus, a systematic review and meta-analysis on the risk of HBVr associated with new classes of immunosuppressants and immunomodulators used for a broad spectrum of diseases and the impact of prophylactic HBV antiviral therapy in reducing that risk to provide guidance to physicians across a wide range of specialties, has been conducted.

More recently, Immune check point inhibitors, tyrosine kinase inhibitors, cytokine inhibitors, CAR T-cell immunotherapies, and corticosteroids have been categorized as presenting high HBVr risk in HBsAg+ patients; cytokine inhibitors, CAR T-cell immunotherapies, and corticosteroids as intermediate risk in HBsAg-/anti-HBc+ patients; and anti-TNF agents and immune check point inhibitors as low risk in HBsAg-/anti-HBc+ patients; based on medium-high quality evidence. NA prophylaxis is recommended when drugs with high HBVr risk are used and monitoring and on-demand NA for drugs with low risk, while either approach may be appropriate for drugs with intermediate risk. It is apparent that there is an ever-increasing number of immunomodulatory and immunosuppressant drugs entering clinical practice and thus the need for even greater vigilance for HBVr.

Suggested Reading:

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外賓演講（8）

H. pylori and Beyond: Pioneering the Microbiome Revolution in Gastroenterology

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The discovery of *Helicobacter pylori* (*H. pylori*) was first reported to the medical community in a letter in Lancet (1983), more than 40 years ago, and has set a milestone in medicine. The bacterium was recognized as primary cause of gastritis, the dogma of the acidic stomach as a sterile organ was turned down and the chapters on gastric pathophysiology and gastroduodenal diseases had to be rewritten.

In the first decade following the discovery, *H. pylori* was identified as principal cause of peptic ulcer disease (PUD) and eradication of *H. pylori* was demonstrated to permanently cure PUD. This eventually became standard of care in management in PUD and for their discovery in this specific context Barry Marshall and Robin Warren 2005 received the Nobel prize for Medicine and Physiology. It was another remarkable achievement that gastric MALT -Lymphoma in early stage became the first malignant disease curable with antibiotics for *H. pylori* eradication.

In the decades thereafter indications for *H. pylori* treatment became extended to other, including extra-digestive, diseases. *H. pylori* gastritis became defined as infectious disease that requires therapy whenever detected.

Intensified basic and clinical research established the insight that *H. pylori* is the main risk factor in the multifactorial pathogenesis of gastric cancer. Doors were opened for gastric cancer prevention through *H. pylori* screen & treat strategies.

The role of *H. pylori* in pioneering the microbiome revolution has gained traction from the introduction of molecular techniques (eg next generation sequencing) for detection and characterization of microbiota along the entire gastrointestinal tract. The presence of *H. pylori* alters the composition and diversity of other gastric microbiota. There is increasing evidence that microbial changes with increase of other proinflammatory and pro-oncogenic bacterial species in the stomach during the progression of *H. pylori* gastritis will assume an important contributing role in gastric carcinogenesis.

The interaction of *H. pylori* with the gastrointestinal microbiome offers a series of other new fascinating insights that include the possible influence of *H. pylori* on pathologies in the colon, on changes in gut microbiota diversity and mechanisms of antibiotic resistance following eradication therapy. Future research will reach out for novel *H. pylori* therapies which might include to recruit candidates from the broad field of probiotic medicine.

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GEST-KSG Joint Symposium

Innovations in Diagnosis and Treatment of Liver Disease

The Integrative Prediction Model of HCC in CHB Patients

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Hepatocellular carcinoma (HCC) remains a major concern for patients with chronic hepatitis B (CHB), even though antiviral therapy significantly reduces its incidence. Developing an integrative HCC risk prediction model is crucial for optimizing clinical management. Such a model could help determine the optimal timing for initiating antiviral treatment in untreated patients and refine HCC surveillance strategies in those receiving therapy.

Several key factors must be considered when constructing an effective prediction model. First HBeAg status serves as an effect modifier and should not be analyzed as a single group, as HCC risk differs significantly between HBeAg-positive and HBeAg-negative patients. In HBeAg-negative individuals, HCC risk increases with viral load and plateaus at ≥5 log10 IU/mL, while in HBeAg-positive patients, a paradoxical decrease in HCC risk is observed when HBV DNA levels are >7 log10 IU/mL. Such different trends are also noted between HBsAg levels and HCC risk.

Second, more biomarkers further enhance risk stratification. Fibrosis markers, such as liver stiffness assessments, are essential, though platelet-based liver fibrosis biomarkers can serve as alternatives when liver stiffness data are unavailable. Viral biomarkers also contribute to refined risk assessment: HBsAg levels help predict HCC risk in immune-tolerant patients, while HBcrAg levels aid in stratifying eAg-negative patients in the grey zone.

Long-term HCC prediction remains crucial, particularly for non-cirrhotic patients and those undergoing antiviral treatment. A well-validated integrative model could improve individualized HCC risk assessment, enabling precision medicine in CHB management and ultimately reducing HCC-related mortality.

GEST-KSG Joint Symposium

Innovations in Diagnosis and Treatment of Liver Disease

Recent Advances in Treatment of MASLD/MASH

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Metabolic-Associated Steatotic Liver Disease (MASLD), equivalent to the original term non-alcoholic fatty liver disease (NAFLD), currently is the most prevalent liver noncommunicable disease globally. The epidemic has particularly been rapidly progressing in the past decades in Asia-Pacific in parallel to the rapid Westernization in the region. MASLD and its extreme form, steatohepatitis (MASH), possess a huge health burden and carry the risks for both liver-related events and non-liver-related events. MASLD and MASH may progress to liver inflammation, fibrosis, cirrhosis and potentially the development of HCC. MASLD had higher overall mortality compared with controls, and most deaths were due to cardiovascular events. Obesity is the main pillar of the risk factors contributing to MASLD/MASH. Therefore, the investigation of the disease course and the optimal patient management is a must for gastroenterologists and hepatologist.

Lifestyle intervention should be the initial step toward patient care of MASLD. Lifestyle modification consisting of diet, exercise, and weight loss has been advocated to be the initial step for management of MASH patients. The strategies have been widely adopted into the major current guidelines. Among them, weight loss has been reported as the most effective one in improving the histology features and regression of MASH. Several studies have evaluated lifestyle changes, particularly diet and exercise in managing MASH.

The adherence of lifestyle modification remains problematic in a large proportion of MASH patients. It is difficult for patients with morbid obesity and musculoskeletal disorders to do sufficient exercise. Besides, the efficacy of lifestyle modification could not be applied to those lean MASH patients. Currently USFDA approved the first effective drug for MASH treatment in 2024. Many anti-diabetics have been actively investigated for the direction. These include peroxisome proliferator-activated receptor gamma agonist, glucagon-like peptide 1 receptor agonists (GLP-1 RAs), etc. The efforts will much change the landscape of patient care and outcome prediction in MASLD/MASH.

GEST-KSG Joint Symposium

Innovations in Diagnosis and Treatment of Liver Disease

Non-invasive Assessment of Fibrosis and Portal Hypertension

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Chronic liver diseases, such as viral hepatitis, alcoholic liver disease, and non-alcoholic fatty liver disease, frequently lead to fibrosis and cirrhosis, significantly impacting morbidity and mortality. Evaluating liver fibrosis and detecting portal hypertension are crucial for patient management. Although liver biopsy has traditionally been the reference standard, its invasiveness, complications, and sampling variability have driven the development of non-invasive alternatives. Various imaging techniques, including transient elastography (TE), magnetic resonance elastography (MRE), and acoustic radiation force impulse (ARFI) imaging, have demonstrated high accuracy in assessing liver fibrosis. TE, widely adopted due to its efficiency, reliably estimates liver stiffness and correlates well with fibrosis severity. MRE offers superior precision, particularly in patients with obesity or heterogeneous fibrosis distribution. ARFI-based methods, such as two-dimensional shear wave elastography (2D-SWE), further refine fibrosis evaluation. In addition to imaging, serum biomarkers and scoring systems provide valuable insights into liver fibrosis severity. Direct biomarkers, including hyaluronic acid, type IV collagen, and tissue inhibitors of metalloproteinases (TIMPs), reflect extracellular matrix remodeling, while indirect markers such as the aspartate aminotransferase-to-platelet ratio index (APRI) and fibrosis-4 (FIB-4) index utilize routine blood tests for fibrosis estimation. Composite scores like the enhanced liver fibrosis (ELF) test and FibroTest exhibit moderate to high diagnostic accuracy in detecting significant fibrosis and cirrhosis.

Portal hypertension, a serious consequence of advanced fibrosis, is a major predictor of liver-related complications, including variceal bleeding, ascites, and hepatic encephalopathy. While hepatic venous pressure gradient (HVPG) measurement is the gold standard for diagnosing portal hypertension, its invasiveness limits widespread use. Alternative non-invasive methods, such as spleen stiffness measurement (SSM) and Doppler ultrasound-based indices, show promise in identifying clinically significant portal hypertension (CSPH). Additionally, surrogate biomarkers like the platelet count-to-spleen diameter ratio and liver stiffness measurement (LSM) via TE have been validated for assessing portal hypertension severity.

Combining multiple non-invasive approaches has improved diagnostic accuracy. Integrating LSM with platelet count enhances cirrhosis and CSPH prediction, while algorithms incorporating elastography and serum biomarkers provide a comprehensive assessment. Furthermore, artificial intelligence and machine learning applications have enabled the development of predictive models that refine fibrosis and portal hypertension evaluation. Despite these advancements, certain limitations remain. Factors such as hepatic inflammation, cholestasis, and obesity can affect elastography accuracy, leading to potential misclassification. Additionally, serum biomarkers, although convenient, are influenced by age, metabolic disorders, and coexisting liver conditions. Further research is required to enhance non-invasive

techniques, optimize risk stratification, and improve their clinical applicability across diverse patient populations.

In conclusion, non-invasive methods for evaluating liver fibrosis and portal hypertension have transformed the management of chronic liver diseases. Imaging-based elastography, serum biomarkers, and integrative diagnostic models have significantly reduced the reliance on liver biopsy while providing reliable diagnostic and prognostic insights. Continuous advancements in technology and further validation studies will refine these approaches, ultimately enhancing patient outcomes and enabling earlier intervention in liver disease progression.

GEST-KSG Joint Symposium

Innovations in Diagnosis and Treatment of Liver Disease

Update on Management of Alcoholic Liver Disease

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Alcohol-associated liver disease (ALD) remains a major cause of liver-related morbidity and mortality worldwide, yet progress in developing effective treatments has been historically slow. However, recent advances in understanding ALD pathogenesis have paved the way for novel therapeutic strategies. Pharmacological interventions continue to be a primary focus, with corticosteroids remaining the standard treatment for severe alcohol-associated hepatitis (AH). However, their benefits are limited to short-term survival, highlighting the importance of early assessment using the Lille score. Recent clinical trials have demonstrated that IL-1 inhibitors failed to show efficacy in phase 2 studies, while TNF-α inhibitors did not provide benefits in phase 3 trials, prompting a shift toward alternative therapeutic approaches.

Although N-acetylcysteine has shown promise in experimental and early clinical studies, it has yet to be evaluated in phase 3 trials, and the role of granulocyte colony-stimulating factor (G-CSF) in ALD management requires further investigation. The gut-liver axis has emerged as a key therapeutic target, with microbiome-based interventions such as fecal microbiota transplantation (FMT) and probiotics showing potential in modulating disease progression. Additionally, nutritional therapy is gaining recognition as an essential component of ALD management, particularly in patients with AH, where protein-energy malnutrition and micronutrient deficiencies significantly impact outcomes.

Sustained alcohol cessation remains the cornerstone of ALD treatment, with integrated psychosocial and pharmacological interventions, including baclofen and acamprosate, proving effective in supporting abstinence. Liver transplantation, traditionally considered a last resort, is now being explored as an early intervention for select patients with severe AH, offering promising survival benefits.

These recent developments emphasize the need for a multidisciplinary approach to ALD treatment, integrating pharmacological advances, microbiome-targeted therapies, nutritional support, and early liver transplantation to improve patient outcomes. Continued research into disease-modifying therapies is crucial to changing the natural course of ALD and addressing its growing global burden.

專題討論（1）

Emerging Concepts in GERD and Esophageal Motility Disorders Symposium

Motility Testing in 2025: Optimizing Point of Care Endoscopy

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Evaluating patients with esophageal symptoms presents a significant challenge due to the overlap and non-specific nature of symptoms, which often complicate the identification of the underlying cause. Common esophageal complaints such as heartburn, dysphagia, regurgitation, chest pain, and food impaction can be attributed to a variety of disorders, including gastroesophageal reflux disease (GERD), achalasia, and eosinophilic esophagitis (EoE). This overlap underscores the importance of a systematic diagnostic approach to differentiate between structural, motility, and functional disorders effectively.

The initial step in assessing esophageal symptoms typically involves obtaining a comprehensive clinical history, which guides further evaluation. Upper endoscopy, with or without biopsies, is a cornerstone of the diagnostic pathway, allowing for the identification of structural abnormalities such as strictures, tumors, inflammatory conditions, and anatomical defects like large hiatal hernias. When structural and inflammatory causes are ruled out, the focus shifts toward distinguishing GERD, motility disorders, and functional conditions. Endoscopic findings such as the presence of luminal contents, esophageal dilation, or a tight lower esophageal sphincter (LES) may suggest an underlying motility disorder. The CARS (Contents-Anatomy-Resistance-Stasis) score, a novel approach that evaluates these endoscopic parameters, can aid in identifying major motor disorders, particularly achalasia, during routine upper endoscopy. However, the CARS approach, while highly specific, lacks sensitivity, as a substantial proportion of patients with achalasia may present with a normal endoscopic appearance.

Functional lumen imaging probe (FLIP) panometry is an emerging diagnostic tool that offers real-time assessment of esophageal distensibility and can be performed during the initial endoscopic evaluation. FLIP provides a unique advantage over high-resolution manometry (HRM) by facilitating the immediate assessment of esophageal motility, helping to confirm or exclude major motor disorders such as achalasia. If FLIP findings are normal, further motility testing may not be required, allowing clinicians to focus on GERD or functional disorders. Conversely, if FLIP findings are abnormal and consistent with achalasia or obstructive motility disorders, appropriate therapeutic interventions can be pursued. In cases where FLIP results are equivocal or inconclusive, HRM remains the gold standard for further characterization of esophageal motility abnormalities.

High-resolution esophageal manometry (HRM) provides detailed pressure topography of esophageal peristalsis and LES function and is interpreted based on the Chicago Classification version 4.0. This classification system helps in diagnosing disorders such as achalasia, esophagogastric junction outflow obstruction (EGJOO), and ineffective esophageal motility (IEM). HRM can also be utilized with adjunctive testing, such as the post-prandial challenge,

to assess for conditions like rumination syndrome and supragastric belching. If HRM findings suggest normal or borderline motility, further evaluation may focus on GERD or functional esophageal disorders, which may require pH-impedance monitoring for definitive diagnosis.

Despite the utility of HRM and FLIP, diagnostic uncertainty may persist in some cases, necessitating additional imaging such as a timed barium esophagram to provide functional and structural insights into esophageal transit and emptying. The integration of these diagnostic modalities allows for a comprehensive and methodical evaluation of esophageal symptoms, ensuring that management strategies are tailored appropriately based on objective findings.

Ultimately, no single diagnostic test is infallible, and the interpretation of results should be considered in the context of clinical presentation and complementary investigations. An optimized approach to the evaluation of esophageal symptoms involves a stepwise and integrated use of endoscopy, FLIP, HRM, and adjunctive testing to facilitate accurate diagnosis and effective patient management.

專題討論（1）

Emerging Concepts in GERD and Esophageal Motility Disorders Symposium

What Is New in GERD Diagnosis: Seoul, Lyon, or Milan?

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The **Lyon Consensus 2.0** revises the definition of **actionable** gastroesophageal reflux disease (GERD) to optimize management strategies for symptomatic patients. A major update is the classification of **Los Angeles (LA) grade B esophagitis** as definitive evidence of GERD, thereby recognizing LA grades B, C, and D esophagitis, biopsy-confirmed Barrett's esophagus, and peptic stricture as conclusive indicators of the disease. Additionally, the revised consensus establishes updated thresholds for **prolonged wireless pH monitoring** and incorporates parameters useful in diagnosing refractory GERD when testing is performed on antisecretory therapy in proven GERD.

This presentation will elucidate the clinical implications and rationale behind these updates, incorporating insights from the **Seoul Consensus**, which highlights specific considerations for GERD in **Asian populations**. Finally, it will also cover the **Milan score**, which utilizes **high-resolution manometry** to stratify the risk and severity of GERD, providing a more comprehensive pathophysiologic assessment of the antireflux barrier. By integrating the latest international GERD consensus statements, this approach aims to advance precision diagnosis and personalized management for GERD patients.

專題討論（1）

Emerging Concepts in GERD and Esophageal Motility Disorders Symposium

Update on Management of Refractory GERD

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Currently, proton pump inhibitor (PPI) remains the most commonly used anti-secretory agent for potent acid suppression, symptomatic relief and mucosa healing in the treatment of gastroesophageal reflux disease (GERD). However, up to 40% of patients have poor responses to PPI. The underlying pathophysiology involved in refractory GERD-like symptoms is complex. Prior studies have reported that poor drug compliance, improper dosing time, delayed gastric emptying, concomitant functional bowel disorder, psychological comorbidity, reduced PPI bioavailability, rapid PPI metabolism, and obesity might affect the treatment response to PPI. Identifying factors that might attribute to the poor treatment response of PPI in GERD is crucial to improve the overall treatment responses. Although endoscopy remains the mainstay of diagnostic tool for patients with reflux symptoms in Taiwan, a great proportion of patients have no esophageal mucosa changes on examination, so call non-erosive reflux disease (NERD). Ambulatory multichannel intraluminal impedance and pH (MII-pH) monitoring has been found to be the most sensitive tool in diagnosing GERD. The MII-pH catheter combines impedance channels to conventional pH catheters and helps to establish the reflux-symptom association with symptoms index (SI) and symptom association probability (SAP), and therefore is useful in clarifying the underlying mechanism of refractory GERD. With the aid of 24-h MII-pH monitoring, traditional GERD patients, who are quite heterogeneous from a pathophysiological point of view, could be further categorized into (1) endoscopic positive, (2) true NERD (patients with an excess of acid reflux), (3) hypersensitive esophagus to acid reflux, (4) hypersensitive esophagus to non-acid reflux, and (5) functional heartburn. For patients who could not tolerate catheter-based ambulatory MII-pH monitoring, utilization of prolonged wireless reflux monitoring off PPI therapy also helps to characterize severity of GERD. Absence of pathologic acid exposure on ambulatory reflux monitoring (AET <4.0% on all 4 days of the prolonged wireless pH study) with a normal endoscopy helps to exclude GERD. Moreover, personal factors focused on visceral anxiety and hypervigilance need to be addressed because these features can affect symptom severity and health care use.

Esophageal motility abnormalities, including transient LES relaxation, ineffective esophageal motility (IEM) and hypotensive LES, have been suggested to play an important role in the pathogenesis of refractory GERD. The close relationship between esophageal motor abnormalities and GERD has been demonstrated in previous studies. Among the various esophageal motility abnormalities, esophageal hypocontractility, such as absent contractility and IEM, impairs esophageal clearance of the refluxate and increases the exposure to noxious gastric contents. High-resolution manometry (HRM) is currently considered as the gold standard for evaluation of esophageal motor function. Application of these novel motility studies, including HRM, MII-pH, and wireless pH monitoring, help to clarify the mechanism of refractory reflux symptoms and tailor treatment strategies, achieving the goal of personalized/precision medicine.

專題討論（2）

Steatotic Liver Disease

Impact of MASLD on Liver Disease in Taiwan: Epidemiology View

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As urbanization accelerates and dietary habits and lifestyles change, the global prevalence of obesity continues to rise, posing a significant challenge to public health due to its strong association with an increased risk of various non-communicable chronic diseases. Over the past few decades, chronic infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) were the primary risk factors for advanced liver diseases. However, with the widespread adoption of vaccination programs and the introduction of antiviral therapies, the disease burden of chronic viral hepatitis has been effectively mitigated. In contrast, obesity-related Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has emerged as a critical focus, now recognized as a major risk factor for advanced liver conditions, including cirrhosis and liver cancer.

This presentation will draw on epidemiological data from Taiwan to examine the prevalence of MASLD and its associated disease risks. MASLD is closely linked to a range of chronic conditions, such as cardiovascular and cerebrovascular diseases, as well as increased all-cause mortality. We will investigate the role of MASLD in these diseases, with a particular emphasis on its contributions to the risks of cirrhosis and liver cancer. Taiwan is characterized by a high prevalence of chronic HBV and HCV infections, offering a unique context to compare the impact of MASLD and viral hepatitis on liver disease outcomes. These findings will inform critical considerations for future liver cancer prevention strategies.

Moreover, although obesity prevalence is relatively lower in Asian populations compared to Western counterparts, individuals of Asian descent are more prone to abdominal fat accumulation. Of particular interest is the subset of “lean” MASLD patients, whose outwardly slim appearance belies significant metabolic risks. The liver disease and cancer risks in this group warrant further investigation. Additionally, while the definition of MASLD excludes individuals with high alcohol consumption, the potential influence of low to moderate alcohol intake on liver disease progression within the MASLD population remains to be clarified.

In summary, the health impact of MASLD is becoming increasingly evident, particularly in the context of successful viral hepatitis control. Future efforts should prioritize multicenter collaborations and large-scale integrative studies to elucidate the interplay between MASLD and other risk factors. These findings will guide the development of more effective prevention and treatment strategies to control the public health burden associated with MASLD.

專題討論（2）

Steatotic Liver Disease

Benefits of Exercise in Management of MASLD Patients

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Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has emerged as a prevalent health concern. To date, there is no approved effective drug therapy for MASLD, and lifestyle modification with dietary changes and exercise remains the foundation of MASLD treatment. Exercise is a subset of physical activity that is planned, structured and repetitive, with a specific goal in mind. Current evidence demonstrated regular exercise is associated with decreased risk of MASLD development. A prospective study recruited participants in the UK Biobank, physical activity was associated with a reduced risk of MASLD (HR: 0.39 [0.21–0.70]),[1] and were inversely associated with hepatic fibro-inflammation.[2] At least 10 distinct mechanisms or cellular targets through which exercise exert a therapeutic effect on MASLD. Exercise, particularly resistance exercise, promotes the utilization of fatty acids as an energy source. It enhances muscle glucose uptake and glycogen storage, thus reducing the burden on the liver to uptake excess blood glucose.[3] Through these mechanisms, exercise improve insulin sensitivity, fatty acid metabolism and enhance metabolic flexibility which prevents hepatic steatosis and its related inflammation and fibrosis.

The benefit of exercise in preventing and treating MASLD has been demonstrated in numerous human studies and across different patient populations, including those with lean MASLD. A recent meta-analysis including seven randomised controlled trials showed that exercise is more likely to reduce MRI-measured liver fat (≥30% relative reduction) (odds ratio 3.51, 95% confidence interval 1.49–8.23, p = 0.004) compared to standard care, independent of weight loss.[4] American College of Sports Medicine (ACSM) suggest at least 150 min/wk of moderate or 75 min/wk of vigorous-intensity exercise are recommended for all patients with MASLD.[5]

In conclusion, exercise remains a cornerstone intervention in the management of MASLD.[6] Further research is needed to refine personalised exercise protocols and investigate their potential synergistic effects with emerging treatments.

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專題討論（2）

Steatotic Liver Disease

Will Treat Obesity Resolve MASLD?

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Metabolic-Associated Steatotic Liver Disease (MASLD), equivalent to the original term non-alcoholic fatty liver disease (NAFLD), currently is the most prevalent liver noncommunicable disease globally. MASLD and its extreme form, steatohepatitis (MASH), possess a huge health burden and carry the risks for both liver-related events and non-liver-related events. MASLD and MASH may progress to liver inflammation, fibrosis, cirrhosis and potentially the development of HCC. MASLD had higher overall mortality compared with controls, and most deaths were due to cardiovascular events. Asian people are more prone to metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM), and hypertension (HTN) than other races with the same BMI value. Obesity is the main pillar of the risk factors contributing to MASLD/MASH. Therefore, the investigation of the disease course and the optimal patient management is a must for gastroenterologists and hepatologist.

Lifestyle intervention should be the initial step toward patient care of MASLD. It is intended to lead to weight reduction through a healthy dietary change and increased physical activity tailored to the individual's tolerance and ability. A weight loss of 5% improves pancreatic β-cell function, insulin sensitivity, and hepatic steatosis. However, a more significant weight loss of 7%–10% is necessary for MASH resolution and fibrosis regression. Early evidence was from a randomized controlled trial in a dietitian-led lifestyle modification program or receive usual care for 52 weeks in Hong Kong. It showed that 97% of patients with weight loss >10% had remission of MASLD. Meanwhile, 41% of those with weight loss of 3.0%–4.9% could also achieve the primary outcome of liver fat <5%. Weight reduction is the most important factor for reducing the risk of incident diabetes in MASLD. For overweight and obese adults with diabetes, a weight reduction of >5% has a significant effect on metabolic alterations. Weight reduction of ≥10% early in the disease trajectory is associated with a doubling of the likelihood of diabetes remission at 5 years in patients with newly diagnosed diabetes. Recently, incretin-mimetics such as glucagon-like peptide 1 receptor agonists (GLP-1 RAs) have beneficial effects on ASCVD and weight loss. GLP-1 RAs normalize aminotransferase levels, decrease HbA1c level, reduce liver fat content, and improve histological manifestations in patients with MASLD.

專題討論（2）

Steatotic Liver Disease

Liver-Targeted Drug Treatment of MASLD: Current and Future

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Metabolic dysfunction steatotic liver disease (MASLD) is the most common etiology of chronic liver disease in the world, with approximately 30% of the world's population suffering from MASLD. MASLD can also cause chronic liver inflammation, liver fibrosis, cirrhosis, liver failure, and liver cancer; it also increases the risk of cardiovascular disease, diabetes, chronic kidney disease, and extrahepatic cancers. Therefore, effective treatment is urgently needed.

The treatment of MASLD includes non-drug and drug treatments. Healthy diet, regular exercise, and weight loss are the most effective non-drug treatments. The dietary principles recommend consuming more olive oil, vegetables, fruits and nuts, beans, whole grains, fish and seafood; consuming less red meat and processed foods, and reducing the intake of sugar and refined carbohydrates. Exercise is performed alternately through aerobic exercise (such as brisk walking, jogging, and cycling) and resistance exercise (such as elastic bands). Literature indicates that for overweight people, losing 5% of their body weight can improve fatty liver, and losing 10% can improve liver fibrosis.

Currently, the only FDA-approved drug treatment is resmetirom, which is a thyroid hormone receptor β agonist that can improve fat and sugar metabolism and reduce fat accumulation in the liver. Other drugs with more diverse mechanisms of action, either as monotherapy or in combination therapy, of Phase II or Phase III clinical trials are undergoing and some of them show promising results. In the future, the treatment of MASLD will no longer be untreatable.

專題討論（3）

Advances in ERCP and EUS

Advanced Endoscopy Meets Molecular Diagnosis of Cholangiocarcinoma

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Biliary Tract Cancer in the Era of Precision Medicine

In the era of precision medicine, the development of new drugs for **biliary tract cancer** has progressed rapidly, with breakthrough advancements in recent years. Since more than half of biliary tract cancer cases are diagnosed at an advanced stage and the tumor tissue tends to undergo extensive fibrosis, early diagnosis and genetic testing often fail or suffer from insufficient sample collection. This poses a significant challenge in the current era of personalized precision medicine that urgently requires breakthroughs. This report will discuss how to enhance the early diagnosis of biliary tract cancer, improve the success rate of genetic testing, and explore new opportunities for follow-up in the age of precision medicine.

專題討論（3）

Advances in ERCP and EUS

What's New in Bile Duct Stricture Management?

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Biliary stricture can be induced by intrinsic narrowing and extrinsic compression, with the majority of cases being malignant. Concurrently, innovative technologies emerge providing fresh insights for the clinical management of these patients. Traditional plastic and metal stents, characterized by their complex application and limited scope, have been unable to fully satisfy clinical needs. The introduction of novel stents and instruments has notably improved this scenario, marking a considerable progression towards precision medicine. Hence, a discussion on the present state and evolving trends of biliary stricture management is presented.

專題討論（3）

Advances in ERCP and EUS

What's New in Dedicated Devices for Therapeutic EUS

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Linear echoendoscopes with large instrument channels enable EUS-guided interventions in organs and anatomical spaces adjacent to the gastrointestinal tract. Novel devices and tools designed for EUS-guided transluminal interventions allow for various new applications and enhance the efficacy and safety of these procedures. Dedicated devices for tract dilatation have been developed to improve technical success rates and reduce complications. Specially designed stents and stent insertion devices facilitate intra- and extrahepatic bile duct and pancreatic duct stenting, as well as gallbladder drainage.

Currently, EUS-guided biliary drainage for obstructive jaundice due to malignant biliary obstruction is considered feasible and safe when ERCP has failed. In the future, it may replace ERCP as the first-line intervention. EUS-guided transmural stenting is regarded as the preferred approach for managing symptomatic peripancreatic fluid collections. Additionally, the creation of new anastomoses between different organs, such as gastrojejunostomy and gallbladder drainage, has become possible with lumen-apposing stents. This presentation focuses on novel devices and specially designed stents for interventional EUS.

專題討論（3）

Advances in ERCP and EUS

EndoHepatology: Current Status and Perspectives

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Lesions such as hepatocellular carcinoma (HCC) or other entities at the caudate or left lobe were located at the deep site of liver, which was not visualized well by transabdominal ultrasound, and there were intervening veins that would have made it not only difficult but also hazardous to attempt percutaneous ablative treatment due to the long trajectory. Endoscopic ultrasonography (EUS) has emerged as a highly sophisticated interventional modality. EUS guided therapy provide the best solution to treat the caudate lobe lesion, i.e., in close proxim¬ity to the stomach, which made it easily accessible by EUS. EUS have been developed for the interventional purpose in addition to the pancreatic disease. EUS-guided liver biopsy, abscess aspiration or ethanol injection or radiofrequency ablation for HCC, owing to its less invasiveness, appears to be a new innovative option for lesions that is difficult to treat by local percutaneous treatment.

專題討論（4）

Viral Hepatitis Treatment Excellence

Unmet Needs of CHB Treatment

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Chronic hepatitis B (CHB) remains a major global health burden with significant unmet treatment needs. Despite advances in antiviral therapy, achieving functional cure, defined as sustained hepatitis B surface antigen (HBsAg) loss, remains difficult. Therefore, establishing a more feasible treatment endpoint that enhances clinical outcomes is an urgent unmet need. Current nucleos(t)ide analogue treatments primarily focus on viral suppression rather than complete virus eradication, necessitating lifelong therapy for most patients. Consequently, determining the optimal timing for antiviral treatment initiation presents another critical challenge.

Given these challenges, partial cure has emerged as a more feasible treatment endpoint. A clinically relevant HBsAg threshold that minimizes HCC risk to a level comparable with the non-HBV/non-HCV general population is needed. Recent large-scale cohort data suggest that an HBsAg level <100 IU/mL could meet this criterion, providing a realistic and practical goal for CHB management.

For HBeAg-positive patients in the immune-tolerant phase, the timing of antiviral treatment initiation remains controversial. While early treatment may reduce HCC risk, evidence from large cohort studies suggests that patients with HBsAg >10,000 IU/mL are associated with delayed HCC development, indicating a potential biomarker for treatment indication.

In HBeAg-negative patients, an interim report from a clinical trial suggests that pre-emptive antiviral therapy may reduce the risk of HCC. However, lifelong oral antiviral therapy is not universally accepted by all patients. The integration of HBV core-related antigen (HBcrAg)-based HCC risk prediction models has provided a novel approach to risk stratification, allowing for more personalized treatment decisions. This model may guide clinicians in determining optimal timing for antiviral treatment initiation to maximize HCC prevention while balancing the need for long-term therapy.

Overall, redefining treatment goals beyond functional cure and incorporating risk-based stratification models are critical steps toward optimizing CHB management and addressing its unmet clinical needs.

專題討論（4）

Viral Hepatitis Treatment Excellence

Update in Treatment of HDV

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For people diagnosed with chronic and active HDV infection, effective treatments for hepatitis D virus infection have been limited to high-dose interferon alfa. Most of the guidelines recommend treatment with peginterferon alfa for at least 48 weeks or longer. However, the response rates are suboptimal, with virologic response rates of 17%–47% with high rates of HDV relapse after stopping therapy. Only a few patients could get a sustained virologic response. Furthermore, interferon-based therapies cannot be used in patients with decompensated liver disease. Therefore, patients have to receive liver transplantation to reduce morbidity and mortality. HDV DNA decline and ALT normalization became important points for clinical benefit in patients treated with interferon-alfa for HDV.

Recently, Bulevirtide and Lonafarnib have demonstrated anti-HDV activity in phase 3 clinical trials. The European Regulatory Agency has approved Bulevirtide in July 2020 based on evidence according to more than 2 log decline in HDV RNA and ALT normalization in phase 2 clinical trials. Further phase 3 clinical trial and real-world evidence have demonstrated clinical benefit in patients with advanced liver disease. Bulevirtide is under consideration by the United States FDA. Lonafarnib also demonstrated interfering on HDV assembly and secretion. In the phase 3 D-LVR randomized controlled trial, patients with active HDV infection treated with Lonafarnib alone (10.1%) or combined with interferon (19.2%) for 48 weeks achieved significantly higher end-of-treatment responses (defined as ≥2 log HDV RNA plus ALT normalization) than those treated with placebo (1.9%). However, the treatment discontinuation occurred in 8%–9% of patients due to gastrointestinal side effects (e.g. nausea, vomiting and diarrhea). Right now, we are still looking forward to seeing additional research to identify more agents targeting HBV and HDV viral replication and augmenting host immune response for HDV cure.

專題討論（4）

Viral Hepatitis Treatment Excellence

Unmet Needs in Management of CHC

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The treatment of chronic hepatitis C (CHC) has revolutionized to an era of all-oral direct-acting antivirals (DAAs) since 2014. Satisfactory treatment efficacy and tolerability can be provided by novel DAAs. Nevertheless, there are still some unmet needs and emerging issues in the treatment of CHC in the DAA era. Certain hard-to-cure populations are prone to have inferior treatment responses, including patients with severe liver decompensation, and hepatitis C virus (HCV) genotype 3(b) (HCV-3[b]) infection and those who experience multiple DAA treatment failures. Hepatitis B virus (HBV) reactivation during and after DAA treatment has raised concern for the use of prophylactic antivirals against HBV throughout DAA treatment. However, the standard strategy for the use of prophylactic antivirals is not uniform across regional guidelines In the post-sustained virological response (SVR) period, hepatocellular carcinoma (HCC) still occurs in a substantial proportion of patients. Attention must also be paid to HCV re-infection, particularly in high-risk populations. Patients with chronic hepatitis C (CHC) infection display a variety of extrahepatic manifestations (EHMs) due to the lymphotrophic nature of hepatitis C virus (HCV). HCV eradication by means of antivirals improves both liver and non-liver related outcomes. Emerging evidence have shown a reduced risk of end-stage liver disease (ESRD), diabetic complications, and lymphotrophic neoplasms in particular non-Hodgkin lymphoma after HCV eradication. As the glycemic control and quality of life (QoL) improves shortly after HCV eradication, discrepant reports existed in the long-term studies while subjects are fighting against the aging process. In the post-sustained virlogical response (SVR) era, extrahepatic malignancy may outweigh due to improvement of liver related outcomes, and non-liver related mortality overwhelms liver related mortality in non-cirrhotic patients in a multinational cohort. Taken collectively, it highlights the importance of multidisciplinary and holistic care of CHC patients in the post-SVR era. The most critical and unmet need for HCV elimination is the large gap in the HCV care cascade at the population level. To accomplish the World Health Organization’s goal for HCV elimination by 2030, the expansion of access to HCV care requires a continuous effort to overcome practical and political challenges.

專題討論（5）

Functional GI Disorders

Role of Food in the Pathogenesis of DGBI

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Disorders of gut–brain interaction (DGBI) affect millions of individuals worldwide. As DGBI are symptom-based diagnoses, their pathogenesis is diverse with abnormalities in motility, visceral sensation, brain-gut interactions, intestinal permeability, immune activation, bile acid metabolism, and the gut microbiome all potentially playing a role. Food can impact upon all of these potential pathophysiological factors through primary or secondary effects. Indeed, the majority of patients with irritable bowel syndrome (IBS) identify food as an important trigger for their gastrointestinal symptoms. Over the past 15–20 years, specific dietary interventions have increasingly become a cornerstone of the multidisciplinary care model for patients with IBS. In this lecture, we will discuss how food plays an important role in the pathogenesis of DGBI and how this knowledge has been leveraged to utilize “food as medicine” in patients with DGBI.

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專題討論（5）

Functional GI Disorders

Dietary Management of Disorders of Gut-Brain Interaction

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The recent decade has seen an increasing scientific approach to unravelling the role of diet in Disorders of Gut-Brain Interaction (DGBI) and the underlying mechanisms. A diet low in fermentable oligo- di- monosaccharides and polyols (FODMAPs) has shown efficacy in **irritable bowel syndrome** (IBS). The low FODMAP diet (LFD) consists of a strict **elimination phase** followed by a gradual reintroduction phase, to determine a long-term personalized diet. Food diaries confirmed a reduced intake of carbohydrates and fats during the LFD, and a positive correlation was found between the response rate and the change in total FODMAP intake. Non-responders to the low FODMAP diet had a significantly lower baseline total FODMAP intake compared to responders. The **reintroduction phase** is time-consuming and highly-subjective. We enrolled responders to a 6-week low-FODMAP diet in a 9-week blinded randomized reintroduction phase with 6 FODMAP powders. The blinded reintroduction revealed a personalized pattern of symptom recurrence, with fructans and mannitol as the most prevalent triggers. The low FODMAP diet is complex and requires repetitive guidance from an experienced dietitian, making it unsuitable for application in primary care IBS. We developed a new **FODMAP lowering self-management smartphone application**, and studied its efficacy in comparison to standard medical therapy in primary care IBS. Symptom improvement at 4, 8 and 16 weeks was superior with the app compared to standard medical therapy. Response to the diet was associated with genetic polymorphisms in eosinophil trafficking and with the change in stool levels of eosinophil derived neurotoxin, implicating a role for immune activation in dietary influences on IBS symptom generation. In patients with **functional disorders of the upper gastrointestinal tract**, dietary measures are classically prescribed as part of the management of patients with, although this has been poorly studied. We also evaluated the effect of a LFD and individual FODMAP-triggers in FD. **A low FODMAP diet** significantly improved FD symptoms, and powder reintroduction identified a large variety in individual FODMAPs and glucose as triggers. In line with a role for duodenal eosinophil activation in FD symptom generation, we demonstrated efficacy of a **six-food elimination diet**. Given the **immune activation component** of dietary factors in DGBI, we are currently exploring the efficacy of a diet based on **confocal laser endomicroscopy** evaluation of **atypical food allergies** in IBS and FD.

專題討論（5）

Functional GI Disorders

The Role of Expert GI Dietitians in Clinical Practice

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Expert GI dietitians can provide a comprehensive assessment and clinical approach to addressing nutritional status and malnutrition risks and mitigating GI symptoms through a shared-decision model. An individualized nutrition plan is fundamental. In disease states in which food intolerance and food-related fears can lead to unintended consequences, dietitian-led care is poised to help enhance food intake and variety and foster a positive relationship with food.

專題討論（5）
Functional GI Disorders

Food and Mental Health: Does What We Eat Affect Our Brain?

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The connection between food and mental health has garnered increasing attention in recent years, highlighting the significant impact diet can have on brain function and emotional well-being. This abstract explores the relationship between nutrition and mental health, investigating whether the foods we consume influence brain structure, function, and behavior. Research indicates that diets rich in nutrients such as omega-3 fatty acids, antioxidants, vitamins, and minerals can positively affect cognitive function and reduce the risk of mental health disorders like depression and anxiety. Conversely, poor dietary choices, including excessive consumption of processed foods, sugar, and unhealthy fats, may contribute to mental health challenges. The gut-brain axis, which links the digestive system and brain, plays a crucial role in this dynamic. This talk will introduce the impact of food on mental health briefly, focusing on depression.

專題討論（5）

Functional GI Disorders

Gut Microbiota-Based Management of DGBI

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Disorders of Gut-Brain Interaction (DGBI), including irritable bowel syndrome (IBS) and functional dyspepsia (FD), are prevalent conditions characterized by chronic gastrointestinal symptoms without identifiable structural abnormalities. Recent research underscores the pivotal role of the gut microbiome in the pathogenesis of DGBI, influencing gut motility, visceral sensitivity, and brain function through metabolic byproducts and neurotransmitter modulation. Modulating the gut microbiota has emerged as a potential therapeutic approach for DGBI. Emerging strategies such as antibiotics, fecal microbiota transplantation, probiotics, prebiotics, and dietary interventions are increasingly utilized in clinical practice. By understanding the complex interactions between the gut microbiome and the brain, future precision management may be developed to improve outcomes for DGBI patients and enhancing quality of life. This talk aims to provide a comprehensive overview of how gut microbiota-based strategies could transform the clinical management of DGBI, offering novel therapeutic avenues for patients.

專題討論（6）

Mastering the Management of IBD

Clinical Pearls for Difference Diagnosis of Inflammatory Bowel Diseases

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Inflammatory bowel disease (IBD) is characterized by repetitive episodes of inflammation of the gastrointestinal tract caused by an abnormal immune response to gut microflora. Ulcerative colitis (UC) and Crohn's disease (CD) are two major forms of IBD. UC involves diffuse inflammation of the colonic mucosa. CD results in transmural ulceration of any portion of the gastrointestinal tract, most often affecting the terminal ileum and colon.

The diagnosis of IBD is based on a combination of clinical, biochemical, stool, endoscopic, cross-sectional imaging, and histological investigations. Since there is no gold standard diagnostic test, there are many disease processes that can be misdiagnosed as IBD, given its often non-specific symptoms.

There is a broad differential diagnosis IBD, however most of the etiologies generally fall into two categories: infectious and non-infectious. Endoscopy is an important diagnostic and therapeutic modality in IBD. Endoscopy is used to make an initial diagnosis of IBD, distinguish CD from UC, assess the disease extent and activity and monitor response to therapy. Clinicians should be familiar with the typical endoscopic findings of IBD. In some cases, however, it is difficult to differentiate IBD due to an atypical presentation. Therefore, not only endoscopic features but also clinical symptoms, as well as laboratory, pathological, and radiological findings should be considered in order to make a correct diagnosis. By the way, a superinfection with cytomegalovirus or Clostridioides difficile can aggravate intestinal inflammation in IBD, especially in patients who are immunocompromised.

A single reference standard for the diagnosis of IBD does not exist. A careful history and physical examination may help to both narrow the differential diagnosis and order specific testing that will culminate in a diagnosis. Reviewing potential differential diagnoses should guide the search for the underlying cause.

專題討論（6）

Mastering the Management of IBD

Positioning Biologics and Small Molecules in the Treatment of Refractory Inflammatory Bowel Diseases

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Refractory inflammatory bowel disease (IBD) represents a significant challenge in the management of patients with Crohn's disease and ulcerative colitis who do not respond adequately to standard or advanced treatments. Refractory IBD is generally defined as 1) Failure of biologics and advanced small molecules with at least two different MoAs; 2) Postoperative recurrence of Crohn's disease after two or more (adult) or one (children) intestinal resections; 3) Chronic antibiotic-refractory pouchitis; 4) Complex perianal disease; 5) A patient's coexisting psychosocial issues that impair adequate clinical management. The current treatment strategies for refractory IBD focus on early diagnosis of IBD, optimizing existing therapies, utilizing advanced therapies earlier, combined advanced therapies, and exploring novel agents. The primary goals of treatment are to reduce symptoms, promote mucosal healing, transmural healing, histologic remission, and improve the overall quality of life for patients. This necessitates a personalized approach that takes into account the specific characteristics of the disease, patient preferences, and potential adverse effects of treatment options. Continued research into the underlying mechanisms of refractory IBD and the development of innovative therapies is essential for improving outcomes in this challenging patient population.

專題討論（6）

Mastering the Management of IBD

Management of Iron Deficiency and Anemia in Inflammatory Bowel Diseases

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Inflammatory bowel disease (IBD), encompassing conditions like ulcerative colitis and Crohn's disease, is characterized by chronic inflammation within the gastrointestinal tract. Anemia is a frequent complication, impacting up to two-thirds of individuals with active IBD. The underlying causes of anemia in IBD are diverse and may involve chronic inflammation, malabsorption, blood loss and drug-induced hematological toxicity. Effective management requires a multi-pronged approach which including treating the Underlying IBD, iron replacement, addressing nutritional deficiencies and blood transfusion.

In Summary, managing anemia in IBD involves a multifaceted approach. Treating the underlying inflammation, addressing nutritional deficiencies (particularly iron), and considering blood transfusions when necessary are key components of successful management.

專題討論（6）

Mastering the Management of IBD

Inflammatory Bowel Disease in Elderly Patients

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The prevalence of IBD among elderly individuals appears to be up to 15% after the age of 60 years. Persons older than 60 years are more likely to have other diagnosis that may mimic symptoms of IBD such as colorectal cancer, ischemic colitis, segmental colitis associated with diverticulosis, nonsteroidal anti-inflammatory drug-induced enteropathy, radiation enteritis or colitis. late-onset IBD patients tend to have atypical presentations and milder severity at initial diagnosis, which may result in a longer time to diagnose. Doctors should be more aggressive in making an earlier diagnosis in elderly adults.

Moreover, elderly adults have higher mortality and rates of surgery. Older patients with IBD have a greater burden of comorbidity than younger patients. Optimization of comorbidity is important to minimize the risks associated with IBD and its treatment and guide selection of the appropriate agent. Medications to control disease activity should be cautiously adjusted and sepsis risk avoided, thereby improving outcomes in individuals with late-onset IBD.

專題討論（7）

Recent Advances in Diagnosis and Management of Neuroendocrine Tumors (NET)

Application of Medical Treatments for NETs by Gastrointestinal Specialists

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Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms originating from neuroendocrine cells distributed throughout the body. NETs are considered rare, with an annual incidence of 1.51 per 100,000 individuals, according to a nationwide population-based study in Taiwan. However, the incidence has been rising in recent years. The most common primary sites of NETs are the gastrointestinal (GI) tract, followed by the lungs, bronchus, and pancreas. Given the high prevalence of GI involvement, gastroenterologists play a pivotal role in the diagnosis and management of these tumors.

The primary treatment strategy for NETs is resection, which may be performed with either curative or palliative intent. In cases of oligometastatic liver involvement, local ablative therapies can also be considered. For functional NETs that secrete bioactive hormones, somatostatin analogs (SSAs) are effective in symptom control. In patients with advanced or metastatic disease, treatment selection depends on various factors, including tumor origin, histopathological differentiation, grading, functional status, and somatostatin receptor (SSTR) expression. Therapeutic options include SSAs, targeted therapy, peptide receptor radionuclide therapy (PRRT), and chemotherapy.

In this discussion, I will provide an overview of the medical management of NETs from a gastroenterologist's perspective and highlight the most advanced treatment options currently available.

專題討論（7）

Recent Advances in Diagnosis and Management of Neuroendocrine Tumors (NET)

Peptide Receptor Radionuclide Therapy (PRRT) for Gastroenteropancreatic Neuroendocrine Tumors (GEP-NET): Key Insights for GI Specialists

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Low- to intermediate-grade, well-differentiated neuroendocrine tumors (NETs), particularly those originating from the gastrointestinal tract or pancreas, frequently express somatostatin receptors (SSTRs), primarily subtypes 2 and 5. The mainstay of initial treatment involves somatostatin analogs (SSAs) like octreotide LAR and lanreotide, which bind these receptors, helping to alleviate hormone-related symptoms and slow tumor growth. Radiolabeled SSAs have expanded the management toolbox by serving both diagnostic (e.g., ^{68}Ga-DOTATOC and ^{68}Ga-DOTATATE PET imaging) and therapeutic purposes (e.g., ^{177}Lu-DOTATATE). The NETTER-1 trial in 2017 demonstrated that ^{177}Lu-DOTATATE significantly improved progression-free survival for patients with advanced, well-differentiated gastroenteropancreatic NETs, leading to its approval in Europe, Canada, and the United States. Treatment choices should be tailored to the patient's specific tumor characteristics and overall clinical profile.

專題討論（7）

Recent Advances in Diagnosis and Management of Neuroendocrine Tumors (NET)

Techniques for Endoscopic Resection of Rectal Neuroendocrine Tumors

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Since the development of endoscopic technology, the main procedure for rectal neuroendocrine tumors (rNETs) are endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Traditional EMR technique is simple, but it seems difficult to guarantee complete resection for rNETs. Therefore, many device-assisted EMR technique have been derived and can be compared to ESD.

The main challenge of traditional EMR is the depth of vertical margin is not fully guaranteed, resulting a positive vertical margin. Therefore, device-assisted EMR method use device to fully attract the lesion and lift the lesion to ensure the depth of vertical margin.

Cap-assisted EMR (EMR-C) uses a transparent hood and a crescent snare to grasp and resect the lesion after submucosal fluid injection under the tumor. EMR with a ligation device (EMR-L) use transparent hood and rubber band to make a pseudopolyp after injection fluid under the tumor, then resect.

ESD is commonly used for lesion resection. It achieved radical treatment, even in lesion involving submucosa and retaining the muscle layer, preserving the local anatomy and function.

專題討論（7）

Recent Advances in Diagnosis and Management of Neuroendocrine Tumors (NET)

Managing Small Pancreatic Neuroendocrine Tumors: Radiofrequency Ablation or Ethanol Injection

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Pancreatic neuroendocrine tumors (PNETs) originated from Enterochromaffin cells located in neuroendocrine tissue. PNETs are classified as functional (10%–30%) and nonfunctional (70%–90%) NETS based on whether they have hormone symptoms or not. The percentage of PNETs is approximately 7% of pancreatic tumors. The annual incidence is approximately 3.2/1,000,000in Taiwan. Analysis of the surveillance, epidemiology, and end results database shows a rising incidence of PNETs, likely attributed to the increased identification of small-sized tumors (<2 cm) on cross-sectional imaging.

Although observation is now generally indicated for most patients with small (<2 cm), incidental, and nonfunctional PNETs, surgical resection is the treatment of choice for larger and functional PNETs. However, surgical therapy caried higher adverse events (AEs).

During the last decade, advances in EUS-guided ablations have enabled a possible alternative to surgical resection. The two most commonly described techniques are radiofrequency ablation (RFA) and ethanol injection (EI). Both techniques have been reported to have variable outcomes in recent small case series or retrospective or prospective studies. However, there is still no data that was comparing the clinical/technical success and safety between these two methods.

According to recent systematic review and meta-analysis which evaluate the success rate and safety of EUS-RFA and EUS-EI in the treatment of PNETs. The data showed the location of PNETs in head/neck of pancreas (P = 0.03) was a positive predictor of clinical success for EUS-RFA. EUS-RFA and EUS-EI have similar effectiveness and safety for pNETs ablation. Head/neck location of pNETs was a positive predictor for clinical success after EUS-RFA. Outcomes of EUS-RFA ablation for PNETs are like EUS-EI. There was still need further study to compare the clinical effectiveness and safety to compare these two EUS-guided local ablations.

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專題討論（8）

Surveillance after Polypectomy: Is Your Practice Evidence-Based?

Optimizing Surveillance Colonoscopy Practices: Understanding the Importance of Surveillance

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Colorectal cancer (CRC) remains a leading cause of morbidity and mortality worldwide, making effective surveillance strategies critical for early detection and prevention. Surveillance colonoscopy plays a pivotal role in identifying precancerous lesions, preventing disease progression, and improving patient outcomes. However, optimizing surveillance practices requires a delicate balance between timely follow-ups, risk stratification, and healthcare resource utilization.

This talk will explore the principles of surveillance colonoscopy, including current guidelines, risk-based intervals, and the latest advancements in predictive tools. We will discuss the impact of overuse and underuse of surveillance, emphasizing the importance of evidence-based decision-making to enhance patient safety and healthcare efficiency.

By the end of this session, attendees will gain a deeper understanding of the significance of surveillance colonoscopy, practical insights for optimizing follow-up schedules, and strategies to improve patient compliance and outcomes.

專題討論（8）

Surveillance after Polypectomy: Is Your Practice Evidence-Based?

International Recommendations on Surveillance Intervals after Polypectomy: A Review of Major Guidelines and Emerging Trends

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Post-polypectomy surveillance guidelines continue to evolve toward more risk-stratified approaches that balance cancer prevention benefits against resource utilization and potential procedural harms. Recent updates to major international guidelines have generally resulted in less intensive surveillance recommendations, with more patients being returned to routine screening rather than entered surveillance programs.

Significant differences remain between guidelines from different regions, particularly regarding patients with lower-risk findings such as small adenomas or those with specific histological features. Further research is needed to address areas of uncertainty, particularly regarding the optimal management of serrated polyps and the long-term surveillance needs after initial follow-up examinations.

The identification of socioeconomic and comorbidity factors affecting surveillance adherence highlights the need for more nuanced, personalized approaches to post-polypectomy follow-up. Future surveillance strategies must move beyond purely polyp-based risk stratification to incorporate patient factors that influence both adherence and outcomes. By addressing these complexities, the gastroenterology community can continue to refine post-polypectomy surveillance approaches to maximize colorectal cancer prevention while minimizing unnecessary procedures and healthcare disparities.

專題討論（8）

Surveillance after Polypectomy: Is Your Practice Evidence-Based?

When Should We Stop Surveillance Colonoscopy? Addressing the Needs of an Aging Population

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Determining the appropriate time to discontinue surveillance colonoscopy in older adults is a complex decision that balances the benefits of early detection against the risks of the procedure and the limited life expectancy associated with advancing age. Current guidelines from major gastroenterology societies recommend individualized assessments, particularly in the 75 to 85 age range, considering the presence of comorbidities, prior polyp burden, family history of colorectal cancer, and overall functional status. For individuals with significant comorbidities or an expected life expectancy of less than 10 years, the potential harms of colonoscopy, such as procedural complications and post-procedure recovery challenges, may outweigh the benefits. Conversely, in healthier older adults with a strong history of adenomatous polyps, continued surveillance may be justified if the probability of detecting clinically significant lesions remains high. Shared decision-making plays a crucial role in this process, ensuring that patient values and preferences are integrated with clinical judgment and evidence-based guidelines. Additionally, emerging risk stratification tools and non-invasive screening modalities, including stool-based tests and emerging biomarkers, may reduce the need for routine colonoscopies in select older adults. Ultimately, the decision to discontinue surveillance colonoscopy in the aging population should be guided by a comprehensive, patient-centered evaluation that thoughtfully weighs individual risk factors, procedural risks, and anticipated life expectancy. Ongoing research aims to refine these approaches by accounting for frailty, cognitive function, and quality of life.

專題討論（8）

Surveillance after Polypectomy: Is Your Practice Evidence-Based?

Surveillance for Populations at Risk of Hereditary Colorectal Cancer

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Hereditary colorectal cancer (HCRC), particularly Lynch syndrome (LS), is a significant challenge in gastroenterology. LS provides a vital model for understanding the carcinogenesis of colorectal cancer (CRC). This presentation examines the molecular mechanisms, surveillance strategies, and clinical challenges of LS, emphasizing the crucial role of gastroenterologists in early detection and prevention.

We will explore how mutations in mismatch repair (MMR) genes contribute to carcinogenesis in LS, providing an overview of the Knudson two-hit hypothesis and the impact of epimutations on tumor development. The intersection of epidemiology and prevention will also be discussed, focusing on how understanding the variants of MMR genes enhances risk assessment and informs surveillance strategies.

Although colonoscopy surveillance offers clear benefits, several challenges persist, including uncertainty about its long-term effectiveness, the procedural burden on patients and endoscopists, and the lack of standardized quality indicators for colorectal surveillance in LS.

In Taiwan, expanding CRC screening programs and utilizing cancer registry databases present new opportunities for enhancing LS detection and management. Incorporating genetic testing, refining risk stratification, and adherence to surveillance guidelines could significantly improve early diagnosis and cancer prevention.

In conclusion, evidence-based surveillance, strict adherence to clinical guidelines, and personalized screening/surveillance strategies are essential for effective management. Future research should focus on refining risk-based approaches and addressing barriers to optimal surveillance, ultimately improving patient outcomes and reducing the burden of HCRC.

專題討論（9）

Hepatocellular Carcinoma

Comparing Treatment Strategies for Liver Cancer: Surgery, Radiofrequency Ablation, and Microwave Ablation

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Hepatocellular carcinoma (HCC) arises in the setting of cirrhosis in most cases, requiring multidisciplinary input to define resectability. In this regard, more precise surgical management considers patient factors and anatomical states, including resection margins, tumor biology, and perioperative therapy. Together with advances in surgical techniques, this integrated approach has resulted in considerable improvements in patient morbidity and oncological outcomes. Despite this, recurrence rates in hepatocellular carcinoma remain high. As the systemic treatment landscape in HCC continues to evolve and locoregional options are increasingly used. Locoregional therapies play a fundamental role in the treatment of patients with early and intermediate and locally advanced hepatocellular carcinomas. Radiofrequency ablation (RFA) has been accepted as the most effective local ablation for small HCC ≤3.0 cm by several HCC guidelines because the technique is minimally invasive, fewer sessions and easily repeatable. The complete response rates for HCCs ≤3.0 cm in size exceeds 90%. However, in prior studies, the complete response rate was reduced to 45%–70% for medium-sized HCCs (3.1–5.0 cm), and it was only 23%–45% for large HCCs (>5.0 cm) by single RF electrode. The strategy to maximize outcomes of RFA is to increase ablation size and target tumor precisely (ex., real-time fusion imaging, contrast-enhanced ultrasonography, artificial ascites…). The methods of local ablation to get adequate safety margin for large HCCs (>5.0 cm) include overlapping method, combined with ethanol, combined with chemoembolization, multiple-electrode mono-polar RF or bipolar RF with switch-controller, RITA RF generator with expandable electrodes and new generation microwave ablation (MWA). An increase in the number of sequential overlapping ablations usually results in an irregular shape of coagulation. Incomplete ablation may occur with irregular ablated zones and it is a common reason for treatment failure. A deployed RF electrode can provide a 5- to 7-cm-diameter ablation zone with a single electrode placement, but the shape of the ablation zone is not circular, and the device's multiple tines have the potential to puncture adjacent vital structures. Recently, MWA is designed to achieve larger areas of necrosis compared to RFA and has a good safety profile among liver cancer treatments. However, conventional MWA systems still have major limitations such as unpredictability of the ablation zone size and the elliptical shape of necrosis. New generation MWA can provide predictable ablation results and outcomes regardless of the target location or tissue type. The 2022 BCLC strategy incorporates an expert clinical decision-making component. It highlights the different concepts and parameters that physicians and multidisciplinary tumor boards should integrate into a personalised HCC treatment approach.

專題討論（9）

Hepatocellular Carcinoma

The Role and Future Development of Immunotherapy in Liver Cancer Treatment

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The systemic treatment of hepatocellular carcinoma (HCC) has incorporated immunotherapy for nearly 10 years. Inhibitors of immune checkpoints, such as PD-L1 and CTLA-4, are now standard treatment options. For patients eligible for immunotherapy, dual immune checkpoint inhibitors (ICIs) and targeted therapy combined with ICIs are recommended as first-line treatments. Additionally, inhibitors of other immune checkpoints, bispecific antibodies, T-cell engagers, and CAR-T therapy are currently being actively researched.

專題討論（9）

Hepatocellular Carcinoma

Optimal Treatment Selection for Intermediate Stage HCC

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Managing intermediate-stage hepatocellular carcinoma (HCC) remains challenging, often requiring a multidisciplinary approach. While transarterial chemoembolization (TACE) is the standard treatment, its long-term efficacy is limited for many patients. Recent advances in immunotherapy have demonstrated promising results, particularly in advanced HCC, raising the question of whether it could redefine treatment for intermediate-stage disease. This presentation will explore the evolving role of multidisciplinary management, especially immunotherapy in intermediate-stage HCC, reviewing its biological rationale, target populations, and emerging clinical trial data on TACE-immunotherapy combinations. We will also address key challenges in integration, including patient selection (TACE-suitable vs. TACE-unsuitable), optimal treatment sequencing, and combination strategies.

專題討論（9）

Hepatocellular Carcinoma

Impact on Liver Reserve by Current HCC Treatment

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Liver function preservation is widely recognized as a key prognostic factor in the treatment of hepatocellular carcinoma (HCC). Current clinical practice guidelines for HCC treatment across various stages emphasize the importance of liver function preservation. Before undergoing curative treatments such as local tumor ablation or liver resection, liver function must be thoroughly evaluated to avoid liver decompensation, which could lead to patient mortality. For patients with curative tumors but compromised liver function, liver transplantation should be considered. For patients with unresectable HCC, palliative treatments such as transarterial chemoembolization, transarterial radioembolization, immune checkpoint inhibitors, or targeted therapy may be recommended. However, because these tumors are typically incurable or prone to frequent recurrence, patients often require repeated treatments. Unfortunately, repeated HCC treatments may result in liver function impairment, decompensation, or even liver failure. Conversely, impaired liver function can delay or halt HCC treatments, potentially leading to disease progression. Thus, balancing HCC treatment strategies with liver function preservation is crucial. Although multiple treatments can be applied simultaneously to manage a large tumor burden, the current approach emphasizes selecting therapies that are both effective and relatively liver-sparing. In this talk, we will review the impact of current HCC treatments on liver reserve, and comprehensively discuss the critical importance of liver function evaluation before selecting HCC treatments and the ongoing monitoring of liver function during treatment to optimize outcomes in HCC management.

專題討論（10）

New Frontiers in Gut Microbiota Research

New Frontiers in Gut Microbiota Research of Gastrointestinal Diseases

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Gut microbiota contribute to the breakdown and assimilation of nutrients, absorption of essential compounds, syntheses of vital biological molecules such as vitamins, provision of necessary energy and nutrients for the body, preservation of intestinal barrier integrity, protection against pathogens, support for immune system development, and regulation of immune responses. Despite the advancements in microbiota research, there are still limitations to current microbiota studies. Firstly, majority of existing investigations were based on observational studies, which may have confounding factors and lack causality. On the other hand, randomized control trials pose challenges in terms of costs, time constraints, and ethical considerations. Secondly, the precise mechanisms through which probiotics regulate immune responses remain unknown.

Mendelian Randomization analysis is a tool that exploits genetic variants as instrumental variables to probe the causal relationship between an exposure and an outcome. Since genetic variations are randomly allocated during conception, MR studies are less prone to common confounding factors and reverse causality issues. The MiBioGen consortium has released a substantial number of microbiome abundance-associated loci, presenting an opportunity to delve into the causality between the gut microbiota and diseases.

Inflammasome signaling is a fundamental aspect of innate immunity and plays a crucial role in maintaining gastrointestinal homeostasis and disease regulation. The antimicrobial role of the inflammasome is primarily attributed to IL-1β, IL-18, and pyroptosis. Uncontrolled inflammasome activity sustains chronic inflammation, which is the pathophysiological basis of gastrointestinal diseases such as inflammation, cancer, and non-alcoholic fatty liver disease. It is evident that the development of intestinal inflammation and cancer is closely tied to impaired inflammasome signaling and/or dysbiosis. Despite the evidence indicating that the inflammasome plays a role in regulating the composition of the gut microbiota, further research is still required. The complex interplay between inflammasomes, pathogens, and the microbiota offers a platform for basic and clinical research, enabling a deeper understanding of health and disease.

專題討論（10）

New Frontiers in Gut Microbiota Research

New Frontiers in Gut Microbiota Research of Liver Diseases

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Gut microbiota plays a crucial role in the development and progression of various liver diseases through the gut-liver axis, such as fatty liver disease, alcoholic liver disease, liver cirrhosis, and liver cancer, etc. Understanding the role of gut microbiota in the development and progression of liver diseases can provide deeper insights into the pathogenesis and treatment strategies for many liver diseases.

This lecture will review the latest concepts and important research findings on the gut microbiota in the development and progression of liver diseases in recent years. It will focus on key discoveries from animal studies and clinical research, as well as discuss relevant clinical applications. This lecture is suitable for scholars interested in gut microbiota and liver disease research, as well as clinicians interested in the potential future applications of microbiota in liver diseases.

專題討論（10）

New Frontiers in Gut Microbiota Research

New Frontiers in Gut Microbiota Research of Metabolic Diseases

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In recent years, the gut microbiota has emerged as a critical factor influencing the onset and progression of cardiometabolic diseases, including obesity, type 2 diabetes, MASLD, and cardiovascular disease. Advanced metagenomic and multi-omics technologies have revealed how genetics, lifestyle, and gut microbial composition interact to shape metabolic disease risk. Emerging evidence indicates that distinct microbial signatures can identify at-risk individuals and guide targeted, personalized interventions. Fecal microbiota transplantation (FMT) is a promising strategy for remodeling the gut microbiome by transferring beneficial microbes from healthy donors to patients. Clinical and experimental studies suggest that FMT can restore disrupted microbial ecosystems, improve metabolic markers (such as insulin sensitivity), and reduce systemic inflammation. However, the lack of standardized quality control in the chemistry, manufacturing, and controls (CMC) process remains a challenge to developing FMT as a biotherapeutic. Next-Generation Probiotics (NGPs) leverage next-generation sequencing and culturomics to discover and isolate bacterial strains with specialized functions. These innovative probiotics may be more effective than traditional formulations in enhancing host metabolism and combating metabolic disorders. Still, the effectiveness of FMT and NGPs varies among individuals, underlining the need for more personalized strategies. This presentation will examine how gut microbiota analysis enables disease prediction and stratification, emphasizing the importance of personalized microbial interventions in metabolic diseases. We will also explore the mechanistic foundations and practical considerations of both FMT and NGPs, addressing challenges and opportunities for their successful translation into clinical practice.

專題討論（10）

New Frontiers in Gut Microbiota Research

New Frontiers in Gut Microbiota Research of Psychiatric Diseases

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Previous studies have investigated the gut microbiota-gut-brain axis and its role in neurodevelopmental psychiatric disorders, including autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). The bidirectional communication between gut microbiota and the brain involves immune mechanisms, the vagus nerve, and microbial neurometabolite production.

Our study involved a large cohort of unaffected siblings (SIB) and compared gut microbial diversity and taxonomy among individuals with autism spectrum disorder (ASD), SIB, and typically developing controls (TDC). The results consistently revealed differences in gut microbial diversity and composition between those with ASD and TDC. Key findings indicated associations between gut microbiome composition and clinical phenotypes of autism, showing significant correlations between altered taxonomic diversity in ASD and autistic symptoms, thought problems, delinquent behaviors, self-dysregulation, and somatic complaints. SIB displayed higher alpha diversity than TDC, suggesting a more stable and diverse gut microbiome. Additionally, we observed an increased abundance of Prevotellaceae and Lachnospiraceae at the family level in SIB, with *Anaerostipes* showing a higher relative abundance linked to less severe autistic symptoms and fewer emotional/behavioral issues, indicating a potential protective role.

Machine learning methods, including SHAP analysis and general linear models, were utilized to identify potential diagnostic biomarkers for ASD based on gut microbiota composition. Specific bacterial strains, such as *Ruthenibacterium lactatiformans*, *Phascolarctobacterium faecium*, and *Gemmiger formicilis*, showed SHAP values significantly skewed toward the ASD group, indicating their potential as diagnostic markers. Conversely, *Bifidobacterium adolescentis* and *Bifidobacterium bifidum* displayed SHAP values favoring the control group, suggesting their potential as therapeutic targets.

In exploring the gut-brain axis in ASD, specific microbial taxa were linked to structural alterations in the cingulate cortex, a brain region implicated in ASD. Increased abundances of *Enterococcaceae* and *Enterococcus* in ASD were associated with decreased cortical thickness in specific cingulate regions and increased surface area in the isthmus cingulate. These microbial markers also positively correlated with autistic symptom severity. Conversely, a reduced abundance of *Dialister* was negatively correlated with cingulate cortex thickness. These findings underscore the potential of gut microbiota as biomarkers and therapeutic targets for ASD.

Additionally, we examined gut microbiota in ADHD. Results indicated an altered gut microbiota composition in children with ADHD, with a significant correlation between the relative abundance of *Cutibacterium acnes* and inattention, executive dysfunction, and hyperactivity/impulsivity.

In conclusion, our findings underscore the vital role of gut microbiota in neurodevelopmental disorders. The identified microbial signatures, their links to clinical symptoms, and neuroanatomical

correlations deepen our understanding of ASD pathophysiology. The unique microbial patterns found in individuals with ASD, along with the potentially protective bacterial taxa in unaffected siblings, indicate both risk and resilience factors. These discoveries pave the way for microbiome-based diagnostic biomarkers and targeted therapeutic interventions, emphasizing the gut-brain axis as a critical consideration in addressing neurodevelopmental issues.

專題討論（11）

Precision Treatment and Prevention of Gastrointestinal Cancers

Optimizing Diagnosis and Treatment for Esophageal Squamous Cell Carcinoma

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Esophageal cancer remains one of the leading causes of cancer-related mortality worldwide, with a particularly high burden in East Asia. Esophageal squamous cell carcinoma (ESCC) accounts for approximately 85% of cases globally, while adenocarcinoma prevalent in Western countries. The aggressive nature and late-stage diagnosis of ESCC make it one of the most challenging malignancies to manage. This speech will focus on the importance of precise diagnostic staging and optimized treatment strategies for advanced ESCC to improve survival and quality of life.

Accurate staging is critical for treatment planning, with CT scans, endoscopic ultrasound (EUS), and fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT playing key roles. CT scans assess tumor size, local invasion, and distant metastasis, while EUS provides detailed evaluation of tumor depth and lymph node involvement. FDG-PET/CT, which integrates functional and structural imaging, is particularly valuable for detecting metastatic disease, assessing treatment response, and monitoring tumor activity with greater sensitivity. Bronchoscopy is crucial for confirming airway invasion and should be performed in in patients with suspected involvement. Nutritional assessment and supplementation should be integrated into the diagnostic workup to optimize treatment tolerance and reduce the risk of severe adverse events.

For locally advanced ESCC, neoadjuvant chemoradiotherapy (CRT) followed by surgery remains the standard of care, offering the best chance for long-term survival. Recent evidence suggests that triplet chemotherapy with cisplatin, 5-fluorouracil, and docetaxel could be an alternative neoadjuvant option. Adjuvant nivolumab significantly improve disease-free survival in patients who do not achieve a pathological complete response after surgery. In patients who are unfit for surgery or have cervical esophageal involvement, definitive CRT serves as an effective alternative.

For metastatic ESCC, recent advances in immunotherapy have reshaped first-line treatment recommendations. The combination of immune checkpoint inhibitors (ICIs) with chemotherapy has demonstrated superior survival outcomes compared to chemotherapy alone, particularly in tumors with high PD-L1 expression.

Preventing severe treatment-related complications, such as aorto-esophageal and broncho-esophageal fistulas, is crucial for reducing morbidity and mortality. Identifying high-risk patients, optimizing radiation planning, implementing preventive aortic or airway stents, and ensuring close clinical monitoring are essential strategies for mitigating these risks.

By refining staging accuracy, tailoring treatment approaches, proactively managing complications within a multidisciplinary framework, we can continue to improve outcomes for patients with advanced ESCC.

專題討論（11）

Precision Treatment and Prevention of Gastrointestinal Cancers

Gastric Cancer Prevention: The Past and Future in Taiwan

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The Taiwan Gastric Cancer Prevention Program has pioneered mass screening initiatives, including the world's first community-based *Helicobacter pylori* screen-and-treat program in the Matsu Islands, dual cancer screening using fecal samples, and a family-based approach in Indigenous communities. Since its launch in 2004, the Matsu program has completed eight screening rounds, reducing *H. pylori* prevalence from 64.2% to 10%. By 2021, gastric cancer incidence had decreased by 56%, with a 36% reduction in mortality. Projections for 2030 estimate further reductions of 69% and 57%, respectively, effectively eliminating gastric cancer as a major health threat in this population. The success of this program has led to its expansion into broader healthcare systems, incorporating systematic process and outcome evaluations. In 2014, a pragmatic randomized trial was launched to integrate *H. pylori* eradication for gastric cancer prevention with colorectal cancer screening. This study, the first screening trial of *H. pylori* in an average-risk population, demonstrated a 21% adjusted reduction in gastric cancer incidence and improved screening participation rates. Recognizing the disproportionate burden of gastric cancer among Indigenous populations, the Taiwan Gastric Cancer Prevention Program initiated the first-ever *H. pylori* screening and eradication program for Indigenous communities in 2018, addressing health disparities through tailored interventions. The development of a real-time data monitoring system has ensured program quality, effectiveness, and equity. Additionally, policy efforts have led to the expansion of *H. pylori* treatment indications, securing national health insurance coverage in 2024. As a model for public health interventions, Taiwan has played a key role in shaping international guidelines.

專題討論（11）

Precision Treatment and Prevention of Gastrointestinal Cancers

Optimizing Diagnosis and Treatment for Gastric Cancer: The Role of Targeted Therapies

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Kaohsiung Medical University Hospital,
Kaohsiung, Taiwan**

This presentation provides a comprehensive overview of the latest advancements in the treatment of gastric and gastroesophageal junction (G/GEJ) adenocarcinoma. The NCCN guidelines recommend performing adequate biopsies using larger forceps to ensure sufficient tissue for accurate diagnosis and treatment planning. Siewert classification is should be described in endoscopy report for GEJ adenocarcinoma.

For resectable gastric cancer, recent trials have introduced immune checkpoint inhibitors (ICIs) or HER2-targeted antibodies to perioperative chemotherapy. Preliminary data indicate a higher pathological complete remission rate with these additions.

The integration of ICIs with chemotherapy has established a new standard of care for metastatic G/GEJ cancer, offering significant benefits, particularly for patients with MSI-high tumors or positive PD-L1 expression. Numerous clinical trials have demonstrated the ability of ICIs to improve survival outcomes in advanced G/GEJ adenocarcinoma, with varying degrees of success. For instance, the KN811 trial confirmed the efficacy of pembrolizumab in combination with trastuzumab and chemotherapy for HER2-positive gastric cancer. Additionally, trastuzumab deruxtecan (T-DXd) has emerged as an effective rescue treatment upon disease progression for HER-2 positive gastric cancer.

Furthermore, the overexpression of FGFR2b (30% prevalence) and CLDN18.2 (35% prevalence) has been successfully targeted by the therapies bemarituzumab and zolbetuximab, respectively. These advancements underscore the ongoing shift toward more personalized treatment strategies.

專題討論（11）

Precision Treatment and Prevention of Gastrointestinal Cancers

Optimizing Diagnosis and Treatment for Pancreatobiliary Cancers

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Pancreaticobiliary (PB) cancers share many common features about morphology, immunohistochemical profile and molecular drivers. The asymptomatic nature of the early stages often leads to delayed detection, resulting in grave prognosis. Existing diagnostic and treatment strategies are relatively limited. However, recent advances in molecular biology and immunology have broadened the improvement pathways.

Imaging studies including ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), endoscopic ultrasound (EUS), and endoscopic retrograde cholangiopancreatography (ERCP) are widely used along with tissue acquisition for the diagnosis of PB cancers. Tumor markers including carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) are used but with limited applications. Liquid biopsy with blood or body fluid samples is less invasive and easier to collect samples than traditional biopsy. Various novel analytical methods for circulating tumor cells, cell-free nucleic acids, secreted proteins and cytokines have been developed, so earlier and more accurate diagnosis of PB cancers may become possible in the near future.

Surgical procedure is appropriate for resectable PB cancers without distal metastases, but only a small percentage of patients are potentially resectable at presentation. Systemic chemotherapy of different combination has long been the mainstay treatment for both pancreatic ductal adenocarcinoma (PDAC) and biliary tract cancers (BTCs), but the treatment efficacy is poor. Targeted and immunotherapy strategies may have the potential to improve the current treatment landscape. For example, DNA damage repair (DDR) genes may serve as targets for treatment of both PDAC and BTCs. There are some promising targets such as isocitrate dehydrogenase 1 (IDH1) and fibroblast growth factor receptor (FGFR) in BTCs. In addition, modulation of cells involving the immune microenvironment such as adoptive cell therapy and cancer vaccines may offer another treatment option for the formidable PB cancers.

In summary, incorporation of various molecular profiling techniques may identify actionable genetic alterations in PB cancers. Combination with novel immunotherapy may further facilitate treatment strategies to enhance PB cancer patient outcomes.

專題討論（12）

Advances in the Management of Cirrhosis Complication

Treatment of Portal Hypertension in Patients with HCC

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Portal hypertension (PHT) is a critical factor influencing the prognosis and management of hepatocellular carcinoma (HCC). This presentation explores the interplay between PHT and HCC, emphasizing the impact of clinically significant portal hypertension (CSPH) on disease progression, treatment outcomes, and patient survival. CSPH is associated with an increased risk of liver decompensation, variceal bleeding, and tumor progression, necessitating precise assessment and targeted therapeutic strategies. While hepatic venous pressure gradient (HVPG) measurement remains the gold standard, noninvasive methods are emerging as viable alternatives for CSPH evaluation.

Primary prophylaxis with nonselective beta-blockers (NSBBs), particularly carvedilol, is recommended to prevent variceal hemorrhage and liver decompensation in cirrhotic patients, including those with HCC. Endoscopic variceal ligation (EVL) has shown superiority over propranolol in preventing initial variceal bleeding in patients with medium-to-large esophageal varices, particularly in early-stage HCC. The presence of PHT significantly influences treatment selection, as surgical resection, transarterial therapies, and systemic treatments can modify liver hemodynamics and exacerbate PHT-related complications. Moreover, systemic therapies, including tyrosine kinase inhibitors and immune checkpoint inhibitors, necessitate careful risk-benefit assessment due to potential bleeding risks, particularly when combined with anti-angiogenic agents like bevacizumab. Emerging evidence suggests that transjugular intrahepatic portosystemic shunt (TIPS) may be feasible in select HCC patients despite prior concerns regarding tumor spread and liver dysfunction.

In this presentation, I will provide insights into optimizing the management of PHT in HCC, focusing on refining screening strategies, enhancing risk stratification, and incorporating novel therapeutic approaches to improve patient outcomes.

專題討論（12）

Advances in the Management of Cirrhosis Complication

Gut Microbiome Based Therapy in Liver Cirrhosis

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Liver cirrhosis is a severe condition characterized by chronic liver damage, often associated with gut microbiota dysbiosis. The gut-liver axis plays a crucial role in disease progression, as disruptions in the gut barrier can lead to increased bacterial translocation and systemic inflammation. Gut microbial therapy, particularly fecal microbiota transplantation (FMT), has emerged as a promising approach to restore microbial balance and improve liver function. By modulating the gut microbiota, FMT helps strengthen the gut barrier and alleviate cirrhotic complications. Recent studies suggest that targeting the gut-liver axis through microbiota-based interventions may offer novel therapeutic strategies for managing liver cirrhosis. In this talk, I will introduce some important studies and some preliminary data from our lab.

專題討論（12）

Advances in the Management of Cirrhosis Complication

Cirrhosis Associated with MAFLD

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Along with universe increase of metabolic dysfunction associated steatotic liver disease (MASLD), the prevalence of metabolic dysfunction associated steatohepatitis (MASH) and consequent cirrhosis would definitely raise. The prevalence of advanced fibrosis or cirrhosis in Asian with non-alcoholic fatty liver disease (NAFLD) was reported to be 4% by a meta-analysis published in 2022. The strongest risk factors predicting fibrosis progression in patients with MASLD are presence of steatohepatitis, type 2 DM and obesity, Patients with MASH-associated cirrhosis are vulnerable to not only hepatic decomepnsation evens and HCC, but also cardiometabolic diseases and extrahepatic malignancy. Ninety percents of cirrhotics could be diagnosed by either vibration-controlled transient elastography, shear-wave elastography, or MR elastography. Liver biopsy, however, could not be abandoned because it provides histological assessment of steatosis and necroinflammatory activity, as well as documentation of alternative cause of liver disease. In the instance biopsy was performed, there would be a diagnostic dilemma while burned-out cirrhosis presents. As for management of MASH associated cirrhosis, lifestyle modification is mandatory and should be adapted to severity of liver disease and nutrition status. Bariatric surgery reduces NASH and fibrosis status, but it's safety and efficacy in MASH cirrhotics requires well-designed studies to establish. Similarly, the safety and efficacy of medicine already proved to diminish steatosis and resolve steatohepatitis in noncirrhotic MASH patients, have not been documented in MASH cirrhotics. Well-designed studies to assess resemetirom, GLP-1 analogs, pioglitazone, and other MASH pipeline drugs in MASH cirrhotic patients are in eagerly demand.

專題討論（13）

Artificial Intelligence in Digestive Diseases

Emerging AI Trends in Abdominal Image Analysis

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Artificial intelligence is transforming abdominal image analysis, improving efficiency, accuracy, and adaptability in clinical workflows. This talk explores key AI advancements driving data interpretation, decision support, and automation in medical imaging. We also examine how AI creates new opportunities, presents challenges, and redefines the role of medical imaging in clinical decision-making and patient care.

專題討論（13）

Artificial Intelligence in Digestive Diseases

Artificial Intelligence in Precision Medicine in Hepatology

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The emergence of artificial intelligence (AI) in clinical medicine has shown incredible potential across a wide range of healthcare fields. With the vast amount of health-related data available, AI technology can analyze this data to provide solutions for disease prediction, diagnosis, prognosis, and management. Liver disease is a prime example of a field where AI can be applied to both research and clinical practice.

The liver serves as a central hub, connecting to other vital organs in the body, making it a complex area to investigate. In routine hepatology practice, multiple sources of clinical data are generated, including electronic medical records (EMRs), laboratory tests, imaging studies (such as abdominal ultrasonography, CT scans, and MRI scans), and liver pathology, all of which may be structured or unstructured. Blood and tissue samples are also valuable for multi-omics analysis, including next-generation sequencing and other advanced tools, enabling investigations down to the single-cell or molecular level and providing unprecedentedly detailed information. AI can be leveraged to analyze this multi-modal data, facilitating the management of liver diseases and driving a paradigm shift toward precision medicine in hepatology.

In this presentation, I will provide several examples demonstrating how AI can be integrated into precision medicine practice in hepatology, particularly through the use of EMRs, radiological imaging, and pathological images.

In summary, the potential of AI in clinical medicine is vast, and liver disease serves as a prime example of its application in analyzing multi-modal data to enhance disease management and improve patient outcomes.

專題討論（13）

Artificial Intelligence in Digestive Diseases

Artificial Intelligence System for Diagnosis of GERD and Barrett's Esophagus

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- **The definition of AI system:**

AI refers to the simulation of human intelligence processes by machines, especially computer systems. These processes include learning (the acquisition of information and rules for using it), reasoning (the use of rules to reach approximate or definite conclusions), and self-correction.

There are different levels of AI training system, such as

1. Machine Learning

researchers use their knowledge to identify relevant features in an existing database, which they then use to train a model

2. Deep Learning

autonomously extracts distinctive attributes of input data using artificial neural networks (ANN)

3. Convolutional neural network (CNN)

unsupervised feature extraction algorithm that use unlabeled data includes convolutional layers

- **The current AI studies of GERD aim several aspects like**

1. AI for GERD management (including medical or surgical decision making)
2. AI in impedance-pH studies interpretation
3. AI to assess the severity of gastroesophageal reflux disease
4. AI prediction of future GERD possibility (Ex: GERD after Sleeve gastrectomy)
5. Laryngo-pharyngeal symptoms or cough related to GERD
6. Neonatal problems of GERD

- **AI in Barrett's esophagus**

The current AI studies of Barrett's esophagus focus on Barrett's esophagus mucosa detection (our expertise area) as Computer-Assisted Detection (CADe) and detection of neoplasia in Barrett's esophagus.

專題討論（13）

Artificial Intelligence in Digestive Diseases

AI-Assisted Colonoscopy and Colorectal Cancer Screening: Where Are We Going?

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Colorectal cancer (CRC) remains a significant global health concern, underscoring the need for effective screening strategies to reduce both incidence and mortality rates. Colonoscopy is considered the gold standard for detecting and removing colorectal neoplastic precursors; however, variations in endoscopist expertise and technique can result in missed lesions and suboptimal patient outcomes. Factors such as inadequate bowel preparation, incomplete examinations, and operator-dependent variability contribute to disparities in screening efficacy.

The integration of artificial intelligence (AI) into endoscopic procedures offers a promising solution to enhance the accuracy, efficiency, and overall quality of CRC screening. AI-driven applications, particularly computer-aided detection (CADe) and computer-aided characterization (CADx), have demonstrated significant potential in improving adenoma detection rates and the precision of optical diagnosis. CADe systems assist in real-time polyp detection, reducing the risk of overlooked lesions, while CADx aids in differentiating between benign and malignant lesions, potentially reducing unnecessary biopsies and improving clinical decision-making.

Beyond lesion detection and characterization, AI-assisted quality control systems play a crucial role in standardizing endoscopic procedures. These systems analyze procedural factors such as withdrawal time, completeness of mucosal inspection, and bowel preparation quality, ensuring more consistent and reliable examinations across different operators and clinical settings.

Despite these advancements, the clinical impact, cost-effectiveness, and long-term benefits of AI-assisted colonoscopy require further validation. Large-scale, multi-center trials are necessary to assess its real-world applicability, determine optimal integration strategies, and address challenges such as data privacy, regulatory approval, and clinician adoption. As AI technology continues to evolve, its role in improving CRC screening outcomes is expected to expand, potentially setting new standards in precision medicine and personalized patient care.

GEST-KSG Joint Symposium (YIA)

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DEEP LEARNING-BASED PREDICTION OF PEPTIC ULCER DISEASES CAUSED BY NSAIDS USING LONGITUDINAL ELECTRONIC HEALTH RECORDS

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Background & Aims: Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used to treat musculoskeletal disorders but are associated with peptic ulcer (PU). Predicting the risk of PUs in NSAID users is vital to minimize adverse effects. This study aims to develop and validate predictive models for NSAID-induced PUs using longitudinal electronic health record (EHR) data.
Methods: We utilized EHR data from Seoul National University Hospital (SNUH) and Seoul National University Bundang Hospital (SNUBH). The cohort included 423,278 patients from SNUH (2001–2022) and 314,548 patients from SNUBH (2004–2021), all of whom had been prescribed NSAIDs for at least seven days. We employed laboratory tests, medication history, and demographic information to train various machine learning and deep learning models, including random forests, gradient boosting machines (GBM), recurrent neural networks (RNN), long short-term memory networks (LSTM), gated recurrent units (GRU), and Transformers. Endoscopy reports were used to more accurately determine the incidence of PU. Model performance was evaluated utilizing the area under the receiver operating characteristic curve (AUROC) and the area under the precision-recall curve (AUPRC).
Results: The GRU model achieved the highest performance, with an AUROC of 0.941 for internal validation and 0.964 for external validation. Significant predictors included hemoglobin levels, duration of medication, and aspirin use. Risk score analysis indicated a sharp increase in risk two months before PU occurrence.
Conclusions: We developed and validated robust predictive models for NSAID-induced PUs using longitudinal EHR data. These models can assist in clinical decision-making for NSAID management and PU prevention. Further studies are necessary to refine these models and expand their application to diverse datasets.

Keywords: NSAIDs, Peptic ulcer, Deep Learning, Electronic Health Records, Prediction Model

②

A PRACTICAL APPLICATION OF LYON 2.0 AND LYON SCORE IN DIAGNOSING GERD: REVISITING THE ROLE OF DEMEESTER SCORE

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Lyon 2.0 國際共識和 Lyon 評分系統在診斷胃食道逆流症的實際應用：重新探討 DeMeester 評分系統的角色

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Background: Lyon Consensus 2.0 metrics for modern GERD diagnosis have been integrated into the novel Lyon score for the characterization of esophageal syndromes into meaningful phenotypes. The DeMeester score aids in identifying GERD that may benefit from antireflux surgery.
Aims: This study aimed to explore whether the DeMeester score has utility in the appraisal of GERD characterized by Lyon consensus 2.0 and Lyon score thresholds.
Methods: Adult patients with typical reflux symptoms underwent 24-hour impedance-pH monitoring off acid suppression therapy, from which the Lyon score (conclusive GERD ≥5.0, normal ≤0.5, borderline GERD ≥3.0) and DeMeester score (abnormal ≥14.72) were calculated. GERD classifications were based on AET thresholds from Lyon consensus 2.0 criteria. Patient-reported outcomes included the GERD Questionnaire (GERDQ) and the esophageal hypervigilance and anxiety scale (EHAS). Mucosal integrity was evaluated using the mean nocturnal baseline impedance (MNBI). The performance characteristics of Lyon and DeMeester scores were calculated using ROC analysis.
Results: Among 428 patients, 49 patients (11.4%) had AET >6%, with 100% demonstrating concordant Lyon Score and 95.9% showing concordance with the DeMeester score. Among 349 (81.5%) with AET <4%, 253 patients (72.5%) had a concordant Lyon score, while 348 patients (99.7%) had a concordant DeMeester score (P = 0.104). Among 30 patients with AET 4%–6%, 18 patients (60%) had DeMeester score >14.72, and 29 patients (96.7%) had a Lyon score within the conclusive GERD range (P = 0.406). MNBI values were <1500 ohms in 17 patients with abnormal Lyon score and normal DeMeester score and in none with normal Lyon score and abnormal DeMeester score (P = 0.668). Median MNBI was higher when the Lyon score was normal compared to when the DeMeester score was normal in discordant cases (MNBI: 2565.7Ω vs. 2293.3Ω, P = 0.440). In Table 1, patients with a DeMeester score ≥14.72 had higher GERDQ scores (P = 0.021), greater esophageal hypervigilance (P = 0.032), elevated AET (P < 0.001), lower MNBI (P < 0.001), more reflux episodes (P = 0.001), higher Lyon scores (P < 0.001), and a greater prevalence of Lyon 2.0-proven GERD (P < 0.001). The optimal DeMeester score cut-offs for no GERD, borderline GERD, and conclusive GERD were <11.13, 11.13–1749, and >17.49 with AUROC of 0.987, 0.862, and 0.990, respectively. EHAS scores did not differ across AET categories or when using Lyon score with a 5.0 cutoff; however, EHAS (hypervigilance) scores were higher when the DeMeester score was >14.72.
Conclusions: The DeMeester score aligns well with the Lyon Score and complements the Lyon Score in diagnosing GERD and predicting hypervigilance. When the Lyon Score and DeMeester score are discordant, MNBI values can help define conclusive GERD. DeMeester thresholds that incorporate borderline GERD may further improve performance characteristics.

③

CHRONIC KIDNEY DISEASE RISK ASSOCIATED WITH METABOLIC ASSOCIATED STEATOTIC LIVER DISEASE: A NATIONWIDE COHORT STUDY IN KOREA

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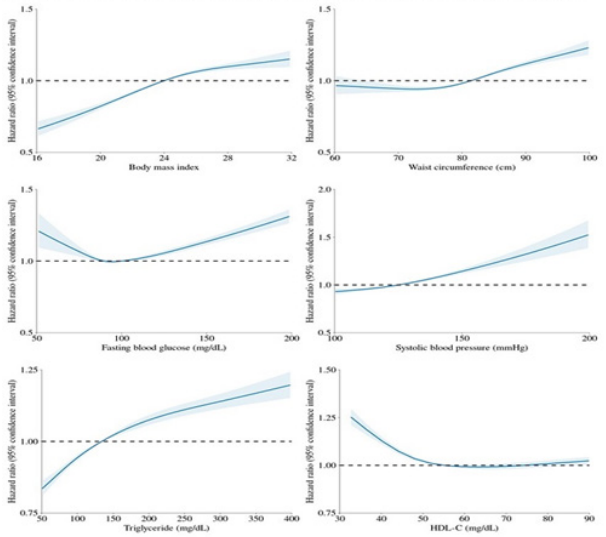
Background & Aims: Nonalcoholic fatty liver disease (NAFLD) and chronic kidney disease (CKD) are linked through inflammation and oxidative stress, which play key roles in CKD progression. The metabolic dysfunction-associated steatotic liver disease (MASLD) terminology has led to a reevaluation of epidemiological trends and CKD risk. This study aims to show that MASLD significantly increases CKD risk compared to those without MASLD.
Methods: Administrative data from the Korean National Health Insurance Service was used to analyze 362,285 individuals aged 40 years or older. Participants were categorized into three groups: No steatotic liver disease (SLD) without cardiometabolic risk factor (CMRF), No SLD with CMRF, and MASLD. Hepatic steatosis was defined as a fatty liver index ≥30. CKD was defined as grade 3 or higher (GFR <60 mL/min/1.73 m²) or the ICD-10 code N18.
Results: This study included 198,661 participants. The participants' characteristics were: No SLD without CMRF, mean age 55.0 years (47.4% males, 52.6% females); No SLD with CMRF, 58.7 years (43.0% males, 57.0% females); MASLD, 58.3 years (68.6% males, 31.4% females) (P < 0.001). During a median follow-up of 8.5 years, 39,277 participants developed CKD (21.46 per 1,000 person-years). Adjusted HRs for CKD were 1.16 (95% CI: 1.12–1.21) for no SLD with CMRF, and 1.39 (95% CI: 1.33–1.45) for MASLD, with no SLD without CMRF as the reference group. Incidence rates were 16.03, 22.53, and 26.12 per 1,000 person-years for the no SLD without CMRF, No SLD with CMRF, and MASLD groups, respectively. A restricted cubic spline analysis revealed a linear relationship, with higher predictor levels associated with increased CKD risk.
Conclusion: This study demonstrates that MASLD is significantly associated with an increased risk of CKD, with metabolic dysfunction playing a critical role in CKD development. The MASLD definition effectively identifies individuals at high risk for CKD, emphasizing the importance of targeted strategies to manage metabolic dysfunction and reduce CKD incidence.

Table. Association between SLD and CKD.

Group	Number	Events	Follow-up duration (person-years)	Incidence rate (per 1000 person-years)	Crude HR (95% CIs, P-value)	Adjusted HR (95% CIs, P-value)
No SLD without CMRF	19424	2760	172152	16.03	1 (Reference)	1 (Reference)
No SLD with CMRF	110265	21310	945891	22.53	1.40 (1.35-1.46, p<0.001)	1.16 (1.12-1.21, p<0.001)
MASLD	68972	15207	582206	26.12	1.63 (1.56-1.70, p<0.001)	1.39 (1.33-1.45, p<0.001)

*The model was adjusted for age, sex, income level, residence, Charlson comorbidity index, hemoglobin level, glomerular filtration rate, smoking and regular exercise status.

Figure. Restricted cubic spline of hazard ratio with 95% confidence intervals for CKD.



*The model was adjusted for age, sex, income level, residence, Charlson comorbidity index, hemoglobin level, glomerular filtration rate, smoking and regular exercise status.

④

GENE ANALYSIS IN LEAN INDIVIDUALS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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代謝功能障礙相關脂肪性肝病於非肥胖個體之基因分析

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Background: While metabolic dysfunction-associated steatotic liver disease (MASLD) is often linked to obesity. Within the MASLD population, 20% of people were lean, tied to visceral fat, metabolic imbalances, and genetic factors such as PNPLA3 and TM6SF2.
Aims: Its genetic basis in Taiwan remains unclear. This study aims to explore these genetic factors.
Methods: This study analyzed 24,632 individuals from the Taiwan Biobank with complete genomic and abdominal ultrasound data to investigate genetic and clinical characteristics of lean MASLD. Genome-wide association studies (GWAS) were conducted using PLINK 1.9, employing logistic regression adjusted for demographic and genetic covariates. Significant variants ($p < 5\times10^{-8}$) were visualized using Manhattan and Q-Q plots. Fibrosis risk (Fibrosis-4 score, nonalcoholic fatty liver disease fibrosis score) and metabolic risk scores (1–5 criteria) were evaluated.
Results: From the Taiwan Biobank, 10,811 individuals with steatotic liver disease (SLD) were identified, of whom 9,846 met cardiometabolic criteria for MASLD, including 1,720 lean and 8,126 non-lean individuals. Lean MASLD patients exhibited significantly worse metabolic profiles compared to healthy controls, including higher BMI, waist circumference, HbA1c, fasting glucose, triglycerides, LDL, and lower HDL levels, as well as elevated liver enzyme and uric acid levels. GWAS identified 47 significant signals for MASLD in the lean population, primarily in PNPLA3 and SAMM50, with rs9625962 in PNPLA3 confirmed as an independent signal. Among these, one known variant, rs12483959, was successfully replicated. Fibrosis risk scores were evaluated revealing positive correlations with metabolic risk scores in both lean and non-lean MASLD groups, emphasizing that higher metabolic risk factors are associated with increased fibrosis risk. These findings highlight genetic and metabolic contributors to fibrosis risk in MASLD, particularly among lean individuals.
Conclusions: Lean MASLD in Taiwanese group is linked to distinct metabolic and genetic profiles, with significant variants in PNPLA3 and SAMM50, and metabolic risk strongly correlating with fibrosis risk, underscoring the need for tailored diagnostic and management strategies.

⑤

MICROBIOTA-METABOLITE INTERACTIONS IN METABOLIC DYSREGULATION AND TUMOR PROGRESSION IN PANCREATIC CANCER

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Background & Aims: While there is growing evidence of gut microbial dysbiosis and metabolic reprogramming are linked to in pancreatic cancer, specific mechanisms by which microbiota-metabolite interactions shape metabolic pathways and contribute to tumor progression remain insufficiently understood. Understanding microbiota-metabolite interactions may contribute to improving the diagnosis and treatment outcomes of pancreatic cancer patients.

Methods: Gut microbial taxa and total gene function were analyzed based on shotgun metagenomic analysis using a pancreatic cancer cohort including patients (n = 54) and healthy individuals (n = 28). Enterotyping was conducted based on the Dirichlet Multinomial Mixtures (DMM) approach on a genus-abundance matrix. Untargeted fecal metabolomics was performed using a non-targeted approach to assess polar metabolites and lipidomes. Associations of the pancreatic cancer, the gut microbial community, and metabolites using various statistical analysis.

Results: Enterotyping analysis identified three enterotypes in the cohort. Of these, we found one enterotype significantly associated with pancreatic cancer and labeled it as a dysbiotic enterotype. This enterotype presented higher levels of oxidative stress and reduced levels of amino acid fermentation functions. Despite the absence of microbial clustering based on host conditions, metabolites demonstrated clear clustering patterns associated with pancreatic cancer, cachexia, and enterotypes.

Conclusion: Specific microbe-metabolite interactions were observed within the gut of pancreatic cancer patients, extending to cachexia and the dysbiotic gut type.

⑥

EXOSOMAL MIRNAS AS NON-INVASIVE BIOMARKERS FOR EARLY DETECTION AND CHEMORESISTANCE IN PANCREATIC DUCTAL ADENOCARCINOMA

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外泌體 miRNA 作為非侵入性生物標記物，用於胰管腺癌的早期檢測和化療抗藥性

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Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies, marked by late diagnosis, limited treatment options, and poor survival rates. Gemcitabine remains the primary chemotherapeutic agent for PDAC, yet its clinical benefit is often constrained by rapid development of resistance. Therefore, identifying biomarkers for early detection and predicting chemoresistance is critical for improving patient outcomes. Liquid biopsy, a minimally invasive technique that analyzes circulating biomarkers in body fluids, has emerged as a powerful tool for real-time monitoring of tumor dynamics in PDAC. Exosomal microRNAs (miRNAs) from serum are particularly promising, offering stability and specificity that reflect the molecular profile of the tumor.

Aims: In this study, we explored exosomal miRNA profiles in the PDAC cell line MIA-PaCa-2 compared with normal human pancreatic duct epithelial (HPDE) cells, aiming to identify miRNAs selectively associated with PDAC.

Methods: Exosomes were harvested from the culture medium of both MIA-PaCa-2 and HPDE cells, and exosomal miRNAs were extracted and subjected to high-throughput sequencing for comprehensive miRNA profiling. In parallel, we analyzed miRNA expression differences between gemcitabine-resistant MIA-PaCa-2 cells and their parental counterparts through sequencing to identify miRNAs associated with chemoresistance.

Results: Moreover, integrating our findings with The Cancer Genome Atlas (TCGA) PAAD cohort data, we identified four miRNAs of interest: hsa-miR-202-5p, hsa-miR-493-5p, hsa-miR-23a-5p, and hsa-miR-181c-5p. These miRNAs were consistently elevated in PDAC samples, detectable in liquid biopsies, and associated with resistance to gemcitabine. Kaplan-Meier survival analysis of these miRNAs indicated a significant association with overall survival in PDAC patients, with a hazard ratio (HR) of 1.53 (95% CI: 1.01–2.3, P = 0.038), underscoring their potential prognostic value.

Conclusions: Our panel of exosomal miRNAs offers a promising liquid biopsy-based biomarker set for early PDAC detection, treatment monitoring, and prognostication. These findings highlight the potential of liquid biopsy to enable personalized treatment approaches by assessing tumor response and resistance to gemcitabine, ultimately improving therapeutic outcomes for PDAC patients.

一般演講

主題：上消化道疾病（一）

①

巴雷特氏食道治療新進展：質子幫浦抑制劑結合內視鏡光動力療法的臨床優勢
ADVANCING BARRETT'S ESOPHAGUS TREATMENT: CLINICAL BENEFITS OF COMBINING PROTON PUMP INHIBITORS WITH PHOTODYNAMIC THERAPY

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Background: Barrett's esophagus (BE), a precursor to esophageal adenocarcinoma, necessitates effective therapeutic strategies. Proton pump inhibitors (PPI) are the standard of care, while photodynamic therapy (PDT), a minimally invasive endoscopic treatment, has been proposed as an adjunct. This study evaluates the clinical outcomes of PPI combined with PDT versus PPI monotherapy using a global real-world database.

Aims: To assess whether the addition of PDT to PPI therapy improves clinical outcomes, including mortality reduction, progression to dysplasia, and the incidence of treatment-related complications.

Methods: This retrospective cohort study utilized the TriNetX Global Collaborative Network, analyzing data from 137 healthcare organizations. Patients diagnosed with BE or related conditions between January 1, 1995, and December 31, 2020, were included. The treatment cohort (PPI + PDT, n = 493) was compared to the control cohort (PPI alone, n = 167,293). Propensity score matching (1:1) balanced baseline characteristics, resulting in 483 patients in each cohort. Clinical outcomes, including mortality, dysplasia progression, and complications (e.g., vitamin B12 deficiency, diarrhea, and iron deficiency), were evaluated using Kaplan-Meier survival analysis, hazard ratios, and risk differences.

Results: After propensity score matching, the treatment and control cohorts demonstrated balanced baseline characteristics. The PPI + PDT cohort showed a trend toward reduced mortality compared to the PPI-only cohort (18.6% vs. 22.8%; risk difference: -4.1%, 95% CI: -9.2% to 1.0%, p = 0.112), with a corresponding hazard ratio of 0.764 (95% CI: 0.578–1.010, p = 0.058). Regarding dysplasia progression, both cohorts exhibited identical risks (2.9%, p = 1.0). However, Kaplan-Meier survival analysis revealed a higher survival probability at the end of the time window for patients in the PPI + PDT cohort (92.57%) compared to those in the PPI-only cohort (84.60%). Complications such as vitamin B12 deficiency and diarrhea showed no statistically significant differences between the cohorts, with a lower incidence of vitamin B12 deficiency in the PPI + PDT cohort (2.5% vs. 3.9%, p = 0.201).

Conclusions: The addition of PDT to PPI therapy demonstrated a favorable trend in reducing mortality and improving survival outcomes in patients with BE. While dysplasia progression and most complications were similar between the cohorts, PDT may confer a survival advantage without significantly increasing adverse events. These findings support PDT as an effective adjunctive treatment for BE. Further studies are warranted to confirm these benefits over the long term and explore its impact on quality of life.

②

食道弛緩不能症的食道肌肉特徵與臨床表現：一個基於高頻內視鏡超音波的前瞻性研究

ESOPHAGEAL MUSCULAR CHARACTERISTICS AND CLINICAL IMPLICATIONS IN PATIENTS WITH ESOPHAGEAL ACHALASIA: A PROSPECTIVE STUDY BASED ON HIGH-FREQUENCY ENDOSCOPIC ULTRASOUND

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Background: Endoscopic ultrasound (EUS) has emerged as an increasingly important tool in the evaluation and management of patients with esophageal achalasia. Muscle thickness, particularly at the esophagogastric junction (EGJ), has recently gained attention for its relevance to achalasia disease severity and treatment response.

Aims: We aimed to investigate the esophageal muscle characteristics with EUS and their relationship with various clinical manifestations, including symptom profiles, endoscopic, manometric and radiographic features in patients with achalasia.

Methods: Consecutive patients who were diagnosed with esophageal achalasia via high-resolution impedance manometry (HRIM) were prospectively enrolled at a tertiary medical center in this study. Patients with prior treatments for achalasia were excluded. All participants underwent a thorough diagnostic evaluation, including validated symptom questionnaires, EUS, timed barium esophagography (TBE), and HRIM. EUS was performed utilizing a high-frequency miniprobe to observe the esophageal muscular features and the muscular thickness at the EGJ, 5 cm and 10 cm above the EGJ was measured. Manometric evaluation was based on the Chicago Classification version 3.0 and 4.0. Patients were compared according to the various clinical characteristics and parameters, with a focus on EUS findings.

Results: Between October 2014 and October 2024, a total of 144 were included in the analysis (56 men; mean age: 51.38 years, range 20–89.2 years). Of these, 52 patients (36.1%) had type I achalasia, 90 patients (62.5%) had type II achalasia, and 2 patients (1.4%) had type III achalasia. Compared to type II achalasia, type I achalasia patients had a longer symptom duration (mean: 74.7 vs. 38.0 months, $p = 0.007$), lower lower esophageal sphincter (LES) resting pressure (24.16 mmHg vs. 41.55 mmHg, $p < 0.001$), and lower LES IRP-4s (16.41 mmHg vs. 28.15 mmHg, $p < 0.001$). Type I achalasia patients also had greater esophageal width on TBE at 1 minute (4.35 cm vs. 3.63 cm, $p = 0.012$), 2 minutes (4.02 cm vs. 3.14 cm, $p = 0.003$), and 5 minutes (3.61 cm vs. 2.82 cm, $p = 0.01$). However, there was no significant difference in muscular thickness, including the inner circular muscle (ICM), outer longitudinal muscle (OLM), or total muscle thickness, at the EGJ, 5 cm and 10 cm above the EGJ between type I and type II achalasia patients. Patients with a symptom duration exceeding one year had a thicker ICM at 10 cm above the EGJ compared to those with a shorter symptom duration (1.53 cm vs. 1.17 cm, $p = 0.024$). Patients with luminal dilation on endoscopy had a thicker ICM at both 5 cm and 10 cm above the EGJ compared to those without luminal dilation (1.66 cm vs. 1.17 cm, $p = 0.034$; 1.49 cm vs. 1.08 cm, $p = 0.047$). LES resting pressure correlated with ICM thickness at EGJ ($r = 0.182$, $p = 0.040$)

Conclusions: This study demonstrates the association of esophageal muscular characteristics with symptom duration and disease severity on manometric and endoscopic examinations in patients with achalasia. Future studies are needed to clarify the role of esophageal muscle in the underlying pathophysiology and natural course of achalasia.

③

改善胃食道逆流症的診斷：對 pH 阻抗監測中不確定的非胃食道逆流指標患者進行分型

IMPROVING GERD DIAGNOSIS: CLASSIFYING PATIENTS WITH INCONCLUSIVE NON-GERD MEASUREMENTS FROM PH-IMPEDANCE MONITORING

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Background: 24-hour pH-impedance monitoring has limitations in capturing day-to-day variability in acid burden, which may underestimate the diagnosis of gastroesophageal reflux disease (GERD) in patients with normal or borderline acid exposure time (AET). While AET <4%, total reflux episodes (TRE) <40, and mean nocturnal baseline impedance (MNBI) >2500 Ω identify conclusive absence of GERD (non-GERD), the implications when these metrics are discordant (inconclusive non-GERD) remain unclear.

Aims: This study compares reflux and esophageal function metrics in symptomatic patients with AET <4%, with a particular focus on better characterizing patients with inconclusive non-GERD.

Methods: Data from patients with GERD symptoms and normal acid exposure who underwent upper endoscopy and high-resolution manometry at Hualien Tzu-Chi Hospital, Taiwan, and Brigham and Women's Hospital, USA, were analyzed. Based on Lyon consensus criteria, patients were categorized into conclusive non-GERD (AET <4%, TRE <40/day, MNBI>2500 Ω) and inconclusive non-GERD groups as follows: (i) Reflux-Like: AET <4% + ≥1 abnormal reflux metric (TRE >80 and/or MNBI <1500 Ω), (ii) Indeterminate: AET <4% + two inconclusive reflux metrics (TRE 40–80 and MNBI 1500–2500 Ω), and (iii) Non-Reflux-Like: AET <4% + one inconclusive and one conclusive non-GERD metric (TRE <40 + MNBI 1500–2500 Ω or TRE 40–80 + MNBI >2500 Ω). Prospectively collected symptom, endoscopic, pH-impedance, and manometric measures were compared.

Results: Among 343 patients (mean 50.3 years, 67% female), 108 (31%) with conclusive and 235 (69%) within conclusive non-GERD were indistinguishable on standard symptom measures. The inconclusive non-GERD group had higher AET, lower MNBI, DeMeester scores, TRE, and RSA, and more hypomotility ($p \leq 0.017$ for each comparison with conclusive non-GERD. Among inconclusive non-GERD patients, the non-reflux-like subgroup resembled the conclusive non-GERD cohort with similar symptom measures (DSI, GSS), but lower than the reflux-like and in determinant subgroups. On physiologic testing, reflux-like subgroup patients had the highest rates of ineffective ($p = 0.013$) and failed ($p = 0.002$) peristalsis and the lowest MNBI ($p < 0.001$). Compared to the combined non-reflux-like and conclusive non-GERD group, the reflux-like group had higher DSI, AET, DeMeester scores, TRE, ineffective and failed peristalsis, along with lower MNBI ($p \leq 0.03$ for each comparison). On multivariable logistic regression, TRE (OR 2.54, CI 1.83–3.52, $p < 0.001$) and MNBI (OR 0.58, CI 0.49–0.69, $p < 0.001$) independently predicted the reflux-like phenotype among patients with AET <4%. A Lyon score cutoff of 2.00 demonstrated high diagnostic accuracy (AUC 0.769, sensitivity 100%, specificity 48.8%) in distinguishing the reflux-like phenotype from non-reflux-like and conclusive non-GERD cohorts.

Conclusions: Phenotyping patients with AET <4% using symptom measures, physiologic parameters and Lyon score may have diagnostic and management implications.

④

食道過度警覺與焦慮程度在氫離子幫浦抑制劑依賴性胃食道逆流症患者中的角色：應用無線酸鹼測定探討依賴機制與治療策略

THE ROLE OF ESOPHAGEAL HYPERVIGILANCE AND ANXIETY SCALE IN PPI-DEPENDENT GERD PATIENTS: INSIGHTS INTO DEPENDENCY MECHANISMS AND MANAGEMENT USING PROLONGED WIRELESS PH MONITORING

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Background: Gastroesophageal reflux disease (GERD) is a prevalent condition, affecting approximately 10%–20% of the population. Proton pump inhibitors (PPIs) remain the standard treatment for GERD. However, more than 40% of GERD patients require prolonged PPI therapy, leading to concerns regarding the risks associated with long-term PPI use and increased healthcare costs. The esophageal hypervigilance and anxiety scale (EHAS), a validated tool for assessing cognitive-affective aspects of visceral sensitivity, has been shown to correlate with reflux symptom severity and psychological stress. Nevertheless, the role of EHAS in PPI-dependent GERD patients remains unclear.

Aims: To evaluate the presence of pathological GERD and the role of EHAS in patients with GERD symptoms who exhibit PPI dependence.

Methods: This study included patients with typical GERD symptoms who were PPI-dependent for at least six months. All participants underwent prolonged wireless pH monitoring after discontinuing PPI therapy. Validated patient-reported outcome measures, including the GERD questionnaire (GERDQ) and EHAS, were recorded.

Results: A total of 22 patients were enrolled, with a mean age of 48.8 years (range 21–64 years), and 27.3% were female. Nine patients had an acid exposure time (AET) <4.0% on all monitored days, while 13 patients had an AET ≥4.0% for at least one monitored day. Patients with AET <4.0% demonstrated significantly higher total EHAS scores and EHAS anxiety subscores compared to those with AET ≥4.0% (total EHAS: 49.2 vs. 28.3, $p = 0.008$; EHAS anxiety subscore: 29.7 vs. 22.5, $p = 0.005$). No significant differences were observed between groups in terms of age, sex, body mass index (BMI), GERDQ scores, or EHAS hypervigilance subscores ($p > 0.05$).

Conclusions: This study revealed that 41% of patients with typical GERD symptoms and PPI dependence did not exhibit pathological GERD. These patients had significantly higher EHAS scores, particularly in the anxiety component, which may contribute to PPI dependence. Targeting the anxiety aspect of EHAS could represent a potential therapeutic strategy to reduce unnecessary PPI usage.

⑤

探討紅辣椒素對逆流症患者其食道功能的影響

INFLUENCE OF CAPSAICIN INFUSION ON ESOPHAGEAL MOTILITY IN PATIENTS WITH GERD

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Background: Capsaicin-containing red pepper sauce suspension can induce heartburn symptoms and augment esophageal peristalsis in healthy adults.
Aims: We aimed to apply high-resolution manometry (HRM) to investigate the hypothesis of whether an acute esophageal infusion of capsaicin-containing red pepper sauce can modulate esophageal sensorimotor function in patients with gastroesophageal reflux disease (GERD).
Methods: 14 GERD patients (mean age 46 years, 8 male) were evaluated for primary and secondary peristalsis using HRM with one mid-esophageal injection port. Primary peristalsis was performed with ten water swallows, while secondary peristalsis was generated with slow and rapid air injections. The study assessed the effects of capsaicin-containing red pepper sauce on esophageal peristaltic physiology. GERD phenotypes were diagnosed based on 24-hour pH impedance. The symptom response to capsaicin infusion was investigated by measuring the intensity (visual analog scale [VAS]) and lag time when there was an initial perception of typical symptoms.
Results: Capsaicin infusion significantly increased distal contractile integral (DCI) of primary peristalsis ($p = 0.004$) and its frequency ($p = 0.03$) (Table 1). Capsaicin infusion significantly increased the resting pressure of the lower esophageal sphincter ($p = 0.001$) and esophagogastric junction contractile integral ($p = 0.002$). Capsaicin infusion also significantly increased DCI of secondary peristalsis during rapid air distensions ($p = 0.038$) but not for slow air distensions ($p = 0.178$). Infusion of capsaicin did not alter the distension threshold for slow air distensions ($p = 0.082$) or rapid air distensions ($p = 0.183$). The frequency of secondary peristalsis during rapid air distension was not altered by capsaicin infusion ($p = 0.075$). Capsaicin infusion also significantly increased DCI of primary peristalsis in patients with normal motility ($p = 0.003$) but not in those with ineffective esophageal motility (IEM) ($p = 0.648$). Capsaicin infusion did not alter the contractile vigor of secondary peristalsis in patients with normal motility or IEM. All patients experienced heartburn sensation subsequent to the administration of capsaicin, but there was no group difference regarding lag time ($p = 0.889$) or VAS score of their heartburn symptom ($p = 0.223$) among different phenotypes of GERD patients.
Conclusions: The acute administration of capsaicin-containing red pepper sauce appears to facilitate primary peristalsis and secondary peristalsis in response to rapid air distension in patients with GERD. The sensory modulation of capsaicin infusion on the subjective perception of heartburn is similar among different phenotypes of GERD patients.

⑥

咽喉逆流症狀和下咽部胃酸逆流患者的上食道括約肌及食道對模擬逆流事件的反應：一項比較性研究

UPPER ESOPHAGEAL SPHINCTER AND ESOPHAGEAL BODY RESPONSES TO SIMULATED REFLUX EVENTS IN PATIENTS WITH LARYNGOPHARYNGEAL REFLUX SYMPTOMS AND HYPOPHARYNGEAL ACIDIC REFLUX: A COMPARATIVE STUDY

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Background: Upper esophageal sphincter (UES) and esophageal body responses are crucial in preventing esophagopharyngeal reflux and its complications. Hypopharyngeal multichannel intraluminal impedance-pH (HMII-pH) technology, which includes two trans-UES impedance channels, may detect pharyngeal reflux. Using this technology, pharyngeal acidic reflux (PAR) episodes—characterized by a pharyngeal pH drop of ≥2 units to <5 within 30 seconds during esophageal acidification—have demonstrated high diagnostic accuracy and strong interobserver reliability. (Chen YY et al. J Neurogastroenterol Motil. 2023;29:49-57). This study investigated UES and esophageal body responses to simulated reflux in patients with laryngopharyngeal reflux symptoms (LPRS) and confirmed PAR episodes.

Aims: This study investigated UES and esophageal body responses to simulated reflux in patients with laryngopharyngeal reflux symptoms (LPRS) and confirmed PAR episodes.

Methods: Patients (≥20 years) with laryngeal symptoms and laryngoscopic signs of reflux undergoing HMII-pH off therapy were divided into 3 groups: Group A: 24 patients with PAR episodes; Group B: 35 patients with excessive esophageal acid reflux alone (EAR); Group C: 24 patients with normal acid exposure, matched for sex and age. Another 24 asymptomatic healthy subjects serve controls (Group D). High-resolution impedance manometry (HRIM) was used to evaluate primary (10 wet swallows of 5 ml saline) and secondary peristalsis (rapid air 20 ml, 10 repetitions; rapid saline 20 ml, 5 repetitions) injections in the distal third of the esophagus. Esophago-UES relaxation reflex (EURR) was defined as UES pressure decreased by >10 mm Hg below baseline within UES analysis window.

Results: The frequency of EURR during rapid saline injection was higher in Groups A and B compared to Groups C and D ($p < 0.05$), with no differences between Groups A and B. The frequency of secondary peristalsis for both air and saline injection was lower in Groups A, B, and C versus Group D ($p < 0.05$), with no difference among Groups A, B, and C. Mean proximal contractile integral was lower in Groups A, B, and C compared to Group D ($p < 0.05$), with no difference among Group A, B, and C. Mean distal contractile integral was lower in Group B compared to Groups A and D ($p < 0.05$), with no difference between Groups A and D.

Conclusions: Patients with LPRS and confirmed PAR episodes exhibit impaired EURR similar to those with EAR alone, indicating overlapping dysfunction. However, a normal mean distal contractility profiles in those with PAR episodes contrasted with a reduced mean distal contractile integral in those with EAR alone, implies distinct pathophysiological mechanisms.

主題：肝腫瘤（一）

⑦

內視鏡超音波導引下射頻燒融治療肝左葉惡性腫瘤的成效分析
THE APPLICATION OF EUS GUIDED RFA TX FOR METASTATIC HEPATIC TUMORS AT LT LOBE

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Background: Endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) is a promising technique for treating small metastatic hepatic tumors at left or caudate lobe, particularly where ablation via percutaneous route is deemed to be technically difficult.
Aims: To assess the safety and efficacy of EUS guided RFA therapy for patients with metastatic hepatic tumors at left or caudate lobe.
Methods: A total of 4 patients with metastatic hepatic tumors at left or caudate lobe underwent EUS guided RFA from 2023-02 to 2024-11 in our hospital. All patients received EUS guided FNA for tissue proof. Three patients are colorectal cancer patients, and among them two patients had hepatic metastasis after one year postoperatively. The other one was found to have hepatic metastasis during the ne-adjuvant therapy. The last one is a victim of esophageal cancer responding well to CCRT and want to receive curative surgery combined with local ablation for hepatic lesions. The EUSRATM catheter is made by Taewoong Co., Korea. We use 19 Gauge needles 1 cm in length. The working station is Combo. The energy is set at 30 watts and the burning duration is 20 to 30 seconds. The ablation time depends upon the controlled energy.
Results: Every patient has two metastatic tumors, which are located at the left lobe, with size between 1-2 cm. A total of 8 tumors are ablated. The average burning time is 5 minutes and 10 seconds. Among 4 cases, two cases had complete ablation at one session, the other two cases had incomplete ablation, and after supplementary ethanol injection ablation, all cases had achieved complete ablation. No adverse events occurred among these patients.
Conclusions: EUS guided RFA is a safe and effective treatment for hepatic left lobe metastatic malignancy. However, the machine setting should be adjusted and standardized according to the different malignant tumor biology.

⑧

局部治療對接受免疫治療不可切除肝細胞癌患者的協同作用
SYNERGISTIC EFFECT OF LOCOREGIONAL THERAPY IN PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA RECEIVING IMMUNOTHERAPY

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Background: Immune checkpoint inhibitors (ICIs) have become a significant part of frontline therapy against unresectable hepatocellular carcinoma (uHCC). However, there is still a substantial portion of patients with uHCC who suffer from progressive disease. Locoregional therapies (LRTs) promote antitumor immunity through local inflammation and by releasing tumor-associated antigens. Immortal time bias should be cautioned in the study design. Time-varying covariate Cox proportional hazards regression models (time-varying analyses) account for the variable initiation dates of ICI therapy and on-demand LRTs in HCC patients and help to overcome immortal time bias.
Aims: To investigate the synergistic effect of LRTs in patients with unresectable HCC receiving ICIs by conducting time-varying analyses.
Methods: 273 consecutive adult patients with uHCC who received at least one dose of immunotherapy, with evaluable follow-up computed tomography, and overall survival (OS) for more than 3 months at China Medical University Hospital, Asia University Hospital, LinKou Chung Gung Memorial Hospital, and New Taipei Municipal TuCheng Hospital were enrolled. An analytic data unit of 3 months was selected because of the regular imaging follow-up interval of HCC. Covariates and the exposures of interest (systemic therapy, LRT, or both systemic therapy and LRT [both Sys-LRT]) were reassessed every 3 months. Both Sys-LRT meant systemic therapy and LRT was used in the same time frame. Cox regression analysis was performed to identify variables associated with progression-free survival

(PFS) or OS.

Results: The median age of the enrolled patients was 64.3 (55.7–69.8) years, and the median follow-up duration was 15.07 (7.45–24.63) months. Among the enrolled patients, 19 (7.0%), 38 (13.9%), and 216 (79.1%) had BCLC stages A, B, and C, respectively. Among the 1051 time frames for PFS analysis, systemic therapy, LRT, and both Sys-LRT were not a predictor of PFS. In the subgroup analysis of LRTs, liver radiotherapy predicted PFS (HR 0.555, 95% CI: 0.339–0.911). Among 1803 time frames for OS analysis, time-varying multivariable Cox regression analysis indicated systemic therapy (HR: 0.198, 95% CI: 0.133–0.294), and both Sys-LRT (HR: 0.158, 95% CI: 0.078–0.321) were independent predictors of OS in addition to other variables. Both Sys-LRT had no additional survival benefit than systemic therapy (HR: 0.798, 95% CI: 0.406–1.569, p = 0.513). In a subgroup analysis, different systemic therapies, including tyrosine kinase inhibitor (TKI), mono-ICI, ICI+TKI, and ICIs (atezolizumab plus bevacizumab or ipilimumab plus nivolumab), were all predictors of OS. In a subgroup analysis of LRTs, curative therapy (radiofrequency ablation and surgery, HR: 0.311, 95% CI: 0.112–0.870) and TACE (HR: 0.416, 95% CI: 0.181–0.953) were predictors of OS.

Conclusions: Systemic therapy or both Sys-LRT (especially ICI-based systemic therapy) was a predictor of OS, but both Sys-LRT had no additional survival benefit than systemic therapy.

⑨

肝細胞癌切除術後的早期和晚期復發預測模型：台灣的前瞻性研究

PREDICTIVE MODEL FOR EARLY AND LATE RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER HEPATECTOMY: A PROSPECTIVE STUDY IN TAIWAN

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Background: Many predictors have been proved to be associated with early or late recurrence of HCC, however, those currently available have limited applicability, robustness and generalizability.

Aims: We aimed to develop a simple scoring system to predict the risk of HCC recurrence among HCC patients after curative hepatectomy.

Methods: A cohort of 2732 patients who underwent curative hepatectomy with pre-operative serum and post-operative pathology-verified HCC samples in Taiwan Liver Cancer Network (TLCN) program between January 2005 and August 2011 was recruited (Figure 1). Nelson-Aalen cumulative hazard estimate and the log-rank test were used to determine the cumulative survival of different recurrence types and the cutoff time between early and late recurrence. A polytomous regression model was also used to assess the influence of putative factors on early and late HCC recurrence.

Results: Early recurrence was associated with the poorest survival rate (Figure 2). Multivariate analysis showed cirrhosis, clinically significant portal hypertension (CSPH), high AFP (>20 ng/mL), large tumor size (>5 cm), multinodularity and hepatitis B virus (HBV) with high viral load (HBV DNA level >10000 copies/mL) significantly increased the risk of early recurrence (< 1 year). In contrast, CSPH, multinodularity and HBV with high viral load were significantly associated with late recurrence (>1 year) (Table 1). A simple risk score based on TLCN program showed fair calibration and discrimination to predict early HCC recurrence after curative hepatectomy (Figure 3).

Conclusions: Our model based on polytomous regression delivers a reliable and reproducible risk score for predicting early recurrence in HCC patients. It may assist in developing optimal surveillance programs and identifying patients who could benefit from adjuvant treatment after curative hepatectomy.

⑩

以演化學習整合像特徵之多模態模型預測肝癌接受手術切除後之早期復發

EVOLUTIONARY LEARNING-DERIVED MULTIMODAL MODELS INTEGRATING COMPREHENSIVE IMAGING FEATURES TO PREDICT EARLY RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER CURATIVE RESECTION

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Background: The accuracy of existing models for predicting early recurrence of hepatocellular carcinoma (HCC) after curative resection remains suboptimal.

Aims: This study aimed to develop artificial intelligence-based models to enhance accuracy by integrating comprehensive imaging features.

Methods: This study enrolled patients with HCC who underwent curative resection with complete clinical data (n=1477), dynamic CT images (n=588), and an external validation cohort from Hong Kong (n=122). Multimodal imaging features, including radiomics, 3D geometric properties, tumor morphology, and deep learning-derived latent features, were analyzed. Two evolutionary learning-based models, EL-CERSL (clinical features only) and EL-MERSL (clinical and imaging features), were developed to predict early recurrence of HCC.

Results: The EL-CERSL and EL-MERSL models provided personalized predictions of recurrence-free survival (RFS). In the test set, the area under the receiver operating characteristic curves (AUCs) for EL-CERSL-preoperative, EL-CERSL-postoperative, EL-MERSL-preoperative, and EL-MERSL-postoperative models were 0.791, 0.774, 0.857, and 0.861, respectively, significantly outperforming the ERASL-pre and ERASL-post models (AUCs 0.733 and 0.747) and high-risk criteria from IMBrave050, KEYNOTE-937, EMERALD-2, and CheckMate-9DX trials (AUCs 0.607, 0.622, 0.643, and 0.543, respectively). In the external validation cohort, the AUCs of the EL-MERSL-preoperative and EL-MERSL-postoperative models were 0.801 and 0.808, respectively. Among IMBrave050-defined high-risk patients, the EL-MERSL-postoperative model reclassified 72.4% as low-risk and 27.6% as high-risk, with corresponding 2-year RFS rates of 70.2% and 20.6%, respectively.

Conclusions: The EL-CERSL and EL-MERSL models demonstrated significantly improved accuracy in predicting early HCC recurrence after resection. These models hold potential for guiding post-resection surveillance strategies and optimizing clinical trial designs by identifying high-risk candidates for adjuvant therapies.

⑪

使用機器學習模型預測接受樂衛瑪治療之不可切除肝細胞癌患者之 1 年和 2 年死亡率
MACHINE LEARNING MODELS FOR PREDICTING 1-YEAR AND 2-YEAR MORTALITY IN PATIENTS RECEIVING LENVATINIB FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA

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Background: Lenvatinib has been an effective treatment for patients with intermediate to advanced stage unresectable hepatocellular carcinoma (HCC). However, tumor response and survival outcomes vary widely. Machine learning (ML) models have been investigated to predict survival outcomes in patients with unresectable HCC treated with lenvatinib alone or in combination with immunotherapy or TACE. Most existing ML models, however, focus on radiomic feature-based prediction. ML models for predicting survival outcomes in unresectable HCC treated with lenvatinib have not been well validated.

Aims: In this study, we aimed to predict 1-year and 2-year mortality using clinical demographics, laboratory tests, radiologic patterns, and tumor response through ML algorithms.

Methods: This multi-center, retrospective study included a total of 205 patients with unresectable HCC treated with lenvatinib as first-, second-, or third-line therapy. Patients without intrahepatic tumors or those receiving concurrent immunotherapy or local therapy were excluded. Demographic data, laboratory tests, radiologic tumor patterns, and tumor response by RECIST (Response Evaluation Criteria in Solid Tumors) 1.1 criteria were collected. Radiologic patterns were classified as infiltrative or nodular beyond or within the Up-to-7 criteria. The entire dataset was randomly divided into training and test sets for 1-year and 2-year mortality prediction. Univariate analysis of the training set was conducted for feature selection, and 5-fold cross-validation was performed for hyperparameter tuning. ML algorithms, including logistic regression, support vector machine (SVM), random forest (RF), XGBoost, and AdaBoost, were implemented. Survival outcomes in terms of 1-year and 2-year mortality were predicted.

Results: A total of 177 and 154 patients were included for 1-year and 2-year mortality prediction, respectively, as their follow-up periods were adequate for analysis. Six input variables (ALBI score, ALT, major vascular invasion (MVI), alpha-fetoprotein (AFP), tumor radiologic pattern, and RECIST) were selected for 1-year mortality prediction, while four input variables (RECIST, ALBI score, tumor radiologic pattern, and main portal vein thrombosis) were chosen for 2-year mortality prediction. Among the ML models, for 1-year mortality prediction, the RF model exhibited the highest AUROC of 0.80, with a sensitivity, specificity, and accuracy of 65.4%, 89.3%, and 77.8%, respectively, in the test set; RECIST, ALBI score, and ALT had the strongest effects on this model. For 2-year mortality prediction, the SVM model exhibited the highest AUROC of 0.91, with a sensitivity, specificity, and accuracy of 84.6%, 77.6%, and 79.0%, respectively, in the test set, with ALBI score, RECIST, and main portal vein thrombosis showing the strongest effects on the model.

Conclusions: For patients with unresectable HCC treated with lenvatinib, without concurrent immunotherapy or local therapy, the RF model and SVM model exhibited high predictive performance for 1-year and 2-year mortality prediction, respectively. These models may be used to guide physicians' treatment decisions in this patient group and provide prognosis evaluations for patients.

⑫

代謝異常對接受肝切除的瘦型和非瘦型肝細胞癌患者預後的影響
THE IMPACT OF METABOLIC ABNORMALITIES ON PROGNOSIS OF LEAN AND NON-LEAN PATIENTS WITH HEPATOCELLULAR CARCINOMA RECEIVING HEPATIC RESECTION

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Background: Ample data now supports obesity was associated with an increased risk of hepatocellular carcinoma (HCC). Whether a higher body mass index (BMI) confers a survival benefit in HCC patients remains elusive. Consequently, we conducted this study aiming to investigate the survival in HCC patients post hepatic resection according to BMI. The impact of metabolic abnormalities on the outcome between lean and non-lean HCC patients was also assessed.

Aims: This retrospective cohort study aimed to evaluate the differences in the 5-year survival rate post-hepatic resection according to BMI in HCC patients and to understand the impact of metabolic abnormalities between lean and non-lean HCC patients.

Methods: This retrospective cohort study recruited pathologically-proven HCC patients receiving surgical resection between 2013-2021 in a medical center in southern Taiwan. 1,208 patients were included.We categorized the patients into four groups: BMI ≥23 (also called non-lean) with ≥1 cardiometabolic risk factor (CMRF) group (A), BMI ≥23 without CMRF group (B), normal BMI (also called lean) with ≥1 CMRF group (C), and normal BMI without CMRF group (D). We analyzed the clinical data, etiologies, fibrosis stage, liver-related events, cardiovascular events and 5-year survival rate of the HCC.

Results: Patients of group C had a significantly lower 5-year survival rate than patients of group A ($p = 0.007$) and group B ($p < 0.001$). In the subgroup analysis, group C had the lowest 5-year survival rate in the HCV subgroup (group A vs. group C: $p = 0.003$; group B vs. group C: $p < 0.001$). This phenomenon was also observed in patients with non-B-non-C etiologies in group C (group A vs. group C: $p = 0.022$). However, there was no statistically significant difference in the 5-year survival rate in the HBV subgroup. Group A patients had a significantly higher risk of coronary artery disease ($p = 0.035$), hepatic failure ($p = 0.008$), and hepatorenal syndrome ($p = 0.018$) than other groups.

Conclusions: Although individuals with a higher BMI are more likely to develop complications such as myocardial infarction, liver failure, or hepatorenal syndrome, the impact of metabolic abnormalities on the prognosis of lean HCC patients should not be overlooked. Therefore, rigorous follow-up with interventions for metabolic abnormalities are recommended for lean patients with HCC.

主題：病毒性肝炎（一）

⑬

產前抗病毒藥物預防於高病毒量之 B 型肝炎孕婦與產後肝炎發作
PERIPARTUM ANTIVIRAL PROPHYLAXIS AND POSTPARTUM HEPATIC FLARES IN HIGHLY VIREMIC PREGNANT PATIENTS WITH HEPATITIS B

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Background: Peripartum antiviral prophylaxis is highly effective in reducing the risk of mother-to-child transmission (MTCT) of hepatitis B virus (HBV). However, studies on postpartum hepatic flares in highly viremic, immune-tolerant pregnant patients who receive antiviral therapy during the third trimester and discontinue treatment one month postpartum are limited. A previous study reported that 36.3% of patients experienced postpartum hepatic flares after Telbivudine therapy.

Aims: This study aims to assess postpartum hepatic flares after the withdrawal of medication in highly viremic pregnant patients.

Methods: This retrospective study recruited highly viremic, Hepatitis B e antigen (HBeAg)-positive pregnant women in between Feb 2018 and Oct 2024 at a single center in Taipei, Taiwan. Prophylactic antiviral treatment was initiated at 28 weeks of gestation. Virological and biochemical markers were assessed before treatment and postpartum. Postpartum HBV flare-up was defined as a 2-fold increase in alanine aminotransferase levels at 8 weeks after delivery.

Results: A total of 24 pregnant patients received prophylactic antiviral therapy, with a mean age of 35.5 ± 4.9 years. The mean baseline viral load was 8.2 log10 IU/mL, and the patients underwent an average of 3.7 months of antiviral treatment. Twenty-one patients (87.5%) were treated with tenofovir. Ten patients were lost to follow-up after delivery. Among the 14 patients (58.3%) who completed follow-up for 3.7 months, 4 patients (28.6%) experienced HBV flare-ups 2.5 months after discontinuing antiviral therapy. The incidence of flare-ups was higher with Telbivudine (50%) compared to Tenofovir (25%). Postpartum hepatic flare rates were 14.3% and 36.7% at 2 and 6 months, respectively, after discontinuing nucleos(t)ide analogues.

Conclusions: A significant proportion of highly viremic, immune-tolerant pregnant patients who received prophylactic antiviral therapy during the third trimester experienced postpartum hepatic flares. This suggests that these patients entered the immune clearance phase after delivery, potentially creating an opportunity to initiate re-antiviral therapy.

⑭

B 型肝炎感染在代謝功能障礙相關脂肪性肝病族群產生骨質疏鬆之風險
RESOLVED HEPATITIS B VIRUS INFECTION AND RISK OF OSTEOPOROSIS IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: Previous research has indicated that patients with metabolic dysfunction-associated steatotic liver disease (MASLD) exhibit a lower risk of osteoporosis and higher bone density. However, the impact of resolved hepatitis B virus (HBV) infection on osteoporosis risk in MASLD patients remains unclear.

Aims: This study aims to elucidate the relationship between HBV infection status (resolved or current) and the development of MASLD, as well as the associated risk of osteoporosis.

Methods: We conducted a cross-sectional study using data from 22,491 participants in the Taiwan Biobank database, spanning January 1, 2009, to December 31, 2019. MASLD diagnosis was based on liver ultrasound findings indicating hepatic steatosis, combined with the presence of cardiometabolic dysfunction markers such as obesity, diabetes, or dyslipidemia. HBV infection status was classified as no infection, resolved infection, or current infection, determined using serological markers including HBsAg, anti-HBc, and anti-HBs. Logistic regression models were applied to assess the prevalence of osteoporosis across these groups. Key analyses included the comparison of osteoporosis prevalence among MASLD and non-MASLD patients, stratified by HBV infection status. Data processing and statistical analyses were performed using R software.

Results: MASLD patients demonstrated a significantly lower prevalence of osteoporosis compared to the non-MASLD group (12.2% vs. 22.1%, $P < 0.001$). Among MASLD patients, those with resolved HBV infection exhibited a higher prevalence of osteoporosis compared

to those with current HBV infection (13.4% vs. 9.8%, P < 0.001). A similar pattern was observed in non-MASLD patients, where osteoporosis prevalence was higher in the resolved HBV infection group than in the current HBV infection group (24.2% vs. 21.2%, P < 0.001). Across all HBV infection statuses, MASLD patients consistently had a lower osteoporosis prevalence than their non-MASLD counterparts (P < 0.001).

Conclusions: Our findings suggest that resolved HBV infection is associated with an elevated risk of osteoporosis in MASLD patients, followed by current infection, while the non-infection group exhibited the lowest risk. This trend was similarly observed in non-MASLD patients. These results underscore the importance of HBV vaccination as a preventative strategy to mitigate osteoporosis risk. Furthermore, early intervention and management of osteoporosis in patients with resolved HBV infection may be critical. Future studies should explore the underlying mechanisms linking HBV infection resolution to bone health deterioration, focusing on immune modulation and metabolic alterations. This research highlights the necessity of integrating osteoporosis risk assessments into the clinical management of MASLD patients with a history of HBV infection.

⑮

比較表面抗原定量值 100 IU/mL 和 ALT to qHBsAg 比例 0.2 預測 e 抗原陰性慢性 B 肝病人停止貝樂克或惠立妥治療後 B 型肝炎表面抗原消失的預測能力

COMPARE THE ABILITY OF PREDICTION FOR HBSAG LOSS AFTER ENTECAVIR OR TENOFOVIR CESSATION BETWEEN HBSAG OF 100 IU/ML AND ALT TO QHBSAG RATIO OF 0.2 IN HBEAG-NEGATIVE PATIENTS WITH CHRONIC HEPATITIS B

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Background: The ALT/qHBsAg ratio is a novel marker that could predict HBsAg loss after entecavir cessation.

Aims: To compared the predictive ability for HBsAg seroclearance after entecavir or tenofovir disoproxil fumarate (TDF) cessation between ALT/qHBsAg ratio and qHBsAg level at the end of treatment (EOT).

Methods: This retrospective cohort study included 715 HBeAg-negative chronic hepatitis B (CHB) patients without cirrhosis who received entecavir (n = 438) or TDF (n = 277) therapy previously. All patients had a follow-up of at least 12 months after treatment cessation and met the stopping criteria proposed by the APASL 2012 guidelines.

Results: The cumulative incidences of HBsAg loss at 5 and 10 years after entecavir or TDF cessation were 13.6% and 33.5%, respectively. Both factors of HBsAg levels of 100 IU/mL and an ALT/qHBsAg ratio of 0.2 at EOT could significantly predict HBsAg seroclearance after entecavir or TDF cessation (p < 0.001). Akaike Information Criterion (AIC) and Byesian Information Criterion (BIC) values were 1273.6 and 1276.4 for HBsAg of 100 IU/mL and were 1305.503 and 1308.273 for ALT/qHBsAg ratio of 0.2. HBsAg of 100 IU/mL showed the significantly lower AIC and BIC values compared to ALT/qHBsAg ratio of 0.2. Furthermore, patients who discontinued entecavir therapy had a higher rate of HBsAg loss than those who discontinued TDF therapy in either criteria of HBsAg > 100 IU/mL (p = 0.034) or ALT/qHBsAg ratio <0.2 at EOT (p = 0.025).

Conclusions: HBsAg levels of 100 IU/mL had a better fit to predict HBsAg loss after entecavir or TDF cessation compared to an ALT/qHBsAg ratio of 0.2 at EOT. Patients discontinuing entecavir therapy had a higher rate of HBsAg loss than those discontinuing TDF therapy in either criteria of HBsAg >100 IU/mL or ALT/qHBsAg ratio <0.2 at EOT.

⑯

腎臟移植患者長期使用 Tenofovir Alafenamide（TAF）之骨及腎安全性：和 Entecavir（ETV）之比較

A LONG-TERM BONE AND RENAL SAFETY OF TENOFOVIR ALAFENAMIDE (TAF) TREATMENT ON RENAL TRANSPLANT RECIPIENTS: A COMPARISON WITH ENTECAVIR (ETV)

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Background: The data on tenofovir alafenamide (TAF) in kidney transplant recipients (KTRs) with chronic hepatitis B virus (HBV) infection is limited.

Aims: The study aims to evaluate the renal safety and bone safety in these patients for 3 years follow up.

Methods: A Retrospective cohort study of HBsAg-positive kidney transplant recipients (KTRs) who received TAF between 2019 and 2022 were included in the analysis, and they were categorized into treatment-naïve and treatment-experienced groups for comparison. Patients who continued entecavir (ETV) use were also analyzed as a control. Dose of ETV was adjusted according to the change of eGRF.

Results: Four treatment-naïve (Group I) and 35 treatment-experienced (Group II) patients received TAF for 26.4 ± 11.3 and 43.7 ± 19.0 months respectively. Both groups show significant HBV DNA reduction, but Group I showed higher rates of undetectable HBV DNA (50%, 75%, 75%, 100% at 6, 12, 24, 30 months respectively, compared with 16.7%, 25.3%, 31.4%, 34.7% in Group II, $p = 0.018$). Group I showed ALT normalization at 4.5 ± 2.1 months, while Group II had normal ALT levels throughout the study. Renal allograft function remained stable during follow-up of 42.0 ± 19.0 months for both groups. The eGFR before initiation of TAF and after 2 years of treatment showed no significant difference in both groups (43.6 ± 11.9 mL/min vs. 47.4 ± 36.2 mL/min in the treatment-naïve group, $p = 0.863$; and 48.2 ± 20.9 ml/min vs. 52.9 ± 20.7 min/mL for the treatment-experienced group, $p = 0.635$). Five patients (12.8%) developed hypophosphatemia. Three (7.7%) and one (2.6%) patients had new-onset osteopenia and osteoporosis, respectively. There was no difference in patient and graft survival between two groups at 5 years ($p = 0.853$ and 0.216 respectively). Finally, we further analyzed 10 patients who continued using ETV until now. The period of treatment ranged from 3.6 to 6.8 years, with a median of 5.2 years. These patients exhibited excellent viral suppression to undetectable HBV DNA 70% at 48 weeks, 100% at 96 weeks and 100% at 144 weeks. Their renal function (eGFR) remained stable throughout the first three years, with no significant changes ($p > 0.05$). There is no difference of viral suppression as well as eGFR evolution when compared ETV with TAF cohort in three years.

Conclusions: Our results suggested favorable efficacy and tolerability of TAF in KTRs.

⑰

HBV RNA 在預測慢性 B 型肝炎患者開始使用核苷（酸）類似物以及停藥後復發風險的角色

THE ROLE OF HBV RNA IN PREDICTING NUCLEOS(T)IDE ANALOGUES INITIATION AND RISK OF RELAPSE AFTER CESSATION IN PATIENTS WITH CHRONIC HEPATITIS B

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Background: The safe cessation of nucleos(t)ide analogues (NUCs) remains challenging in patients with chronic hepatitis B (CHB).
Aims: We aimed to investigate the potential role of novel biomarkers in predicting risk of NUCs initiation and off-therapy relapse.
Methods: From November 2020 to September 2023, we prospectively enrolled 133 CHB patients who did not receive NUCs as cohort 1, and 45 CHB patients who received NUCs and met cessation criteria as cohort 2. The correlation of novel biomarkers including quantitative hepatitis B surface antigen (qHBsAg), hepatitis B core-related antigen (HBcrAg) and hepatitis B virus RNA (HBV-RNA) was studied. Risk factors associated with suitability for National Health Insurance (NHI)-indicated antiviral therapy (cohort 1) and off-NUCs relapse (cohort 2) were also analyzed.
Results: The mean ages of cohort 1 and 2 were 53.4 and 58.9 years, respectively. 132 of 133 (99.2%) CHB patients were HBeAg-negative in cohort 1, and 13 of 45 (28.9%) CHB patients were HBeAg-positive in cohort 2. Hepatitis B virus DNA (HBV-DNA) and HBV-RNA were highly correlated ($r = 0.795$, $p < 0.001$), while qHBsAg and HBV-RNA were moderately correlated ($r = 0.485$, $p < 0.001$) in patients without antiviral therapy. During a median follow-up period of 37.8 months, 18 (13.6%) HBeAg-negative CHB patients in cohort 1 were eligible for NHI antiviral therapy. Baseline HBV-RNA ≥ 3 log (copies/mL) was associated with the risk of further antiviral therapy (HR = 2.910, $p = 0.047$). During a median follow-up of 21.2 months, 36 (80%) patients experienced virological relapse, and 31 (68.9%) patients experienced clinical relapse after discontinuation of NUCs in cohort 2. HBV-RNA ≥ 3 log at end of treatment (EOT) (HR = 2.258, $p = 0.025$) and off-treatment month 3 (HR = 2.227, $p = 0.021$), and HBcrAg ≥ 4 log (U/mL) at month 3 (HR = 2.558, $p = 0.009$) were associated with virological relapse. In contrast, HBcrAg ≥ 4 log at EOT (HR = 4.494, $p < 0.001$) and month 3 (HR = 9.349, $p < 0.001$) were factors associated with clinical relapse. The combination of HBV-RNA and HBcrAg levels significantly differentiated the risk of relapse after treatment, and the prognostic power of the prediction model at month 3 was better than that at EOT. Lastly, we found that kinetics changes in novel biomarkers after cessation of NUCs differed significantly between patients with or without off-treatment relapse.
Conclusions: HBV-RNA levels predict risk of NUCs initiation or relapse after treatment. The combination of HBV-RNA and HBcrAg can be used to identify patients who can safely discontinue NUCs therapy.

⑱

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 有較高的表面抗原下降和消失率

HBV GENOTYPE C IS ASSOCIATED HIGHER HBSAG DECLINE AND 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) decline and loss rate between HBV genotype B and genotype C after cessation of nucleos(t)ide analogues remain unclear.

Aims: To compare HBsAg decline and 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 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: A generalized estimating equations analysis showed that HBV genotype C exhibited larger post-treatment HBsAg declines than genotype B in both the overall patient group and propensity score (PS) matched patients (both, $p < 0.001$), including those without clinical relapse or retreatment after discontinuing entecavir or TDF therapy. A multivariate analysis showed that HBV genotype C was an independent factor of post-treatment HBsAg decline for all and PS matched HBeAg-negative patients. 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 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. Patients with HBV genotype C had a higher HBsAg loss rate than those with HBV genotype B among all and PS matched HBeAg-negative patients ($p = 0.001$). The Cox regression analysis showed that HBV genotype was an independent factor of HBsAg loss after adjusting for other factors.

Conclusions: HBeAg-negative patients with HBV genotype C infection have higher HBsAg decline and HBsAg loss rates than patients with HBV genotype B infection, after cessation of entecavir or TDF therapy in HBeAg-negative CHB patients.

主題：脂肪肝相關疾病

⑲

飲酒造成代謝功能障礙相關脂肪肝的診斷標準中不必要訂定酒精攝取量上限
UNNECESSARY UPPER LIMIT OF INCREASED ALCOHOL INTAKE FOR DIAGNOSTIC CRITERIA OF METALD

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Background: The diagnostic definition of increased alcohol intake for metabolic dysfunction-associated steatotic liver disease (MASLD) with increased alcohol intake (MetALD) is 210 to 420 grams per week for men and 140 to 350 grams per week for women.
Aims: Unlike the traditional definition of increased alcohol consumption, which does not impose an upper limit, this definition includes both lower and upper limits. The new criteria deserve validation.
Methods: Participants from Taiwan Biobank database after exclusion those with positive for HBsAg, anti-HCV, and former drinkers were selected. MASLD is defined as hepatic steatosis on liver ultrasound plus any of cardiometabolic risk factors (CMRF). MetALD* is defined as MASLD plus alcohol consumption exceeding 140 g/week for women and 210 g/week for men, which is a traditional definition. “MASLD with heavy alcohol consumption” is defined as MASLD plus alcohol consumption of >350 g/week for women and >420 g/week for men. The fibrosis 4 (FIB-4) score was used to assess the severity of liver fibrosis, and carotid plaques on duplex ultrasound were employed to diagnose atherosclerosis.
Results: In a total of 18,160 (mean age 55.28 ± 10.41; 33.2% males) participants, there were 7,316 (40.3%) MASLD patients, 209 (1.2%) MetALD*, and 130 (0.72%) patients. The participants with MetALD* were younger and male predominant. After propensity score matching for age and gender, MetALD* patients had higher AST, GGT, fatty liver index (FLI), and FIB-4 score and tended to have a higher proportion of carotid plaques than MASLD patients (Table 1). Compared with MASLD patients, MetALD patients have a higher proportion of males and tend to have younger age. After propensity score matching for age and gender, they had higher triglyceride, GGT, and FLI than MASLD patients. The proportion of carotid plaques and the level of FIB-4 score were comparable between two groups (Table 2). “MASLD with heavy alcohol consumption” patients had higher HDL levels than MetALD patients, The proportion of carotid plaques and the level of FIB-4 score were comparable between two groups (Table 3).
Conclusions: The inclusion of an upper limit for alcohol consumption in the diagnostic criteria for MetALD has drawbacks compared to the traditional definition of increased alcohol intake. It is recommended to adopt the traditional definition and remove the upper limit.

⑳

以進行減重手術之病態性肥胖大鼠模式探討飲食與運動模式對非酒精性脂肪肝進程之影響

EFFECTS OF DIETARY AND EXERCISE MODELS ON PROGRESSION OF NONALCOHOLIC FATTY LIVER DISEASE IN MORBIDLY OBESE RATS UNDERGOING BARIATRIC SURGERY

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Background: The global rise in metabolic syndrome, obesity, and diabetes has contributed to the increased prevalence of non-alcoholic fatty liver disease (NAFLD). Obesity, characterized by excessive fat accumulation, significantly contributes to NAFLD, posing a major public health concern due to its adverse effects on overall health. Treatment strategies for obesity include lifestyle modification of diets and exercise, pharmacotherapy, and bariatric surgery, with surgery being particularly effective for long-term weight control in morbidly obese patients.

Aims: This study aims to model NAFLD in morbidly obese rats and evaluate the effects of bariatric surgery, dietary changes, and exercise on liver pathology and lipid metabolism.

Methods: A total of 102 male Wistar rats (8 weeks old) with morbid obesity and fatty liver were used. After 14 weeks of diet induction, the rats underwent sleeve gastrectomy. Following surgery, they were subjected to 18 weeks of calorie-restricted diets (CRD), non-ketogenic low-carbohydrate diets (LCD), and exercise. Blood and liver samples were collected every 6 week period for analysis, including biochemical values and inflammation-related blood factors.

Results: At 18 weeks post-surgery, body weight in the high-fat diet (HFD) group continued to increase and remained significantly higher than in all other groups. The CRD group showed significantly lower body weight compared to the LCD group. After a 14-week diet induction for morbid obesity and fatty liver, liver weight, perirenal fat weight, and epididymal fat weight were significantly higher in the HFD group compared to the control group ($p < 0.05$ for all). At 18 weeks post-gastrectomy, no significant differences in liver weight were observed between the groups. In terms of blood biochemistry, after 14 weeks of diet induction, serum SGOT and SGPT levels were significantly higher in the HFD group compared to the control group ($p < 0.05$ for both). At 18 weeks post-surgery, SGOT, SGPT, and triglyceride (TG) levels in the HFD group were significantly lower than those at week 0 post-surgery ($p < 0.05$ for all). Histopathological liver analysis revealed that the HFD induced hepatic lipid accumulation and resulted in a significantly higher NAFLD score than the control group. Sleeve gastrectomy and dietary interventions reduced both lipid accumulation and NAFLD scores.

Conclusions: Sleeve gastrectomy improved liver fat and NAFLD-related biochemical markers in rat models. Among the dietary interventions, the calorie-restricted diet was more effective in reducing body weight and visceral fat compared to the non-ketogenic low-carbohydrate diet.

㉑

精瘦型和非精瘦型代謝功能障礙相關脂肪性肝病（MASLD）的臨床特徵
CLINICAL FEATURES OF LEAN AND NON-LEAN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

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Background: Metabolic-dysfunction assocciated steatotic liver disease (MASLD) has become one of the major causes chronic liver disease worldwide, with an incidence of approximately 15 to 30%. The prevalence of MASLD also increases in Taiwan. However, the clinical manifestation of lean and non-lean MASLD patients is insufficient.

Aims: The aim of this study is to evalute the clinical manifestation, body composition and fibrosis severity of lean and non-lean MASLD patient in Taiwan.

Methods: Patients with clinically diagnosed MASLD were consecutively enrolled. All of the patients were divided into lean (BMI < 23 kg/m²), non-lean (BMI ≥ 23 kg/m²) body mass. The clinical features, including anthropometric parameters, clinical and biochemical characteristics, body composition as well as fibrosis and steatosis severity were collected. Non-invasive assessment for hepatic fibrosis included fibroscan, M2BPGi and FIB-4 score. The data of body composition included body mass index (BMI), percent of body fat (PBF), body fat mass (BFM), skeletal muscle mass (SMM), fat tissue index (FTI) and lean tissue index (LTI). Statistical analyses were performed by chi-square test, Fisher's exact test, Student's t test.

Results: A total of 300 patients with MASLD were enrolled. There were 44 (14.7%) lean-MASLD and 256 (85.3%) were non-lean MASLD. There were no significant difference in terms of prevalence of DM, hypertension, chronic hepatitis B and C between two groups. The lean-MASLD were older (59.64 ± 7.84 y/o vs. 53.66 ± 11.8 y/o, P < 0.001), and had significantly higher ratio of female gender (61.36% vs. 32.03%, P = 0.001) and HDL levels (52.68 ± 13.04 mg/dl vs. 52.68 ± 13.04 mg/dl, P = 0.029), lower triglyceride levels (116.86 ± 58.49 mg/dl vs. 170.49 ± 243.47 mg/dl, P = 0.003), HOMA-IR (2.59 ± 1.90 vs. 3.61 ± 2.28, P = 0.007), lower proportion of cardiometabolic risk factors >3 (9.09% vs. 40.27%, P = 0.001) than non-lean MASLD. The non-invasive fibrosis assessment revealed that there was no difference in terms of M2BPGi and FIB-4 socre between the lean and non-lean MASLD patients. However, the non-lean MASLD had significantly higher elastrogrphy stiffness (5.10 ± 2.63 kPa vs. 4.44 ± 1.32 kPa, P = 0.022), controlled Attenuation Parameter (CAP) (305.57 ± 45.42 db/m vs. 267.92 ± 62.9 db/m, P = 0.001), the proportion of severe steatosis (>290 db/m) (61.69% vs.36.84%, P = 0.001) than lean MASLD. In subgroup analysis, there were 182 patients (33/18.1% lean MASLD and 149/81.9% non-lean MASLD) received body composition measurement by Inbody. The lean MASLD had significantly lower PBF (28.56 ± 6.76% vs. 34.08 ± 7.38%, P = 0.001), FTI (6.26 ± 1.63 kg/m² vs. 9.43 ± 2.70 kg/m², P < 0.0001) and LTI (8.77 ± 1.42 kg/m² vs. 10.07 ± 1.27 kg/m², P < 0.0001).

Conclusions: The prevalence of lean MASLD was 14.7% in our cohort. Non-lean MAFLD patients had more cardiometablic risk factors, higher HOMA-IR and higher elastrography stiffness than non-lean MASLD. The insulin resistance may promote hepatic inflammation and fibrosis in non-lean MASLD.

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代謝功能異常相關脂肪肝疾病的遺傳易感性：一項基於人群的全基因組關聯研究
GENETIC PREDISPOSITION OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE: A POPULATION-BASED GENOME-WIDE ASSOCIATION STUDY

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Background: Although metabolic dysfunction-associated steatotic liver disease (MASLD) has been proposed to replace the diagnosis of non-alcoholic fatty liver disease (NAFLD) with new diagnostic criteria since 2023.
Aims: The genetic predisposition of MASLD remains to be explored.
Methods: Participants with data of genome-wide association studies (GWAS) in the Taiwan Biobank database were collected. Patients with missing data, positive for HBsAg, anti-HCV, and alcohol drinking history were excluded. MASLD was defined if having hepatic steatosis on ultrasound, plus at least one of cardiometabolic criteria. The Taiwan biobank used two genetic chips during the period of data collection: Taiwan biobank version 1 (TWBv1) as the initial chip and TWBv2 specifically designed for the Taiwanese population. TWBv2 was used as test group and TWBv1 as validation group. NAFLD fibrosis score (NFS) was used to assess the degree of liver fibrosis, and carotid plaques on duplex ultrasound were employed for the diagnosis of atherosclerosis.
Results: In a total of 16,407 (mean age 55.35 ± 10.41; 29.6% males) participants, 6,722 (41.0%) had MASLD (Figure 1). Eleven single-nucleotide polymorphisms (SNP) were identified to be associated with MASLD (Figure 2). Their functions were exonic in two and intronic in nine (Table 1). They were related to the PNALA3, and SAMM50 genes located on chromosome 22. The linkage disequilibrium showed a high correlation with each other (Figure 3). Four SNPs of PNALA3 and SAMM50 genes had increased risk of MASLD and higher levels of AST/ALT. In addition, there was no association of these two genes with glucose metabolism, but better lipid profiles in SAMM50 (Table 2, 3).
Conclusions: This large GWAS study indicates that eleven SNPs of PNPLA3 and SAMM50 genes predispose the development of MASLD in Taiwanese population.

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腸道特異性剔除過氧化物酶體增殖物活化受體γ惡化脂肪肝小鼠之胰島素抗性
INTESTINAL PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA DEFICIENCY DETERIORATES INSULIN RESISTANCE IN MICE WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOSIS

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Background: Peroxisome proliferator-activated receptor gamma (PPARγ), is a highly expressed nuclear receptor in intestinal epithelium. Recent studies found that PPARγ agonist protected mice from intestinal inflammation in experimental colitis. Intestinal inflammation and bacterial translocation (BT) contributed to the progression of metabolic dysfunction-associated steatosis (MASH).
Aims: We aimed to investigate the impact of intestinal PPARγ on BT, liver injury and metabolic dysfunction.
Methods: Intestine-specific PPARγ knockout mice (PpargΔIEC) and control mice (Ppargfl/fl) were fed with fast food diet (FFD) to induce obesity, insulin resistance and MASH, or normal chow diet for 24 weeks.
Results: Mice fed with FFD displayed characteristics of MASH, including obesity, insulin resistance, liver steatosis, inflammation and fibrosis. Although PpargΔIEC mice and Ppargfl/fl mice had similar severity of liver injury on an FFD, intestine-specific PPARr deficiency increased gut permeability with increased serum LPS levels. Expression of tight junction proteins, including claudin-2 and occludin in small intestine and colon were reduced in PpargΔIEC mice through upregulation of iNOs. Intestinal expression of pro-inflammatory cytokine and chemokine were also increased in PpargΔIEC mice. In addition, PpargΔIEC mice had more severe insulin resistance compared to Ppargfl/fl mice with decreased phosphorylation of Akt and IRS-1 in skeletal muscle.
Conclusions: Intestinal PPARγ deficiency leads to intestinal inflammation, increased gut permeability and worsen insulin resistance in mice fed with FFD. Intestinal inflammation may be a therapeutic target of metabolic dysfunction in MASH.

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代謝異常相關脂肪肝病族群之地中海飲食遵從性與肝臟纖維化
ASSOCIATION BETWEEN ADHERENCE TO MEDITERRANEAN DIET AND LIVER FIBROSIS IN PEOPLE WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: Mediterranean diet has been well studied for its improvements in insulin resistance and hepatic steatosis. Positive association between Mediterranean diet and liver fibrosis in patients with non-alcoholic fatty liver disease had been reported in previous cross-sectional analyses using non-invasive scoring system.

Aims: We aim to evaluate the relationship between vibration-controlled transient elastography (VCTE) defined liver fibrosis and adherence to the Mediterranean diet among individuals with metabolic dysfunction-associated steatotic liver disease (MASLD). The potential influence on this association by the number of cardiometabolic factors will also be examined.

Methods: This cross-sectional study analyzed data from a nationally representative dataset from the National Health and Nutrition Examination Survey (NHANES) 2017 to March 2020, which included VCTE for the assessment of liver steatosis and fibrosis. We included participants aged 18 years or older who met the MASLD definition based on the latest nomenclature. First, we ensured they had complete controlled attenuation parameter (CAP), alcohol, and nutrient intake data. We then identified individuals with steatotic liver disease (CAP ≥ 248 dB/m). Those with MASLD must meet the criteria of at least one cardiometabolic risk factor and alcohol consumption less than 30 g/day for men and 20 g/day for women. Cardiometabolic factors were defined as: (1) body mass index ≥25 kg/m² (≥23 kg/m² in Asian ethnicity) or waist circumference >94 cm in man and >80 cm in woman, (2) HbA1c ≥ 5.7%, fasting plasma glucose ≥ 100 mg/dL or under the treatment of diabetes, (3) triglycerides ≥150 mg/dl or under lipid-lowering treatment, (4) high-density lipoprotein-cholesterol ≤39 mg/dL in man and ≤50 mg/dL in woman, (5) blood pressure ≥130/85 mmHg or under treatment for hypertension. For outcome measure, significant liver fibrosis was defined if liver stiffness measurement (LSM) was 8 kPa or higher. For predictor variable, participants' adherence to the Mediterranean diet was evaluated using NHANES dietary questionnaire data. Adherence was estimated using the aMED score, which ranges from 0 to 9, with higher scores reflecting greater adherence. Scores were grouped into three categories: 0–2, 3–4, and 5–9. Baseline descriptive analysis was performed, followed by multivariate logistic regression to examine the association between aMED score and significant liver fibrosis, after adjusting for age, sex, smoking status, and alcohol intake. Risk stratification for significant liver fibrosis was performed based on the number of cardiometabolic factors and different aMED score levels.

Results: Among 15,560 participants, a total of 3,600 MASLD individuals were identified. The MASLD sample consisted of 53.6% (n = 1928) males with a mean age of 52.4 ± 16.5 years. In these individuals, lower body mass index was observed with higher adherence to the Mediterranean diet ($p < 0.01$). Conversely, higher LSM values was detected in individuals with lower aMED scores, with mean LSM values of 7.01 ± 6.34 kPa, 6.91 ± 6.62 kPa, and 6.26 ± 4.42 kPa in the low, moderate, and high aMED score groups, respectively ($p < 0.05$). The proportion of participants with advanced fibrosis was also significantly higher in the low Mediterranean diet adherence group, at 18.9%, 16.2%, and 14.9% in the low, moderate, and high aMED score groups, respectively. When considering the number of cardiometabolic factors alongside Mediterranean diet adherence, a joint effect was observed in evaluating the risk of advanced liver fibrosis; the proportion of significant fibrosis was 4.4% in the high aMED score group with 1 cardiometabolic risk factor, compared to 24.4% in the low aMED score group with 4 to 5 cardiometabolic risk factors. In the crude analysis, high aMED score group demonstrated a significant lower risk of advanced fibrosis compared to the low aMED score group (cOR: 0.75, 95% CI: 0.60–0.95, $p = 0.016$). In the multivariate analysis, this association remained statistically significant after adjusting for age, sex, smoking status, and alcohol intake (aOR: 0.77, 95% CI: 0.60-0.99, $p = 0.039$).

Conclusions: In individuals with MASLD, those with higher adherence to the Mediterranean diet may have a lower risk of advanced liver fibrosis. Additionally, increasing number of cardiometabolic factors may also have an additive effect on the risk of advanced fibrosis in these individuals.

主題：膽胰疾病（一）

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使用抗血小板藥物患者進行 ERCP 時，內視鏡乳頭球囊擴張術的有效性與安全性研究
EFFECTIVENESS AND SAFETY OF ENDOSCOPIC PAPILLA BALLOON DILATION IN ERCP: FOCUS ON PATIENTS UNDER ANTIPLATELET THERAPY

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Background: Antiplatelet agents are widely used for the prevention of cardiovascular and cerebrovascular events but pose challenges in endoscopic procedures due to bleeding risks. Patients undergoing endoscopic sphincterotomy (EST) while on antiplatelet therapy are at increased risk of post-procedural bleeding. Alternative strategies, such as postponing EST or placing an initial biliary stent followed by a second ERCP, may mitigate this risk but extend hospitalization and increase complications. Endoscopic papillary balloon dilation (EPBD), associated with low bleeding rates, may serve as an alternative for this patient group.

Aims: To evaluate the safety and effectiveness of EPBD for patients undergoing ERCP while on antiplatelet therapy.

Methods: We conducted a retrospective review of patients who underwent ERCP between January 2020 and March 2023. All patients with a naïve papilla who received EPBD were included. Data on patient characteristics and endoscopic findings were collected. The antiplatelet group included patients who underwent ERCP without a 7-day discontinuation of antiplatelet agents, contrary to guidelines recommending cessation before high-risk procedures. Difficult cannulation was defined as a cannulation time exceeding 5 minutes, and dilation with a balloon diameter >1.2 cm was classified as endoscopic papillary large-balloon dilation (EPLBD). ERCP-related complications were defined according to the 1991 consensus guidelines.

Results: A total of 61 patients underwent EPBD, 42.6% of whom were male, with a mean age of 66.7 ± 16.3 years. Nine patients had end-stage renal disease (ESRD). The primary indication for EPBD was biliary stone removal (approximately 90%). Difficult cannulation occurred in 30% of cases, and EPLBD was performed in 11%. Stone clearance was unsuccessful in 2 cases due to multiple large stones. Post-ERCP pancreatitis occurred in 3.3%, and acute bleeding was observed in 85.2% of cases, though only 1 ESRD patient experienced delayed bleeding. Minimal ERCP-related complications were reported, with a single case of cholangitis. No delayed bleeding occurred in the antiplatelet group, and no significant differences in outcomes were observed between patients on and off antiplatelet therapy.

Conclusions: Endoscopic papillary balloon dilation is a safe and effective technique for ERCP, even in patients who cannot adequately discontinue antiplatelet therapy.

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困難膽管插管患者中經胰管支架輔助後括約肌切開術與括約肌整形術之比較
A COMPARISON BETWEEN SPHINCTEROTOMY AND SPHINCTEROPLASTY OVER PANCREATIC DUCT STENTS IN PATIENTS WITH DIFFICULT BILIARY CANNULATION

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Background: When endoscopic retrograde cholangiopancreatography (ERCP) is performed, unintended contrast medium or guide wire entrance to the pancreatic duct more than one time increases the risk of post ERCP pancreatitis (PEP). Wire-guided biliary cannulation and a pancreatic duct stent could increase biliary cannulation success and prevent PEP. Then, needle knife sphincterotomy (NKST) or balloon dilation sphincteroplasty (BDSP) over the pancreatic stent can be applied for biliary cannulation, stone retrieval or biliary stenting.

Aims: This study aimed to compare the success rates of biliary cannulation, incidence of PEP, and procedure-related bleeding between the NKST and BDSP techniques performed over pancreatic stents.

Methods: From August 2018 to July 2024, 2309 patients who received ERCP and 227 (9.8%) patients with pancreatic duct stent placement were enrolled. Finally, 109 patients in the NKST group and 80 patients in the BDSP group were included in the analysis. In this study, successful biliary cannulation was defined as successful biliary sphincterotomy or sphincteroplasty. The study also analyzed factors such as procedure-related bleeding, PEP incidence, and the retention status of pancreatic stents using univariate and multivariate logistical regression analyses.

Results: Although the success rate was higher in the NKST group (84/109, 77.1%; overall 95/109, 87.1%) than in the BDSP group (66.3%, 53/80; overall 66/80, 82.5%), no significant difference in success rates was found between the NKST and BDSP groups ($p > 0.05$). According to the univariate analysis, success was negatively correlated with procedure-related bleeding ($\rho = -0.153$, $p = 0.036$). PEP was positively correlated with procedure-related bleeding ($\rho = 0.189$, $p = 0.009$). Multivariate analysis between the success rate and other factors, including age, sex, the use of a unilateral or bilateral flanged stent, the use of an NKST or BDSP, the cannulation time, the presence of an active duodenal ulcer and the presence of a periampullary diverticulum, revealed that there was no significant difference according to logistical regression analysis. Post-ERCP pancreatic stent retention for more than 4 weeks was found in 23 patients (23/122, 18.9%). The major reasons for pancreatic stent retention for more than 4 weeks were patients lost to outpatient follow-up or surgeons not being reminded to check the status of the pancreatic stents following cholecystectomy.

Conclusions: Conclusive wire guidance and pancreatic stent placement could prevent PEP. Over a pancreatic stent, both the NKST and BDSP could be performed for biliary stone retrieval. Biliary cannulation success and procedure-related bleeding or pancreatitis were comparable between the NKST and BDSP groups. The status of stent dislodgement or retention was checked, especially for patients receiving bilateral flanged pancreatic duct stent placement.

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比較胰管鏡碎石和 Frey 手術治療困難胰管結石的臨床成效：一醫學中心的經驗

CLINICAL OUTCOMES OF PANCREATOSCOPY-ASSISTED LITHOTRIPSY AND FREY SURGERY 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). Extracorporeal shock wave lithotripsy (ESWL) and surgery including Frey operation are the main treatment for such difficult pancreatic duct stones. Recently, pancreatoscopy-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 pancreatoscopy-assisted lithotripsy and Frey surgery in patients with difficult pancreatic duct stones.

Methods: From January, 2018 to December, 2024, a total of 18 (15 male and 3 female) consecutive patients, 51 (38–71) years old, with large and/or impacted pancreatic duct stones undergoing single-operator pancreatoscopy-assisted lithotripsy using EHL and/or LL, and 14 (10 male and 2 female) consecutive patients, 48 (33-62) years old, undergoing Frey surgery in a medical center were retrospectively analyzed. Clinical outcomes including stone size, lithotripsy and surgery procedures, ductal clearance, complications, and length of hospital stay were evaluated.

Results: In the group of pancreatoscopy-assisted lithotripsy, 16 (89%; 16/18) patients were successfully treated in 27 (median 1; range 1-3) sessions including LL (n = 16) and EHL (n = 11) to achieve ductal clearance (Clinical success). The technical success rate was 94% (17/18). Eleven (61%; 11/18) patients with pancreatic duct stones were successfully treated at the first session of pancreatoscopy-assisted lithotripsy. The median procedure time was 1.1 (0.6–2.5) hours. After the procedure, mild pancreatitis occurred in 4 (22%; 4/18) patients. The median length of hospital stay was 4.0 (1.0–11.0) days. In the group of Frey surgery, 11 (78.6%; 11/14) patients underwent the surgery successfully. The median procedure time was 5.7 (3.7–7.5) hours. Adverse events after Frey surgery occurred in 3 (21.3%; 3/11) patients, including intra-abdominal abscess, peritonitis and bacteremia, respectively. The median length of hospital stay was 15.5 (7.0–58.0) days.

Conclusions: Pancreatoscopy-assisted lithotripsy is an effective and safe modality for difficult pancreatic duct stones. Comparing with Frey surgery, endoscopic lithotripsy provides a minimally invasive therapy and can be a first-line treatment for selective patients with difficult pancreatic duct stones.

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內視鏡超音波導引下酒精注射或射頻燒融對於胰臟胰島素瘤的安全性與有效性分析
THE SAFETY AND EFFECTIVENESS OF ENDOSCOPIC ULTRASOUND GUIDED ETHANOL INJECTION THERAPY OR RADIOFREQUENCY ABLATION FOR PATIENTS WITH PANCREATIC INSULINOMA

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Background: Endoscopic ultrasound (EUS) guided tumor injection therapy is emerging as a safe and effective treatment for pancreatic neuroendocrine tumors. We aimed to analyze our data of EUS-guided radiofrequency (RFA) and ethanol injection (EI) for the treatment of pancreatic insulinoma (PI).
Aims: To assess the safety and efficacy of EUS guided RFA or ethanol injection therapy for patients with PI.
Methods: A total of 9 patients with pancreatic insulinoma underwent EUS guided intervention from 2015 to 2024 in our hospital. All patients received EUS guided FNA for tissue proof and the grading of all tumors is grade 1 according to the WHO classification. Before 2023-11, a total of five patients received EI therapy. The ethanol concentration is 99.5% and the injected volume estimated summation of long and short radius divided by two. Since 2023-12, due to the advent of RFA catheter and approved in Taiwan for therapy of pancreatic tumor, EUS guided RFA is applied on four patients. The EUSRATM catheter is made by Taewoong Co., Korea. We use 19 Gauge needles 1 or 0.5 cm in length, which needle to use is decided upon the tumor size. The ablation time depends upon the controlled energy. Ultrasound contrast agent, Sonazoid, is used before and after ablation to evaluate whether effect is adequate or not. The hypo- or no-enhancement pattern of tumor after treatment was thought to be complete.
Results: The gender ratio of male to female is 4:5. The tumor size is 10.6 ± 2.3 mm in diameter. The ablation time of EI is 70.6 ± 6.5 seconds, whereas the RFA time is 166.8 ± 16.8 seconds. All patients have reached normalized blood sugar; however, two EI group patients need two sessions of injections. Each group has one adverse event of pancreatic pseudocyst. These two patients recovered completely after supportive management.
Conclusions: EUS guided tumor injection therapy is a safe and effective treatment for pancreatic insulinoma. In comparison with EI, RFA costs longer ablation time. No major adverse event occurs.

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機器學習發展之膽管癌患者存活分析與風險分級
MACHINE LEARNING-BASED SURVIVAL ANALYSIS AND RISK STRATIFICATION FOR PATIENTS WITH CHOLANGIOCARCINOMA

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Background: Patients with cholangiocarcinoma (CCA) have relatively dismal outcomes, and the prognostic factors for CCA is not fully elucidated till now. There is no universally applicable predictive tools for CCA.
Aims: To identify prognostic factors for patients with CCA and assess the performance of novel machine learning (ML)-based survival analysis models in predicting outcomes and stratifying risk.
Methods: A total of 693 treatment-naïve CCA patients diagnosed at Taipei Veterans General Hospital from 2014 to 2022 were retrospectively analyzed. Patients were randomly divided into a training cohort (n = 485) and a validating cohort (n = 208). The primary endpoint was overall survival (OS). Non-invasive biomarkers and image features obtained at diagnosis were analyzed using a Cox proportional hazards model to identify independent prognostic factors. Prognostic models were developed in the training cohort using Extreme Gradient Boosting (XGBoost), Random Survival Forest (RSF), Decision Tree (DT), and Logistic Regression (LR). Model performance was validated in the validation cohort and compared based on predictive accuracy. Shapley Additive Explanations (SHAP) were used to identify key predictors in the ML-based models. Kaplan-Meier (KM) survival analysis was performed to validate the ability of the models to stratify patient risk groups.
Results: After a median follow-up of 33.0 months (interquartile range 29.6–36.4 months), 480 patients had died, with a 5-year OS rate was 12.0%. Independent risk factors for OS included advanced tumor stage, intrahepatic CCA, lack of treatment, non-surgical modalities, prothrombin time international normalized ratio (PT INR), serum cancer antigen 19-9 (CA 19-9) levels, serum gamma-glutamyl transpeptidase (GGT) levels, albumin-bilirubin (ALBI) grade, and fibrosis-4 (FIB-4) grade. Among

the models, RSF demonstrated the best performance in predicting OS (AUROC 0.791, 95% CI: 0.717–0.865), outperforming XGBoost, DT, and LR. SHAP analysis highlighted surgery, advanced tumor stage, absence of treatment, serum GGT, and CA 19-9 levels as the top five predictors in the RSF model. KM survival analysis confirmed the RSF model's robust ability to stratify patients into distinct risk groups ($p < 0.001$).

Conclusions: Machine learning-based survival analysis, particularly the Random Survival Forest, provided accurately prognostic predictions and risk stratification for CCA patients. These tools could support individualized treatment planning and optimize disease management strategies.

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腎功能不全會增加延遲性內視鏡壺腹切開後出血反覆內視鏡止血的發生率

RENAL INSUFFICIENCY INCREASES THE INCIDENCE OF REPEATED ENDOSCOPIC HEMOSTASIS FOR DELAYED POST-ENDOSCOPIC SPHINCTEROTOMY BLEEDING

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Background: Delayed post-endoscopic sphincterotomy bleeding occurred around 1%–3% in ERCP, and endoscopic hemostasis is the first line therapy. However, situations sometimes occur that require repeated endoscopy to stop bleeding.

Aims: To identify the risk factor of repeated endoscopic hemostasis for delayed post-endoscopic sphincterotomy bleeding.

Methods: We retrospectively reviewed the medical records of 109 patients who had been treated by endoscopic hemostasis for delayed post-endoscopic sphincterotomy bleeding between April, 2015 and March, 2024. The patient characteristics and laboratory data before and after sphincterotomy and the way of endoscopic hemostasis, including age, gender, underlying diseases, biochemistry data, severity of bleeding, mono or duel hemostasis therapy, and endoscope type, were analyzed to identify the risk factors of repeated endoscopic hemostasis.

Results: A total of 4904 patients underwent endoscopic sphincterotomy and 109 (2.2%) patients who suffered post-endoscopic sphincterotomy bleeding received endoscopic hemostasis therapy. Twenty-five (23%) patients underwent endoscopic treatment more than once. Univariate analysis revealed that renal insufficiency (GFR <30 or dialysis), low hemoglobin before ERCP and initial bleeding severity were significant predictors of re-bleeding, and by multivariate analysis, renal insufficiency (OR: 4.32, $p = 0.009$), bleeding severity (OR: 4.33, $p = 0.029$) and mono hemostasis therapy (OR: 3.02, $p = 0.052$) were the independent risk factors. There were no patients requiring further trans-arterial embolization or surgical intervention, though one patient died of bleeding because of underlying decompensated liver cirrhosis.

Conclusions: Renal insufficiency, bleeding severity and mono hemostasis therapy are the risk factors of failed endoscopic hemostasis therapy for post-endoscopic sphincterotomy bleeding. Duel or combined hemostasis therapy should be considered when delayed post-endoscopic sphincterotomy bleeding occurred.

主題：上消化道疾病（二）

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介於 1.5 與 2.0 公分被視為胃基質瘤的胃黏膜下病灶的病理組織分析
THE HISTOLOGY OF GASTRIC SUBEPITHELIAL LESIONS CONSIDERED AS GASTROINTESTINAL STROMAL TUMORS WHICH SIZE BETWEEN 1.5 CM AND 2 CM

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Background: Subepithelial lesions are divided into benign subepithelial and potentially malignant gastrointestinal stromal tumors. It is difficult to distinguish benignancy from malignancy between these tumor types.
Aims: To evaluate the malignant potential of patients with gastric subepithelial lesions (GSEL) which size between 1.5 cm and 2 cm by contrast-enhanced harmonic (CEH) endoscopic ultrasonography (EUS) and fine needle aspiration/biopsy (FNB).
Methods: A total of 16 patients with GSEL underwent CEH-EUS with histological evaluation. We use Sonazoid 0.015ml/Kg for contrast-enhanced hormonic EUS assessment. Three patients received EUS/FNB and followed by surgery, another received endoscopic biopsy and then surgical removal, and the other eleven patients underwent EUS/FNB only. The puncture needles used are ProCore 20G, Cook Co., Salem, or Acquire 22G, Boston Sci Co., USA. The malignant potential was assessed according to the modified Fletcher classification system. The clinical characteristics and EUS/CEH-EUS features were recorded.
Results: The gender ratio of male to female is 6:10. The tumor size is 17.6 ± 4.7 mm in diameter. One SEL is an aberrant pancreas, two are leiomyoma, two histology none made and the other eleven SELs are GIST. Hyper-enhancement vascular pattern is observed in the fifteen SELs from the 4th layer of stomach wall. Heterogeneous perfusion echogenicity was also observed in the fifteen SETs from the 4th layer of stomach wall. The CEH-EUS of aberrant pancreas is iso-enhancement and homogeneous echogenicity. The malignant potential of all eleven GISTs is very low risk.
Conclusions: Not all GSELs, which are sizes larger than 15 mm, are GISTs. Histological evaluation is important before endoscopic or surgical removal.

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投予利多卡因噴霧後進行胃鏡插入的最佳時機：隨機對照試驗
THE OPTIMAL TIMING OF THE ENDOSCOPE INSERTION AFTER ORAL LIDOCAINE SPRAY: A RANDOMIZED CONTROLLED TRIAL

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Background: Esophagogastroduodenoscopy (EGD) is a critical diagnostic tool for assessing upper gastrointestinal disorders, yet it can induce significant discomfort due to gag reflexes and pain. For patients with a higher risk for sedation, topical lidocaine spray at the hypopharynx is an alternative method. Yet, no standardized protocol exists regarding the optimal waiting period between administering lidocaine spray and commencing EGD.
Aims: This study investigates the optimal waiting time between the application of topical lidocaine spray and the initiation of EGD to enhance patient comfort and procedural efficacy.
Methods: Conducted as a single-center randomized controlled trial at our hospital, the research involved 160 patients who were divided into two groups based on waiting times of 1 minute or 3 minutes post-lidocaine application. Both objective and subjective discomfort levels were evaluated during the procedure. Objective discomfort assessment included the elevation of heart rate and systolic blood pressure. Subjective discomfort assessment included throat pain, nausea sensation, and abdominal fullness recorded from the patient's questionnaire.
Results: The study indicated that a 3-minute wait significantly reduced both objective measures of discomfort, such as heart rate and blood pressure elevations, and subjective discomfort ratings, including throat pain and nausea. Furthermore, patients in the 3-minute group expressed a lower willingness to undergo future sedated endoscopies, highlighting the importance of minimizing sedation-related risks in high-risk populations.
Conclusions: The study findings suggest that extending the waiting period after lidocaine administration improves patient outcomes during EGD, advocating for a standardized protocol of 3 minutes to optimize analgesia and procedural comfort.

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糖尿病患者的症狀是否能預測胃排空延遲：重新探討胃輕癱的多中心研究
CAN SYMPTOMS PREDICT DELAYED GASTRIC EMPTYING IN DIABETIC PATIENTS: A MULTICENTER STUDY TO REVISIT GASTROPARESIS

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Background: The relationship between the subjective Gastroparesis Cardinal Symptom Index (GCSI) and delayed gastric emptying in diabetic patients remains uncertain.

Aims: This study aimed to assess whether specific symptoms from the GCSI could predict delayed gastric emptying and to establish the prevalence of gastroparesis (GP) in this population.

Methods: Diabetic patients were recruited from a multicenter prospective cohort. Each participant underwent esophagogastroduodenoscopy, symptom assessment using the GCSI, and solid-meal gastric emptying scintigraphy (GES). GP was defined by GES data showing a T1/2 of 85 minutes and/or gastric retention of 8% at 3 hours.

Results: Among 138 diabetic patients, those with abnormal GES results were notably younger (mean age 54.55 years vs. 60.50 years, $p = 0.028$), had a higher incidence of nephropathy (51.72% vs. 22.02%, $p = 0.001$), and lower albumin levels (3.91 g/dL vs. 4.18 g/dL, $p = 0.009$). Cardinal symptoms such as nausea ($p = 0.011$), vomiting ($p = 0.004$), stomach fullness ($p = 0.001$), fullness after meals ($p = 0.024$), and loss of appetite ($p = 0.043$) were more prevalent in patients with abnormal GES. A higher overall GCSI score was found to independently predict delayed gastric emptying ($p = 0.028$) in multivariate analysis. The area under the receiver operating characteristic curve for the GCSI in predicting GP was 0.672, with an optimal cut-off value of 1.78 (sensitivity 79.31%, specificity 49.54%). The prevalence of GP, defined by both GCSI ≥ 1.78 and abnormal GES, was 16.67%.

Conclusions: Diabetic patients exhibiting symptoms such as nausea, vomiting, stomach fullness, fullness after meals, and loss of appetite should be considered for GES evaluation, as the overall GCSI score independently predicts delayed gastric emptying. This study suggests that the GCSI may be useful as a screening tool rather than a diagnostic method for diabetic gastroparesis.

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使用 GLP-1 RA 之肥胖患者的胃食道逆流風險：一項比較 BMI ≥40 與 BMI 25~40 族群的世代研究

COMPARATIVE RISKS OF GERD IN OBESE PATIENTS USING GLP-1 RECEPTOR AGONISTS: A PROPENSITY-MATCHED POPULATION-BASED STUDY OF PATIENTS WITH OBESITY (BMI ≥40) VS. LESS OBESE PATIENTS (BMI 25~40)

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Background: GLP-1 receptor agonists (GLP-1 RA) are widely prescribed for the management of both diabetes and obesity. However, there is a growing concern regarding their potential to induce gastroesophageal reflux disease (GERD), particularly in obese individuals, who are already at a higher risk for GERD and non-erosive reflux disease (NERD). However, real-world data comparing their safety profiles of are limited.

Aims: This study aimed to investigate the potential risk of developing GERD and NERD in obese patients (BMI ≥40) undergoing treatment with GLP-1 RA, compared to less obese patients (BMI 25 ~ 40) who are also treated with the same medications.

Methods: This research employed a population-based cohort study utilizing de-identified data from the TriNetX database, which encompasses over 117 million U.S. patients. The study population included nearly one million individuals with obesity or overweight who were undergoing GLP-1 RA treatment. Patients with a prior history of gastrointestinal cancers, GERD, or any previous gastric surgery were excluded. Participants were divided into two groups: an obese group (BMI ≥40) and a less obese group (BMI 25 ~ 40). Propensity score matching (PSM) was employed to balance the two cohorts, considering demographics, comorbidities such as type 2 diabetes, hypertension, and hyperlipidemia, smoking status, baseline characteristics, such as age, sex, and the use of proton pump inhibitors. The primary outcomes assessed were the incidence of both GERD and NERD. Logistic regression models were used to estimate relative risks (RR) and their corresponding 95% confidence intervals (CIs).

Results: After adjusting for confounders, the study results indicated that patients with a BMI ≥40 had a slightly higher risk of developing both GERD (RR: 1.157; 95% CI: 1.109, 1.206) and NERD (RR: 1.162; 95% CI: 1.114, 1.211) compared to patients with a BMI between 25 and 40.

Conclusions: In conclusion, this study suggests that obese patients with a BMI greater than 40 taking GLP-1 RA medications may have a slightly higher risk of developing GERD and NERD compared to patients with a less obese patients (BMI 25 ~ 40) on the same medication. The differences, though statistically significant, were relatively small. These findings highlight the importance of monitoring for GERD and NERD in obese patients using GLP-1 RA medications. Long-term follow-up studies are warranted to validate the findings.

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優化胃黏膜腸化生的內視鏡風險分級
OPTIMIZING THE ENDOSCOPIC RISK STRATIFICATION FOR ADVANCED GASTRIC INTESTINAL METAPLASIA

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Background: Gastric intestinal metaplasia (IM), a precancerous lesion, requires precise assessment for surveillance. The Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) staging system, based on histopathology, is the international standard for IM risk stratification. ESGE guidelines recommend endoscopic surveillance for advanced IM (OLGIM stages 3/4). Developed as a substitute, the Endoscopic Grading of Gastric Intestinal Metaplasia (EGGIM) score assesses IM across five gastric regions using a 30% threshold. However, its performance remains unrefined.

Aims: To optimize the EGGIM scoring system by refining threshold criteria and incorporating IM morphology.

Methods: In this retrospective cohort study, patients undergoing structured gastroscopy at the National Taiwan University Cancer Center were analyzed from February 2022 to September 2024. EGGIM scoring used high-resolution white-light and narrow-band imaging, with histopathological confirmation per the updated Sydney protocol. The original EGGIM score (0–10) from five gastric regions using a 0–2 scale (0: no IM; 1: focal IM <30%; 2: diffuse IM ≥30%) was simplified by combining the highest scores from two antral and two body locations, along with the angle score (total score 0–6). The refined EGGIM score (0–15) expands the original to a 0–3 scale (0: no IM; 1: IM <30%; 2: 30%–60%; 3: ≥60%). Additionally, IM morphologies (small patches, large patches, and carpet-like lesions) were incorporated into the analysis. Based on histopathologically defined advanced IM, the diagnostic accuracy of the refined and simplified scores was compared to the original EGGIM score.

Results: Among 944 patients (56% female; median age: 64 years), 6% (64/944) had pathological proven advanced IM (OLGIM stage 3 and 4). The refined EGGIM score achieved an AUC of 0.82 for predicting advanced IM, compared to the original EGGIM score with AUC of 0.83 (p = 0.42). The simplified EGGIM score (AUC 0.80) performed similarly to the original (AUC 0.83; p = 0.96), reducing false positives at an optimal cutoff (≥4 vs. ≥5). Incorporating morphology into the EGGIM score yields an AUC of 0.86 in a random forest model, compared to 0.89 for the original EGGIM score (p = 0.27). Feature importance analysis highlights the original EGGIM score as the most predictive variable (0.786) over morphology-based factors.

Conclusions: While neither detailed refinement on area cutoffs nor morphology outperformed the original, the simplified EGGIM score offers similar accuracy while reducing false positives, providing a practical alternative for advanced IM assessment.

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水下法與傳統內視鏡黏膜下剝離術治療胃腸道間質瘤的比較：一項前導研究
UNDERWATER VERSUS CONVENTIONAL ENDOSCOPIC SUBSEROSAL DISSECTION FOR GASTRIC GASTROINTESTINAL STROMAL TUMORS: A PILOT STUDY

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Background: Gastric gastrointestinal stromal tumors (GISTs) are potentially malignant and endoscopic resection has been recommended as an alternative option for gastric GISTs <20 mm and remains challenging if the tumor size >30 mm. The water pressure method (WPM) is a technique to improve submucosal visualization and overcome difficult locations or severe fibrosis.

Aims: This study aims to evaluate the efficacy and safety of endoscopic subserosal dissection (ESSD) with WPM for gastric GISTs when compared to conventional ESSD techniques.

Methods: Between March 2020 to December 2024, patients with gastric GISTs who underwent ESSD at our tertiary medical center were retrospectively reviewed. The patients were divided into two groups with one group receiving underwater ESSD with the WPM while the other group underwent conventional ESSD. The clinicopathologic characteristics, endoscopic characteristics, and therapeutic outcomes including adverse events were analyzed.

Results: A total of 21 patients were enrolled with the overall technical success 100% in both groups. The mean specimen size were 12.6 ± 7.7 mm and the mean procedure times were 99.2 ± 7.7 minutes. The en-bloc resection rates were 80% for those receiving ESSD with WPM (Group1) and 87.5% for the conventional ESSD (Group2) while R0 resection was 80% and 56.25%, respectively. The rate of conversion to endoscopic full-thickness resection (EFTR) was 0% in Group 1 and 37.5% in Group 2. The procedure-related perforation rates were 0% in Group 2 and 50% in Group 2, respectively. In univariate analysis, the conventional ESSD demonstrated a higher en-bloc resection rate (OR: 1.75, 95% CI: 0.12–24.65), but a lower margin-free resection rate (OR: 0.36, 95% CI: 0.03–3.56). Regarding EUS growth patterns, the exophytic pattern was associated with lower margin involvement (OR: 0.54, 95% CI: 0.08–3.76) and fewer complications (OR: 0.42, 95% CI: 0.07–2.66), although none of these were statistically significant.

Conclusions: For patients with gastric GISTs, ESSD with WPM is a safe and feasible treatment that offers a higher margin-free resection when compared to the conventional group.

主題：肝硬化及其他肝病

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褪黑激素重新編程因母體暴露於高脂飲食和微塑膠而引起的雄性幼崽的肝損傷
MELATONIN REPROGRAM LIVER INJURY IN MALE PUPS CAUSED BY MATERNAL EXPOSURE TO A HIGH-FAT DIET AND MICROPLASTICS

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Background: Prenatal exposure to a high-fat diet (HFD) or microplastics can impact liver fat accumulation in offspring.
Aims: This study examines the protective effects of prenatal melatonin on liver injury in male offspring caused by maternal exposure to a high-fat diet and microplastics.
Methods: Pregnant Sprague-Dawley rats were fed either an HFD or a normal chow diet, with some addi-tionally exposed to microplastics alone or in combination with melatonin. Male pups were eval-uated on postnatal day 7.
Results: Results indicated that pups in the HFD-microplastics group (HFD-H) exhibited increased liver lipid accumulation (observed in histological staining), apoptosis (elevated cleaved caspase 3, phospho-AKT, and TUNEL staining), inflammation (higher IL-6 and TNF-α), and oxidative stress (elevated malondialdehyde). Conversely, melatonin treatment (HFD-H+M) significantly reduced these effects, including lipid accumulation, apoptosis, and inflammation, while enhancing anti-oxidant enzyme glutathione peroxidase activity and improving lipid metabolism (reduced SREBP-1 expression).
Conclusions: These findings suggest that melatonin mitigates liver injury caused by maternal HFD and mi-croplastics through its anti-inflammatory, antioxidative, and lipid-regulating properties, under-scoring its potential hepatoprotective role.

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肝硬化患者之β受體阻斷劑反應者的血清代謝物能降低膽管結紮肝硬化大鼠的門脈壓力及肝纖維化
SERUM METABOLITE FROM BETA-BLOCKER RESPONDERS IN CIRRHOSIS REDUCES PORTAL PRESSURE AND LIVER FIBROSIS IN BILE DUCT LIGATION CIRRHOTIC RATS

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Background: Nonselective β-blockers (NSBBs) are widely used to prevent esophageal variceal bleeding in cirrhosis. Our research identified distinct differences in serum metabolite levels between NSBB responders and non-responders among patients with cirrhosis and high-risk esophageal varices before treatment. Notably, the metabolite phenylbutazone (PBZ) was elevated in responders but decreased in non-responders following NSBB use.
Aims: This study aimed to investigate the effects of PBZ on portal hemodynamics and its therapeutic potential in cirrhotic models.
Methods: Rat T6 hepatic stellate cells were treated with various concentrations of PBZ to assess its antifibrotic effects in vitro. In vivo, male Sprague-Dawley rats underwent bile duct ligation (BDL) or sham surgery to induce cirrhosis. PBZ was administered at doses of 1 mg/kg and 10 mg/kg, or a vehicle control, for two weeks. Hemodynamic examinations were then performed for assessment of the portal pressure.
Results: In vitro, PBZ treatment significantly reduced TGF-β1-induced expression of fibrosis markers, including collagen 1α1 and α-SMA, in T6 cells at concentrations ranging from 10^{-6} M to 10^{-4} M. In vivo, PBZ significantly decreased portal pressure in BDL rats at both 1 mg/kg and 10 mg/kg compared to vehicle-treated controls. Though there were no significant differences in liver fibrosis markers observed between PBZ-treated and vehicle-treated BDL rats on Sirius Red staining for collagen, Western blot analysis showed a reduction of α-SMA protein expression in PBZ-treated BDL rats. However, serum AST and ALT levels were unaffected by PBZ treatment.
Conclusions: PBZ reduced portal pressure in BDL cirrhotic rats. PBZ may be a potential therapeutic agent for treatment of portal hypertension.

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預防性抗生素對肝硬化患者接受選擇性胃靜脈曲張硬化術的療效：一項隨機對照試驗
EFFICACY OF PROPHYLACTIC ANTIBIOTICS IN ELECTIVE GASTRIC VARICEAL OBTURATION FOR PATIENTS WITH CIRRHOSIS: A RANDOMIZED CONTROLLED TRIAL

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Background: Antibiotic prophylaxis is a cornerstone in managing acute variceal bleeding in cirrhotic patients. However, its role in patients undergoing elective gastric variceal obturation (GVO) without acute gastric variceal bleeding (GVB) remains unclear.
Aims: This randomized trial aimed to evaluate the benefit of prophylactic antibiotics in this population.
Methods: Cirrhotic patients with gastric varices but without acute GVB, scheduled for elective GVO, were prospectively enrolled at Taipei Veterans General Hospital. Patients were randomized 1:1 to receive prophylactic antibiotics (ertapenem 1 g IV 30 minutes before GVO) or no antibiotics. The primary outcome was the incidence of bacteremia within 24 hours post-GVO. Secondary outcomes included infection, GVB, and overall survival within two months post-GVO.
Results: Between November 2019 and December 2023, 62 patients were randomized equally into antibiotic (n = 31) and control (n = 31) groups. Of these, 19.3% had concurrent hepatocellular carcinoma (HCC). Baseline characteristics were similar between groups, and all patients completed the assigned treatments successfully. Blood cultures at 30 minutes, 4 hours, and 24 hours post-GVO were negative in both groups. Cumulative incidences of infection (p = 0.160) and GVB (p = 0.609) within two months were not significantly different between groups. Multivariate analysis identified concurrent HCC as the only independent risk factor for post-GVO infection (HR 13.414, 95% CI 1.412–127.399, p = 0.024) and GVB (HR 8.880, 95% CI 1.144–68.922, p = 0.037). No deaths occurred in either group within two months post-GVO.
Conclusions: Prophylactic antibiotic administration does not confer additional benefits for cirrhotic patients undergoing elective GVO without acute GVB. Concurrent HCC is the primary independent risk factor for post-GVO infection and GVB.

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在不同酒精暴露下的脂肪性肝病的肝病嚴重性和心血管風險－台灣的一項全國性研究
LIVER DISEASE SEVERITY AND CARDIOVASCULAR RISK OF STEATOTIC LIVER DISEASE WITH DIFFERENT ALCOHOL EXPOSURE – A NATIONWIDE STUDY IN TAIWAN

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Background: Recent nomenclature of steatotic liver disease (SLD) stratify subjects based on the cardiometabolic risk factors (CMRFs) and alcohol consumption. SLD subjects carrying CMRFs and with moderate alcohol consumption (daily intake of 20 to 50 g for females and 30 to 60 g for males) are named as metabolic dysfunction-associated SLD (MASLD) with excessive alcohol consumption (MetALD), whereas those with heavy alcohol consumption (daily intake >50 g for females and >60 g for males) are viewed as having alcoholic liver disease (ALD) regardless CMRF carriage.

Aims: The study aims to address the prevalence, liver disease severity and cardiovascular risk in SLD patients with different alcohol exposures and CMRF carriage in Taiwan.

Methods: Eligible subjects were those retrieved from a nationwide-based health check-up system in Taiwan from 1997 to 2019. Subjects were excluded if they were seropositive for hepatitis B surface antigen and antibodies to hepatitis C virus. SLD was evaluated by sonography and/or having hepatic steatosis index greater than 36. Alcohol consumption was judged by questionnaires and transformed into daily exposure. CMRF was defined as having at least one of the five items, including (1) body mass index (BMI) ≥23 kg/m² (2) fasting plasma glucose ≥100 mg/dL, glycated hemoglobin (HbA1C) ≥5.7% or type 2 diabetes history with or without treatment; (3) blood pressure ≥130/85 mmHg or specific antihypertensive drug treatment; (4) plasma triglycerides ≥150 mg/dL or lipid-lowering treatment; and (5) plasma high-density lipoprotein cholesterol (HDL-C) ≤40 mg/dL for males and ≤ 50 mg/dL for females or lipid-lowering treatment. Liver disease severity was evaluated by fibrosis-4 index (FIB-4) and the cardiovascular risk was calculated by Framingham risk score (FRS).

Results: A total of 501,863 subjects were recruited, and 162,689 (32.4%) subjects had SLD (mean age 44.0 years, male: 63.6%). Of the SLD subjects, the proportion of subjects without alcohol use or with social drinking (Group A), moderate alcohol consumption (Group B) and heavy alcohol consumption (ALD, Group C) was 93.3% (n = 151,747), 4.0% (n = 6,597) and 2.7% (n = 4,345), respectively. The proportion of CMRF carriage was 96.0% (MASLD), 98.1% (Met-ALD) and 97.9% among the 3 groups, respectively. Subjects in Group B and Group C were older and had a higher proportion of male gender and metabolic disarrangements. The FIB-4 value progressively increased from Group A (0.85 ± 0.58), Group B (0.96 ± 0.80) to Group C (1.20 ± 1.13) (Ptrend <0.001). While subjects were divided by the CMRF carriage, those with CMRF carriage had a significantly higher FIB-4 than those without in each subgroup (All P value <0.001). Group A subjects without CMRF had the lowest FIB-4 value (0.71 ± 0.36) whereas Group C subjects with CMRF had the highest FIB-4 value (1.21 ± 1.14). Logistic regression analysis revealed that factors independent associated with significant fibrosis (FIB-4 > 2.6) included alcohol exposure (Odds ratio [OR]/95% confidence intervals [CI]: 2.00/1.91-2.11, P < 0.01 for Group B; OR/CI: 2.61/2.46-2.77, P < 0.01 for Group C, compare to Group A) and CMRF carriage (OR/CI: 4.94/4.27-5.71, P < 0.01 for 1-2 CMRF carriage; OR/CI: 27.78/24.03-32.09, P < 0.01 for > 3 CMRF carriage, compared to no any CMRF carriage). Coincidently, FRS progressively increased from Group A (6.95 ± 7.08), Group B (9.60 ± 8.56) to Group C (10.79 ± 9.33) (Ptrend <0.001). Group A subjects without CMRF had the lowest FRS (2.45 ± 2.21) whereas Group C subjects with CMRF had the highest FRS value (10.93 ± 9.36). Alcohol exposure was independently associated with a higher cardiovascular risk (OR/CI: 1.64/1.53-1.75, P < 0.01 for Group B; OR/CI: 1.74/1.60-1.90, P < 0.01 for Group C, compared to Group A).

Conclusions: Despite the classification of Met-ALD and ALD taking CMRF carriage into consideration, almost all the SLD subjects with moderate or heavy alcohol consumption carried at least one CMRF. Both alcohol exposure and CMRF carriage were independently associated with liver disease severity and cardiovascular risk in Taiwanese SLD subjects.

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肝臟精準投予 Riociguat 對肝硬化大鼠之門脈高壓及相關血流動力學異常的影響
EFFECTS OF LIVER-TARGETED DELIVERY OF RIOCIGUAT ON PORTAL HYPERTENSION-RELATED HEMODYNAMIC DERANGEMENTS IN CIRRHOTIC RATS

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Background: Portal hypertension is a severe complication of liver cirrhosis, arising from increased hepatic vascular resistance (HVR) and hyperdynamic circulation. The development of vasoconstriction in the liver and extrahepatic vasodilation plays a significant role in this condition. Riociguat, a soluble guanylate cyclase stimulator, has proven effective in treating pulmonary hypertension through its vasodilatory effects. In our previous study, asialoglycoprotein receptor-targeted poly (lactic-co-glycolic acid) nanoparticles (ALPNDs) were developed to deliver chemical compounds specifically to the liver. However, the effects of liver targeted delivery of riociguate on portal hypertension was never surveyed.

Aims: The present study aims to evaluate the effects of liver-targeted delivery of riociguat using ALPNDs on portal hypertension and associated hemodynamic abnormalities in cirrhotic rats.

Methods: Male Sprague-Dawley rats underwent common bile duct ligation (BDL) to induce liver cirrhosis and portal hypertension, while sham-operated rats served as surgical controls. From the 15th to the 28th day post-operation, the rats were randomly assigned to receive vehicles, riociguat, ALPNDs, or riociguat-loaded ALPNDs. On the 28th day, hemodynamic measurements were performed.

Results: The results showed that cirrhotic rats had significantly higher hepatic vascular resistance (HVR), portal pressure (PP), and splanchnic inflow, along with lower systemic vascular resistance (SVR), compared to sham-operated rats. Riociguat reduced portal pressure and splanchnic inflow by further decreasing SVR and arterial pressure. In contrast, liver-targeted delivery of riociguat using ALPNDs lowered portal pressure by attenuating HVR. Compared to the riociguat group, liver-specific delivery of riociguat more effectively ameliorated portal hypertension while relatively preserving SVR and arterial pressure.

Conclusions: In conclusion, systemic administration of riociguat reduced portal pressure but exacerbated peripheral vasodilation. Conversely, liver-targeted delivery of riociguat alleviated portal hypertension by restoring abnormal HVR. Liver-specific delivery of riociguat represents a promising therapeutic strategy for portal hypertension and warrants further clinical investigation.

主題：下消化道疾病（一）

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內視鏡技術在炎症性腸病中對結直腸腫瘤監測的應用：系統性回顧與網絡 Meta 分析
ENDOSCOPIC APPROACHES FOR COLORECTAL NEOPLASIA SURVEILLANCE IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Background: Patients with inflammatory bowel disease (IBD) have a higher risk of developing colorectal cancer compared to the general population, making colonoscopy surveillance for neoplastic lesions critically important. Dye-based chromoendoscopy (DCE) has traditionally been considered the preferred image-enhanced endoscopy (IEE) for colonoscopy surveillance. However, clinical adherence to DCE is low, with white light endoscopy (WLE) frequently used for surveillance instead. With advancements in endoscopy, various virtual chromoendoscopy (VCE) techniques have emerged as alternatives for colonoscopy surveillance.

Aims: This network meta-analysis aim to investigate the superior endoscopy techniques for IBD patient surveillance.

Methods: Sixteen RCTs involving 2,514 patients were included in the analysis, comparing different endoscopy techniques in IBD patient colonoscopy surveillance: DCE, high-definition WLE (HD-WLE), standard-definition WLE (SD-WLE), i-scan, NBI, FICE, and AFI. We assessed the per patient neoplastic detection rate (NDR), precision rate, and withdrawal time between different endoscopy techniques. Subgroup analysis was conducted to compare the NDR of DCE, VCE, and HD-WLE with either target or random biopsy protocols.

Results: In the comparison of NDR, only DCE (OR: 2.56 [95% CI: 1.17–5.59]) significantly increased the NDR compared to SD-WLE. The subsequent rankings were HD-WLE, NBI, FICE, i-scan, and AFI. Moreover, the precision rates of DCE, VCE, and HD-WLE showed no significant difference compared to SD-WLE. However, DCE required a significantly longer withdrawal time. In the subgroup analysis, DCE with random biopsy (OR: 4.42 [95% CI: 2.26–8.65]) or target biopsy (OR: 2.01 [95% CI: 1.12–3.61]) and HD-WLE with target biopsy (OR: 3.33 [95% CI: 1.51–7.31]) had superior NDR compared to SD-WLE with random biopsy.

Conclusions: DCE has a significant advantage over SD-WLE in NDR, where random biopsy may offer substantial benefits. DCE does not have a lower precision rate that would cause higher biopsy costs, but it does require more withdrawal time. If performing DCE for surveillance colonoscopy is challenging, using HD-WLE with target biopsy also shows a trend of benefit, while other VCE techniques do not necessarily offer significant advantages.

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篩檢大腸鏡中 ADR 與 APC 的評估：年齡、操作經驗與大腸鏡數量的影響
EVALUATING ADR AND APC IN SCREENING COLONOSCOPIES: IMPACT OF AGE, OPERATOR EXPERIENCE, AND COLONOSCOPY VOLUME

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Background: Adenoma Detection Rate (ADR) and Adenoma Per Colonoscopy (APC) are key metrics for assessing colonoscopy quality, but their variability and interrelationship remain unclear.
Aims: To evaluate trends in ADR and APC across age groups, operator experience levels, and colonoscopy volumes.
Methods: Participants undergoing colonoscopy during health checkups (2014–2020) were included. ADR, the proportion of colonoscopies detecting at least one adenoma, and APC, the average number of adenomas per colonoscopy, were analyzed across age groups (<40, 40-49, 50-59, 60-69, >70 years), operator groups (senior: >10 years, mid-level: 5-10 years, junior: <5 years of experience), and colonoscopy volumes (total procedures per operator). Statistical analyses included ANOVA, linear regression, and Pearson's correlation coefficient (r), with a p-value <0.05 considered significant.
Results: Among 33,064 colonoscopies, ADR averaged 29.1% and APC 0.457. ADR increased with age, from 14.6% (<40 years) to 39.5% (>70 years) ($p = 0.01$). APC rose from 0.200 (<40 years) to 0.691 (>70 years) ($p < 0.01$). ADR and APC were strongly correlated ($r = 0.958$, $p < 0.01$). Junior operators demonstrated the highest ADR (35.4%) and APC (0.574). Colonoscopy volumes were moderately negatively correlated with ADR ($r = -0.677$, $p < 0.01$) and APC ($r = -0.637$, $p < 0.01$), reflecting reduced detection rates in high-volume settings.
Conclusions: ADR and APC are complementary metrics for colonoscopy quality, with APC addressing the "one-and-done" phenomenon, a limitation of ADR. Higher detection rates among junior operators and low-volume practitioners underscore the influence of operator experience and workload on detection quality. Continuous training, quality assurance, and workload management are essential to optimize detection rates and advance colorectal cancer prevention in screening programs.

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利用內視鏡與組織發炎活性預測潰瘍性大腸炎病人之預後
PREDICTING OUTCOMES BASED ON ENDOSCOPIC AND HISTOLOGICAL INFLAMMATORY ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS

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Background: Ulcerative colitis (UC) is a condition of chronic relapsing inflammation in colorectum. With advancements in medical treatment, mucosal healing could be achieved which predicts better outcomes. However, discrepancies exist between mucosal healing and histological inflammation.
Aims: We aimed to investigate the correlation between endoscopic and histological inflammation as well as their prediction for disease prognosis.
Methods: Patients diagnosed with UC who underwent colonoscopy with mucosal biopsy were consecutively recruited from January 1, 2023, to June 1, 2024, at Far Eastern Memorial Hospital. Clinical characteristics, Mayo endoscopic subscore (MES), and Nancy histological index (NHI) were analyzed, where mucosal healing (MH) was defined as a MES of 0 to 1, and histological remission (HR) was defined as a NHI of 0 to 1. The outcomes included escalation of conventional medication doses, initiation of biologic therapies, and UC-related hospitalization and surgery within one year following the colonoscopy.
Results: A total of 42 patients were enrolled, with a mean age of 44.81 years, a disease duration of 4.79 years, and a C-reactive protein level of 1.37 mg/dl. The baseline disease activity by Montreal classification was E1 in 22 patients (52.38%), E2 in 16 patients (38.10%), E3 in 4 patients (9.52%). There were 4 (9.52%), 17 (40.48%), 12 (28.57%) and 9 (21.43%) patients with MES 0, 1, 2, and 3, respectively. Regarding to the NHI, 9 (21.43%), 6 (14.29%), 11 (26.19%), 8 (19.05%) and 8 (19.05%) patients with NHI grade 0, 1, 2, 3 and 4, respectively. Six patients (14.29%) achieved histo-endoscopic remission (HEMR) following proactive care. The Pearson correlation coefficient between MES and NHI was 0.608. Among the 21 patients with MH, 11 (52.38%) also achieved HR, and had a fewer rate of escalation of conventional medication (18.18% vs. 50%, $p = 0.12$), although without statistically

significance, and biologics (0% vs. 40%, p = 0.02). Among those with HR, fewer patients who attained MH needed an escalation of conventional medication (18.18% vs. 100%, p < 0.01) and biologics (0% vs. 75%, p < 0.01). Achieving HEMR was predictive of a lower need for escalation of conventional medication doses (OR 0.06, 95% CI 0.01–0.37, p = 0.002) and the initiation of biologic therapy (OR 0.06, 95% CI 0.01–0.37, p = 0.002). No subjects enrolled experienced UC-related hospitalization or surgery during the one-year follow-up period.

Conclusions: MES and NHI were moderately correlated. Endoscopic inflammation activity seems to be more correlated with clinical decision for step-up medication than histological findings. Patients with UC who achieved HEMR had more stable disease.

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糞便潛血陽性患者行大腸鏡之腺瘤偵測率與惡性腫瘤診斷率：醫學中心及區域醫院之比較

ADENOMA DETECTION RATE (ADR) AND MALIGNANCY DIAGNOSIS RATE IN SCREENING COLONOSCOPIES FOR POSITIVE FECAL OCCULT BLOOD TESTING (FBOT) BETWEEN A MEDICAL CENTER AND A DISTRICT HOSPITAL IN TAIWAN

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Background: Studies have indicated that approximately 40% of individuals with a positive fecal occult blood test (FOBT) result are diagnosed with colorectal cancer or adenoma during subsequent colonoscopy. However, the comparison of adenoma detection rates (ADR) and malignancy diagnosis rates between medical centers and district hospitals has not been fully explored.

Aims: To compare ADR and malignancy diagnosis rates between medical centers and district hospitals.

Methods: We conducted a retrospective study from January 2019 to September 2024 at Changhua Christian Hospital (a medical center) and Yuanlin Christian Hospital (a district hospital). A total of 4,618 colonoscopy events for individuals aged 50–75 at the medical center and 3,116 at the district hospital were included.

Results: Significant differences were observed between the two groups in patient characteristics: sex (45% female at the medical center vs. 48% at the district hospital, p = 0.012), age (62.8 vs. 62.35 years, p < 0.001), bowel preparation quality (excellent, good, fair, poor: 10.3%, 74.5%, 11.6%, 3.4% vs. 12.3%, 79.6%, 6.4%, 1.7%, p < 0.001), physician qualifications (93% vs. 86% with >5 years of experience, p < 0.001), and physician specialty (72.6% vs. 75.73% gastroenterologists, p = 0.002). In terms of ADR, no significant difference was found when only gastroenterologists were included (57.71% vs. 56.23%, p = 0.266). Similarly, the malignancy diagnosis rates were comparable between the groups (4.07% vs. 3.82%, p = 0.578).

Conclusions: Despite differences in patient characteristics and physician qualifications, screening colonoscopies conducted at district hospitals appear feasible without compromising diagnostic outcomes.

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HLA-C*03:04:01 與台灣發炎性腸道疾病患者抗 TNF 藥物抗體產生有較高風險相關性
HLA-C*03:04:01 LINKED TO HIGHER RISK OF ANTI-TNF IMMUNOGENICITY IN TAIWANESE PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Anti-tumor necrosis factor (anti-TNF) therapies are effective and widely used for inflammatory bowel disease (IBD). However, many patients undergoing anti-TNF therapy eventually develop anti-drug antibodies (ADA), which are a major contributor to loss of treatment efficacy and adverse drug reactions. In European populations with Crohn's disease (CD), the genetic variant HLA-DQA1*05 has been linked to the development of antibodies against infliximab.

Aims: This study explores the association between HLA genotypes and ADA formation in non-European IBD patients receiving anti-TNF, anti-integrin, or anti-IL-12/23 therapies.

Methods: This prospective cohort study enrolled patients with IBD receiving anti-TNF, anti-integrin, or anti-IL-12/23 therapy between January 2022 and March 2024. NGS-based HLA genotyping was performed for all participants. The occurrence of ADAs was assessed, and the frequencies of specific HLA alleles were compared between patients who developed ADAs and those who did not. Additionally, HLA allele frequencies in ADA-positive patients were analyzed against the general population in Taiwan.

Results: The study included 95 patients with IBD and HLA genotype data from 1,097 control individuals from the Taiwan Biobank. Among the IBD patients, 58 received anti-TNF therapy, 27 underwent anti-integrin therapy, and 10 were treated with anti-IL-12/23 therapy. In Taiwan, reimbursement criteria require prior treatment with conventional therapy, and biologics are covered only after an inadequate response or adverse effects. As a result, all 95 patients were on combination therapy with biologics and immunosuppressive agents (either thiopurine or methotrexate). Among the 58 patients on anti-TNF therapy (38 with infliximab and 20 with adalimumab), 21 developed ADAs (18 infliximab-related and 3 adalimumab-related). A comparison of patients with and without ADAs identified a significant association between the HLA-C03:04:01 allele and ADA development (33.3% vs. 10.8%, $p = 0.035$), while no such association was found for the HLA-DQA105 allele (52.3% vs. 51.4%, $p = 0.940$). The frequency of the HLA-C*03:04:01 allele also showed a trend toward being higher in IBD patients compared to the general Taiwanese population (16.8% vs. 10.5%, $p = 0.05$). Notably, no ADA development occurred in patients treated with anti-integrin or anti-IL-12/23 therapies.

Conclusions: This study highlights ethnic differences in HLA loci associated with ADA development in IBD patients. While HLA-DQA105 has been implicated in European populations, our findings identify HLA-C03:04:01 as significantly associated with an increased risk of anti-TNF antibody formation in Taiwanese IBD patients.

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換水大腸鏡檢查合併人工智慧系統對大腸腺瘤偵測的影響：一項多中心前瞻性隨機分組試驗期中分析結果

EVALUATION OF ARTIFICIAL INTELLIGENCE FOR ADENOMA DETECTION IN WATER EXCHANGE COLONOSCOPY: INTERIM ANALYSIS OF THE WEAID RANDOMIZED CONTROLLED TRIAL

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Background: Low adenoma detection rate (ADR) and adenomas per colonoscopy (APC) are crucial predictors of interval colorectal cancer (CRC). Water exchange (WE) and artificial intelligence (AI)-based computer-aided detection (CADe) improve ADR and APC. However, the association between adding CADe to WE on APC is unclear.

Aims: We performed an interim analysis of a prospective randomized controlled trial (RCT) (WEAID, WE-AI-assisted Detection) to determine if combining WE with CADe led to a significantly higher APC than WE alone.

Methods: The WEAID trial was a parallel RCT conducted by 7 endoscopists in 2 hospitals in Italy and Taiwan using separate commercially available AI system: Endo-AID (OIP-Ce-1 version 1.00.02, Olympus, EU) was used in the Italian site; CAD-EYE (EW10-EC02 V1, Fujifilm, Japan) was used in the Taiwanese site. Data for the analysis were collected between December 2023 and December 2024. Consecutive patients, aged 45–75 years, were randomized to the WE with CADe-assisted colonoscopy group or the WE control group. Neoplastic lesions included malignancy, adenomas, and clinically significant serrated polyps (CSSPs). CSSPs comprised sessile serrated lesions (SSLs), traditional serrated adenomas, hyperplastic polyps (HPs) measuring ≥10 mm anywhere in the colon, or HPs measuring 6–9 mm in the proximal colon. The primary outcome was APC, with an original planned enrollment of 752 patients.

Results: A total of 560 patients (men: 53.4%; mean age: 59.4 ± 7.7 years; 279 with CADe) were included in the analysis, representing 74.5% of the planned enrollment. Both groups had similar demographic and clinical characteristics. APC was significantly higher in the WE-CADe group than that in the WE group (1.39 vs 1.05 with an adjusted incidence rate ratio [IRR] of 1.33; 95% confidence interval, 1.15–1.55; $P < 0.001$). When stratified by colonoscopy indication, APC was also significantly higher in the WE-CADe group than that in the WE group (1.35 vs 1.04 with an IRR of 1.26 [1.04–1.53] for screening and surveillance colonoscopies; 1.46 vs 1.07 with an IRR of 1.35 [1.05–1.74] for FIT/gFOBT+ colonoscopies). There were no significant differences in ADR, SSL detection rate (SSLDR) and CSSP detection rate (CSSPDR) between the WE-CADe and WE alone groups (54.1% vs 50.2% for ADR, $P = 0.35$; 3.6% vs 3.6% for SSLDR; 9.3% vs 11.6% for CSSPDR, $P = 0.35$). Both groups had a similar withdrawal time for procedures without intervention (10.4 min vs 10.3 min) and a comparable mean number of non-neoplastic lesions resected per colonoscopy (0.52 vs 0.52).

Conclusions: This interim analysis of a multicenter RCT found that including CADe in WE colonoscopy significantly increased APC without prolonging the withdrawal time compared with WE alone. These findings suggest that a combination of WE and CADe improving APC has the potential in preventing interval CRC. The significant difference documented in this analysis justifies the early termination of the study.

主題：幽門螺旋桿菌

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南台灣左氧氟沙星與甲硝唑為基礎的鉍四聯療法在幽門螺旋桿菌根除中的療效比較：一項回溯性真實世界研究

COMPARATIVE EFFECTIVENESS OF LEVOFLOXACIN- VS. METRONIDAZOLE-BASED BISMUTH QUADRUPLE THERAPY AS SECOND-LINE TREATMENT FOR *HELICOBACTER PYLORI* IN SOUTHERN TAIWAN: A RETROSPECTIVE REAL-WORLD STUDY

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Background: *Helicobacter pylori* (*H. pylori*) is a Gram-negative, microaerophilic bacterium associated with gastritis, peptic ulcers, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma. Its eradication is essential to prevent these severe complications. However, increasing resistance to antibiotics, particularly clarithromycin, has significantly reduced the success rates of first-line treatments worldwide. As the failure of initial therapies becomes more frequent, the need for effective second-line regimens has grown critical.

Aims: This study aims to compare the efficacy and complications of levofloxacin-based BQT (EBTL) and metronidazole-based BQT (EBTM) in achieving *H. pylori* eradication as second-line therapies.

Methods: This retrospective study enrolled patients who experienced first-line treatment failure for *H. pylori* and subsequently underwent second-line therapy between January 2010 and September 2024. Patients with incomplete medical records were excluded from the analysis. A total of 160 patients were divided into two treatment groups. The EBTL group received a 10-day regimen of esomeprazole 40 mg twice daily, bismuth 120 mg four times daily, tetracycline 500 mg four times daily, and levofloxacin 500 mg once daily. The EBTM group was treated with esomeprazole 40 mg twice daily, bismuth 120 mg four times daily, tetracycline 500 mg four times daily, and metronidazole 500 mg three times daily. Follow-up endoscopy or urea breath testing was conducted 6 weeks post-treatment to assess response. The primary outcome was the eradication rate, evaluated using intention-to-treat (ITT) and per-protocol (PP) analyses. Secondary outcomes included the incidence of adverse events and compliance rates.

Results: During the follow-up period, 5 patients from the EBTL group and 3 patients from the EBTM group were lost, leaving 75 patients in the EBTL group and 77 in the EBTM group. Baseline characteristics between the two groups were comparable, with no significant differences in age, gender, or comorbidities. The ITT eradication rate was 86.3% (95% confidence interval [CI]: 76.8% to 93.0%) in the EBTL group and 90.0% (95% CI: 81.2% to 95.6%) in the EBTM group, while the PP rates were 92.0% (95% CI: 83.4% to 97.0%) and 93.5% (95% CI: 85.5% to 97.9%), respectively, showing no statistically significant differences (P = 0.720). Adverse events were more frequent in the EBTL group (57.3% vs. 39.0%, P = 0.023), particularly constipation (24.0% vs. 7.8%, P = 0.006). Despite this, compliance remained excellent at 100% in both groups. The positive yield rate of culture was approximately 60.9% (28/46). Levofloxacin resistance was significantly higher in the EBTL group (6/7 cases, 85.7%) compared to the EBTM group (9/21 cases, 42.9%) (P = 0.049). Eradication rates for metronidazole-resistant (Met-R) and levofloxacin-resistant (Lev-R) strains in EBTL and EBTM regimens. In the Met-R group, the eradication rate was 50.0% for EBTL compared to 71.4% for EBTM, with no statistically significant difference observed (P = 0.477). In the Lev-R group, the eradication rates were 83.3% for EBTL and 77.8% for EBTM, also showing no significant difference (P = 0.792).

Conclusions: Both levofloxacin-based and metronidazole-based bismuth quadruple therapies demonstrated high eradication rates for *H. pylori* as second-line treatments in a real-world clinical setting, with no significant differences in efficacy.

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BAP 療法：相比鉍劑四合一療法更好的單一抗生素幽門螺旋桿菌根除新療法
BAP THERAPY: A NOVEL, SUPERIOR MONO-ANTIBIOTIC APPROACH FOR *H. PYLORI* ERADICATION COMPARED TO BISMUTH QUADRUPLE THERAPY

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Background: The efficacy of high-dose amoxicillin and potassium-competitive acid blocker (PCAB) dual therapy for *H. pylori* infection varies across countries. Bismuth salts possess a synergistic effect on antibiotics, potentially increasing the eradication rates of high-dose amoxicillin/PCAB therapy for *H. pylori*. Our pilot study showed high-dose amoxicillin-vonoprazan-bismuth triple therapy achieved a high eradication rate in a Taiwanese population with high clarithromycin resistance.

Aims: To compare the efficacy and safety of a novel 14-day bismuth/high-dose amoxicillin/PCAB (BAP) therapy with a 10-day bismuth quadruple therapy as first-line treatments for *H. pylori* infection.

Methods: We conducted a retrospective cohort study of patients with *H. pylori* infection treated with either 14-day BAP therapy (tripotassium dicitrato bismuthate 300 mg four times daily, amoxicillin 750 mg four times daily, and vonoprazan 20 mg twice daily) or 10-day bismuth quadruple therapy (tripotassium dicitrato bismuthate 300 mg four times daily, rabeprazole 20 mg twice daily, tetracycline 500 mg four times daily, and metronidazole 500 mg four times daily) between January 2019 and September 2024 at five hospitals in Taiwan. Post-treatment *H. pylori* status was assessed at least four weeks following eradication therapy.

Results: The study included 101 patients in the BAP therapy group and 272 in the bismuth quadruple therapy group. Intention-to-treat analysis showed that BAP therapy had a significantly higher eradication rate compared to bismuth quadruple therapy (97.0% vs. 90.4%, P = 0.048; 95% confidence interval: 1.8% – 11.8%; 95% confidence interval: 2.5% – 8.1%). Per-protocol analysis confirmed these findings (100.0% vs. 94.7%, P = 0.023). Adverse events were significantly fewer in the BAP group (7.9% vs. 33.1%, P < 0.001), while drug adherence was comparable between groups (98.0% vs. 93.0%, P = 0.076).

Conclusions: Fourteen-day BAP therapy achieves higher eradication rates with fewer adverse events compared to 10-day bismuth quadruple therapy, supporting its use as an effective and well-tolerated first-line treatment for *H. pylori* infection.

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Vonoprazan 的高劑量雙聯療法、Vonoprazan 的三聯療法與 Rabeprazole 的混合療法在幽門螺旋桿菌感染一線治療中的臨床比較：一項多中心、開放標籤、隨機試驗

VONOPRAZAN-BASED HIGH-DOSE DUAL THERAPY, VONOPRAZAN-BASED TRIPLE THERAPY AND RABEPRAZOLE-BASED REVERSE HYBRID THERAPY FOR FIRST-LINE TREATMENT OF *HELICOBACTER PYLORI* INFECTION: A MULTICENTER, OPEN-LABEL, RANDOMIZED TRIAL

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Background: *Helicobacter pylori* is the most common chronic bacterial infection worldwide.

Aims: This study aimed to compare the efficacy and safety of 14-day vonoprazan-based high-dose dual therapy, vonoprazan-based triple therapy and rabeprazole-based reverse hybrid therapy for the first-line treatment of *H. pylori* infection in areas with high clarithromycin resistance.

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

Results: Between December 2021 to April 2024, 906 patients were recruited. The eradication rates were 83.8% (253/302 [95% CI: 79.6 to 88.0%]) for vonoprazan high-dose dual therapy, 90.1% (272/302 [95% CI: 86.9 to 93.3%]) for vonoprazan triple therapy, and 89.1% (271/302 [95% CI: 85.6 to 92.6%]) for rabeprazole reverse hybrid therapy in intention-to-treat analysis. Vonoprazan high-dose dual therapy was inferior to both vonoprazan triple therapy (95% CI: 1.1 to 11.5%; p = 0.022) and rabeprazole reverse hybrid therapy (95% CI: -0.2 to 10.7%; p = 0.031). There were no differences in the overall proportions of patients experiencing adverse events in vonoprazan high-dose dual, vonoprazan triple and reverse hybrid groups (10.3% [95% CI: 6.9 to 13.7%], 15.2% [95% CI: 11.2 to 19.3%], and 15.6% [95% CI: 11.1 to 20.1%], respectively).

Conclusions: Vonoprazan triple therapy and rabeprazole reverse hybrid therapy are preferable to vonoprazan dual therapy for first-line treatment of *H. pylori* infection in areas with high clarithromycin resistance.

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比較 Vonoprazan 與 Esomeprazole 為基礎的高劑量雙重療法用於一線幽門螺旋桿菌根除的療效：隨機對照試驗

THE EFFICACIES OF VONOPRAZAN BASED AND ESOMEPRAZOLE BASED HIGH DOSE DUAL THERAPIES IN THE FIRST LINE *HELICOBACTER PYLORI* ERADICATION IN TAIWAN: A RANDOMIZED CONTROLLED TRIAL

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Background: Successful eradication of *Helicobacter pylori* (*H. pylori*) infection depends on maintaining an intragastric pH > 6 and addressing antibiotic resistance. Proton pump inhibitor (PPI)-based high-dose dual therapy, using esomeprazole and amoxicillin, has shown promising eradication rates due to sustained gastric acid suppression and low resistance to amoxicillin. Vonoprazan, a potassium-competitive acid blocker (PCAB), offers stronger and more consistent acid suppression than PPIs, potentially improving eradication outcomes. However, the efficacy of vonoprazan-based high-dose dual therapy compared to PPI-based high-dose dual therapy in first-line *H. pylori* treatment remains uncertain.

Aims: This study aimed to (1) compare the efficacy of 14-day vonoprazan-based high-dose dual therapy (VA) versus esomeprazole-based high-dose dual therapy (EA) for first-line *H. pylori* eradication and (2) assess the impact of antibiotic resistance on treatment outcomes.

Methods: This randomized controlled trial enrolled 121 adult patients with confirmed *H. pylori* infection from Kaohsiung Chang Gung Memorial Hospital. Patients were randomly assigned, using a computer-generated randomization sequence, into two treatment groups. The VA group (n = 61) received vonoprazan 20 mg twice daily (bid) and amoxicillin 750 mg four times daily (qid) for 14 days. The EA group (n = 60) received esomeprazole 40 mg three times daily (tid) and amoxicillin 750 mg four times daily (qid) for 14 days. During the study, 4 patients in the VA group and 2 patients in the EA group were lost to follow-up, resulting in 57 patients in the VA group and 58 patients in the EA group completing the study. Drug compliance and adverse events were evaluated at week 2, and *H. pylori* eradication was assessed using the ^{13}C-urea breath test at week 8. Antibiotic susceptibility testing was performed on cultured isolates. Eradication rates, adverse events, and compliance were compared between groups using the chi-square test, and multivariate analysis was used to assess factors influencing treatment efficacy.

Results: Baseline demographic and clinical characteristics were comparable between the VA and EA groups. In the intention-to-treat (ITT) analysis, eradication rates were 85.2% (95% confidence interval [CI]: 75.2%–92.0%) in the VA group and 81.7% (95% CI: 71.3%–89.4%) in the EA group (P = 0.596). Per-protocol (PP) analysis showed eradication rates of 91.2% (95% CI: 81.8%–96.7%) for VA and 84.5% (95% CI: 73.8%–92.1%) for EA (P = 0.269), indicating no statistically significant difference. Adverse events were mild and similar between groups (5.3% in VA vs. 5.2% in EA, P = 0.983), with constipation and diarrhea being the most reported. Both groups achieved 100% compliance. Antibiotic resistance testing (n =13) revealed no resistance to amoxicillin or tetracycline in either group. Clarithromycin resistance was observed in 33.3% of the VA group and 14.3% of the EA group (P = 0.416), while metronidazole resistance was absent in the VA group but present in 28.6% of the EA group (P = 0.155). Levofloxacin resistance was found in 33.3% of the VA group and 14.3% of the EA group (P = 0.416).

Conclusions: Both 14-day vonoprazan-based and esomeprazole-based high-dose dual therapies demonstrated comparable *H. pylori* eradication rates, excellent compliance, and minimal adverse events. However, vonoprazan based high dose dual therapy attained >90% of eradication rate in the per-protocol analysis.

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益生菌補充對於改善幽門桿菌除菌治療之副作用及腸道菌叢失衡的效果 ー 一項多中心雙盲隨機分派對照試驗

THE EFFICACY OF PROBIOTIC SUPPLEMENTATION IN REDUCING ADVERSE EFFECTS AND DYSBIOSIS DURING *HELICOBACTER PYLORI* ERADICATION THERAPY: A DOUBLE-BLIND, MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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Background: *Helicobacter pylori* (*H. pylori*) eradication reduces peptic ulcer recurrence and gastric cancer risk. However, eradication therapy often causes adverse effects, such as diarrhea and abdominal discomfort, contributing to gut dysbiosis. The impact of probiotics on alleviating these effects and restoring gut microbiota remains inconsistent.
Aims: This study aimed to evaluate whether the probiotic Vigiis 101-LAB (*Lactobacillus paracasei*) during 14-day *H. pylori* sequential therapy reduces adverse effects, mitigates gut dysbiosis, and maintains eradication efficacy.
Methods: We conducted a multicenter, open-label, randomized controlled trial in Taiwan. Eligible *H. pylori*-infected subjects naïve to treatment were randomized to receive either a 14-day quadruple therapy combined with a 2-month course of Vigiis 101-LAB probiotics or a placebo. The 14-day quadruple therapy consisted of esomeprazole 40 mg and amoxicillin 1 g twice daily from days 1 to 7, followed by esomeprazole 40 mg, clarithromycin 500 mg, and metronidazole 500 mg twice daily from days 8 to 14. The eradication rates using the intention-to-treat (ITT) and per-protocol (PP) analyses in both groups were compared. The adverse events were graded and stool samples were collected for gut microbiota analysis via shotgun metagenomics respectively at baseline, 2 weeks, 2 months, and 1 year of eradication. The α-diversity was evaluated using species richness indices, while β-diversity was assessed based on the Principal Coordinates Analysis (PCoA).
Results: Eradication rates were similar between the probiotics and placebo groups (ITT: 84.0% vs. 87.0%, p = 0.547; PP: 87.5% vs. 92.6%, p = 0.246). Adverse effects were consistently lower in the probiotics group (e.g., 34% vs. 42.3% during Days 1–14; 16.5% versus 9% during Days 15–28; 12.4% versus 8% during Days 29–42; 7% vs. 13.4% during Days 43–56). Both groups experienced significant reductions in species richness and α-diversity at 2 weeks compared to baseline (species richness, p = 9.5e-17 vs. p = 1.2e-07; species evenness, p = 0.0088 vs. p = 0.12; Shannon index, p = 1.7e-09 vs. p = 1.9e-05; Simpson index, p = 7.8e-06 vs. p = 0.0011). Gradual recovery was observed by 2 months and 1 year, but it did not fully return to baseline levels. Bray-Curtis and weighted PCoA analyses revealed significant differences across time points (PERMANOVA, p = 0.001), with no significant differences between two treatment groups.
Conclusions: Adding *Lactobacillus paracasei* probiotics to 14-day quadruple therapy modestly reduces adverse effects but shows no significant impact on eradication efficacy and gut dysbiosis recovery post-*H. pylori* eradication.

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幽門桿菌感染篩檢最佳策略 ー 多中心隨機對照試驗

IDENTIFICATION OF THE OPTIMAL SCREENING STRATEGY FOR IDENTIFICATION OF *HELICOBACTER PYLORI* INFECTION- A MULTICENTER, RANDOMIZED CONTROLLED TRIAL

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Background: The optimal tools for mass screening of *Helicobacter pylori* (*H. pylori*) to prevent gastric cancer remain uncertain.
Aims: This study aimed to compare the effectiveness and compliance of three non-invasive tests for detection of *H. pylori* in this prospective, multicenter, randomized controlled trial.
Methods: Eligible adult participants undergoing *H. pylori* serology testing were randomly assigned in a 1:1:1:1 ratio to one of the following screening strategies: (A) urea breath test (UBT), (B) *H. pylori* stool antigen test (HpSA), (C) HpSA combined with UBT (standard control), or (D) a two-stage screening method (UBT for serology positive subjects) (Figure 1). In groups A and B, *H. pylori* status was determined by the results of UBT and HpSA, respectively. In group C, participants were considered *H. pylori*-positive if at least two of the three tests (serology, UBT, HpSA) were positive (standard group). In group D, serology screening was conducted first, followed by a confirmatory UBT for individuals with positive serology results. All participants were instructed to discontinue proton-pump inhibitors and histamine-2 blockers for at least two weeks prior to testing. Detection rate differences between groups were analyzed using non-inferiority analysis with a pre-specified non-inferiority margin of 5%.
Results: Among 2,900 participants who completed at least the serology test, the detection rates were 22.7% (162/714, 95% CI: 19.6%–25.8%) in UBT group (A), 25.7% (173/673, 95% CI: 22.4%–29.0%) in HpSA group (B), 24.3% (168/691, 95% CI: 21.1%–27.5%) in standard group (C), and 18.0% (126/699, 95% CI: 15.2%–20.9%) in serology-UBT two stage group (D) (Figure 2). When compared to the standard control group C, the differences in detection rates were -1.6% between UBT group and standard group (95% CI: -5.4% to 2.1%, non-inferiority p = 0.068), 1.4% between groups HpSA and standard group C (95% CI: -2.5% to 5.3%, non-inferiority p = 0.003), and -6.3% between two-stage groups D and standard group C (95% CI: -9.9% to -2.7%, non-inferiority p = 0.772). The detection rate of HpSA and UBT for *H. pylori* is not inferior to standard methods. However, two stage strategy of UBT in subjects with positive serology showed lower detection rate (p = 0.004) than standard group.
Conclusions: HpSA or UBT, but not serology test, can be used in mass screening of *H. pylori* for gastric cancer prevention.

主題：其他消化道疾病

⑭

內視鏡超音波導引下胃小腸吻合術治療胃出口阻塞的成效分析
THE EXPERIENCE OF GASTROENTEROSTOMY WITH HOTAXIOS TO RELIEVE GASTRIC OUTLET OBSTRUCTION IN A COMMUNITY HOSPITAL

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Background: Enteral self-expanding metal stents and surgical gastrojejunostomy are effective for the management of gastric outlet obstruction (GOO) but limited by high complication rates and short-term efficacy. Endoscopic ultrasound-guided gastrojejunostomy (EUS-GJ) is a novel alternative option.
Aims: To evaluate the safety and effectiveness of EUS-GJ for relief of gastric outlet obstruction.
Methods: Patients who underwent EUS-GJ between May 2021 and July 2024 presented as gastric outlet obstruction were included. Technical success was defined as successful placement of a gastrojejunal lumen-apposing metal stent. Clinical success was defined as the ability of the patient to tolerate an oral diet. Post-procedural adverse events were recorded.
Results: The study included 12 patients, of whom 7 (58%) were female. Technical success was achieved in 12 patients (100%). Clinical success was achieved in 11 patients (91.7%). Of the one patient clinical success was not achieved, despite a patent EUS-GJ and required surgical GJ for nutrition. One case is chronic peptic ulcer with bulb deformity. Adverse event of mis-deployment occurred in one patient (8.3%).
Conclusions: EUS-GJ is an emerging procedure that demonstrates efficacy and safety comparable to current treatment options, positioning it as a promising minimally invasive alternative for patients with gastric outlet obstruction.

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Nivolumab 結合化療在晚期胃癌及胃食道交界癌中的長期存活及安全性：隨機對照試驗的系統性回顧與統合分析
LONG-TERM SURVIVAL AND SAFETY OF NIVOLUMAB PLUS CHEMOTHERAPY IN ADVANCED GASTRIC AND GASTROESOPHAGEAL CANCER: A SYSTEMIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Gastric cancer (GC) and gastroesophageal junction cancer (GEJC) are significant global health burdens, with poor survival outcomes in advanced stages. Nivolumab, a PD-1 inhibitor, combined with chemotherapy, has emerged as a promising first-line treatment.
Aims: This meta-analysis aimed to evaluate the efficacy and safety of nivolumab plus chemotherapy for advanced GC and GEJC, focusing on overall survival, progression-free survival and treatment-related adverse events.
Methods: This study adhered to PRISMA 2020 guidelines. A systematic search was conducted in PubMed, Embase, Cochrane CENTRAL, Web of Science, and ClinicalTrials.gov up to December 7, 2024. Randomized controlled trials (RCTs) comparing nivolumab plus chemotherapy with chemotherapy alone in advanced GC and GEJC were included. Data were analyzed using a random-effects model to calculate effect sizes (Hedges' g) for primary outcomes and odds ratios for TRAEs. Sensitivity analyses and publication bias assessments were performed to ensure robustness.
Results: Five RCTs with 4109 participants were included. Nivolumab combined with chemotherapy significantly improved OS (Hedges' g = 0.140, 95% CI: 0.056–0.224, $p = 0.001$, $I^2 = 32.54\%$), PFS (Hedges' g = 0.113, 95% CI: 0.051–0.175, $p < 0.001$, $I^2 = 0\%$). TRAEs were more frequent in the nivolumab group (OR = 1.620, 95% CI: 1.284–2.045, $p < 0.001$, $I^2 = 47.83\%$), but no new safety concerns were identified.
Conclusions: Nivolumab plus chemotherapy significantly improves survival outcomes in advanced GC and GEJC, with manageable safety profiles. These findings support its integration as a first-line treatment and highlight the need for further research on biomarkers, combination therapies, and long-term outcomes.

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維他命 D 濃度與內視鏡異常發現之關聯
THE RELATIONSHIP BETWEEN VITAMIN D LEVEL AND ENDOSCOPY FINDING: A RETROSPECTIVE STUDY IN A SINGLE CENTER

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Background: Recently, arising evidence suggests that vitamin D is related to immune modulation and tumor suppression. However, the relationship between serum vitamin D levels and findings on esophagogastroduodenoscopy remains poorly understood. Additionally, how the anti-inflammatory effects of vitamin D perform in the gastrointestinal tract remains unknown.
Aims: To explore this uncertain area, we conducted a single-center retrospective study to seek answers and provide insights into the potential role of vitamin D in gastrointestinal health.
Methods: This is a single-center, retrospective study. We included patients who were above 18 years old. The inclusion criteria consisted of patients who underwent esophagogastroduodenoscopy between December 31, 2009, and April 28, 2023, and had their serum vitamin D levels measured within one year before or after the endoscopy examination. Endoscopy reports were reviewed manually, and the findings were compared with serum vitamin D levels.
Results: A total of 2726 patients were included in this study. Among all the patients, 1650 had low vitamin D levels, defined as serum vitamin D levels below 20 ng/mL, while 1076 patients had normal vitamin D levels. Reviewing the baseline characteristics of the two groups revealed that those with lower serum vitamin D levels had higher white blood cell counts and C-reactive protein levels, indicating a higher incidence of systemic inflammation. They also had higher creatinine levels, suggesting worse renal function; lower serum calcium and phosphate levels; and lower cholesterol, triglyceride, and low-density lipoprotein cholesterol levels, indicating poorer nutritional status. Regarding endoscopic findings, the incidence rates of esophageal varices, esophageal ulcer, Barrett's esophagus, Forrest III gastric ulcer, portal hypertensive gastropathy, and gastric cancer were significantly related to vitamin D concentrations.
Conclusions: A lower vitamin D level was associated with systemic inflammation. There was also a relationship between serum vitamin D levels and some abnormal findings on endoscopy. Whether additional vitamin D supplementation benefits gastrointestinal health requires further investigation.

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原發性小腸癌的臨床病理學研究：中台灣一醫學中心之經驗
CLINICOPATHOLOGICAL STUDY OF PRIMARY SMALL INTESTINAL CANCER: A SINGLE INSTITUTE EXPERIENCE IN TAIWAN

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Background: The small intestine occupies 75% of the length of the digestive tract and 90% of mucosal surface, but the primary small intestine cancer remain rare and only represent around 3% of digestive cancers. In the past time, because of endoscopic inaccessibility, the primary small intestine tumor was difficulty approach compare to stomach and colon. In addition, four main histologic types of small intestine including adenocarcinomas, neuroendocrine tumors, stromal tumors and lymphomas. The distribution of histologic type is different between Asian and Western country.

Aims: The aim of the study was to investigate the epidemiological data and clinical presentation of primary small bowel intestine cancer in a single institute experience in Taiwan.

Methods: From January 2008 to Novermber 2024, we retrospectively reviewed the medical charts at China Medical University Hospital. Patients who were diagnosed as primary small intestine cancer via double balloon enteroscopy (DBE) were included into this study. Clinical data were obtained from the medical records and from the physicians responsible for patient care. Epidemiological data included histologic type, age, gender, symptoms, tumor location and outcomes.

Results: A total of 70 patients with primary small intestine were enrolled into this study. There were 39 males and 31 females, with a male-to-female ratio of 1.25:1. The mean age was 59.4 years (range, 23-86 years). The histologic type of small intestine cancer, including 34 case (34/70, 48.5%) with GIST, 18 case (18/70, 25.7%) with lymphoma, 15case (15/70, 21.4%) with adenocarcinoma. The three other type have one neuroendocrine tumors, one Kaposi sarcomas, and one angiosarcoma. In our present study, as regards clinical symptoms, 67 patients were symptomatic. Only three asymptomatic patient including two GIST and one adenocarcinoma. These three asymptomatic patients was found accidentally during health examination. In 67 symptomatic patients, they most commonly presented with GI bleeding (54 patients, 80%). Followed by abdominal pain in seven, fever in three, and weight loss in two and diarrhea in one patient. Primary small intestine cancer involved the duodenum in 19 (27.1%) of 70 patient, the jejunum in 39 (55.7%) of 70 patients, and ileum in 12 (17.1%) of 70 patient. In our study, three major histologic type of small intestine cancer were GIST, lymphoma and adenocarcinoma. In term of mean age, the patient with adenocarcinoma is oldest (65.5 y/o), the following is lymphoma with mean age 63.7 y/o and GIST with mean age 58.3 y/o. The gender did not have significant difference between three major small intestine cancer. In term of tumor location, jejunal tumor is most common (GIST: 23/34, 67.6%; Adenocarcinoma: 8/15, 53.3%; Lymphoma: 9/18, 50%) and following is duodenal tumor (GIST: 6/34, 17.6%; Adenocarcinoma: 7/15, 46.6%; Lymphoma: 4/18, 22.2%), the ileal tumor is least (GIST: 5/34, 14.7%; Adenocarcinoma: 0/15, 0%; Lymphoma: 5/18, 27.7%). The prognosis of primary small intestine cancer, total 16 patients expired including seven case with adenocarcinoma, the following is six cases with lymphoma, one case with GIST, one case with Kaposi sarcomas and one case with angiosarcoma. The mortality rate have significant difference between three major type of small intestine cancer, the GIST have lowest motality rate (1/34, 2.9%), lymphoma (6/18, 33.3%) and adenocarcinoma have highest rate (7/15, 46.6%).

Conclusions: In conclusion, the results of our present study showed different prognosis between histologic type of primary small intestine cancer. And distribution of histologic type of primary small intestine cancer in our study are similar as in Taiwan and other Asian country, but is quite different from western country. These patients who suffered from primaly small intestine cancer usually old age and have symptoms.

主題：病毒性肝炎（二）

⑤⑧

糖尿病與 COVID-19 相關胰臟炎有關：TriNetX 資料庫的回顧性研究
DIABETES MELLITUS IS ASSOCIATED WITH COVID-19-RELATED PANCREATITIS: A RETROSPECTIVE COHORT STUDY FROM THE TRINETX COLLABORATIVE NETWORK

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Background: The COVID-19 pandemic, spanning from 2019 to 2023, has been linked to various complications, including pancreatitis.
Aims: This study investigates the association between diabetes mellitus (DM) and COVID-19-related pancreatitis using the TriNetX network database.
Methods: Data were obtained from the TriNetX Collaborative Network, comprising medical records between January 1, 2019, and December 31, 2023. From this cohort, 3,609,987 individuals (>20 years old) who underwent SARS-CoV-2 infection were included. Participants were divided into two groups based on ICD-10 codes for COVID-19 diagnosis with or without diabetes. Patients with a diagnosis of acute pancreatitis within three years prior to the COVID-19 index date were excluded. Acute pancreatitis cases occurring within one month of a COVID-19 diagnosis were included for analysis.
Results: There were 653,593 COVID-19 patients in each group with and without diabetes mellitus were matched by propensity score for age and sex. After analysis, 633 (0.098%) patients with acute pancreatitis was diagnosed within one month of COVID-19 in 644,325 patients with diabetes and 285 patients (0.044%) with acute pancreatitis in 649,790 without diabetes. The odds ratio for developing COVID-19-related pancreatitis in patients with diabetes was 2.241 (95% confidence interval: 1.949–2.578).
Conclusions: COVID-19-related pancreatitis is a rare complication of COVID-19 infection. However, patients with diabetes mellitus have a significantly increased risk of developing this condition.

⑤⑨

接受治療之慢性 B 型肝炎的肝癌風險整合分層：脂肪性肝病與心代謝危險因子的影響
INTEGRATED RISK STRATIFICATION FOR HCC IN TREATED CHRONIC HEPATITIS B: THE IMPACT OF STEATOTIC LIVER DISEASE AND CARDIOMETABOLIC RISK FACTORS

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Background: Chronic hepatitis B (CHB) remains a leading cause of hepatocellular carcinoma (HCC) worldwide, even in patients receiving antiviral treatment. Emerging evidence suggests that coexisting steatotic liver disease (SLD) and cardiometabolic risk factors (CMRFs) may significantly alter HCC risk in treated CHB patients, underscoring the need for refined risk stratification strategies.
Aims: This study investigated the impact of coexisting SLD on the risk of HCC in CHB patients receiving long-term oral antiviral therapy.
Methods: SLD was identified through ultrasound or biopsy evidence of hepatic steatosis. CMRFs included body mass index (BMI), prediabetes or diabetes, hypertension, hypertriglyceridemia, and high-density lipoprotein-cholesterol (HDL-C) levels. HCC risk stratification was performed using Cox regression analysis.
Results: A total of 1,012 patients with CHB who had undergone oral antiviral therapy were enrolled in the study, with a median follow-up period of 5.5 years. A total of 73 HCC events occurred. Patients with both CHB and SLD (n = 702) were younger and had a lower proportion of cirrhosis (26% vs. 41%), as well as lower levels of AST, AFP, FIB-4 (1.94 vs. 3.17), triglycerides, and HDL-C. In contrast, they exhibited higher BMI and platelet counts compared with the non-SLD group (n = 310). Multivariable Cox regression analysis identified SLD (hazard ratio (HR): 0.434, 95% CI: 0.263–0.715, p = 0.001), number of CMRFs (≥2 versus <2, HR: 1.927, 95% CI: 1.179–3.151, p = 0.009), FIB-4 (≥3.25 versus <3.25, HR: 1.949, 95% CI: 1.208–3.143, p = 0.006), and treatment duration (per year, HR: 0.868, 95% CI: 0.793–0.949, p = 0.002) as the independent predictors of HCC occurrence. The combination of SLD and CMRFs (n ≥ 2) effectively stratified HCC risk. In this model, patients with SLD (-) and CMRFs ≥ 2 had a significantly higher risk of developing HCC compared with

those with SLD (+) and CMRFs < 2 (HR: 4.872, 95% CI: 2.347–10.12, p < 0.001). The cumulative incidences of HCC for patients with SLD (-)/CMRFs ≥ 2 and those with SLD (+)/CMRFs < 2 at 3 and 5 years of treatment were 12.5% versus 1%, and 21.4% versus 3.4%, respectively.

Conclusions: Coexisting SLD and CMRFs significantly influence HCC risk in CHB patients receiving antiviral therapy. Incorporating SLD and CMRFs into risk models provides more accurate stratification for optimizing future individualized HCC surveillance strategy.

⑥⓪

HBeAg 陰性慢性 B 型肝炎患者中，再次有限期核苷類治療加速 HBsAg 下降率並提高 HBsAg 低於 100 IU/mL 的比例

ACCELERATED HBSAG REDUCTION RATE AND INCREASED PROPORTION OF HBSAG <100 IU/ML THROUGH REPEATED FINITE NUC THERAPY IN HBEAG-NEGATIVE CHRONIC HEPATITIS B PATIENTS

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Background: Finite therapy is known to increase HBsAg loss rates, but its impact on HBsAg kinetics and reduction among HBeAg-negative chronic hepatitis B (CHB) patients experiencing off-Nuc clinical relapse and undergoing retreatment with finite therapy remains unclear.

Aims: The aim is to evaluate the impact of repeated finite therapy on HBsAg kinetics and reduction in HBeAg-negative CHB patients experiencing off-Nuc relapse and retreatment.

Methods: This analysis included treatment-naïve HBeAg-negative CHB patients who underwent retreatment due to off-Nuc clinical relapse and received at least one additional course of finite Nuc therapy. Nuc cessation followed the APASL stopping rule, requiring at least one year of undetectable HBV DNA before discontinuation. Clinical relapse was defined as ALT >2 times the upper limit of normal with HBV DNA >2000 IU/mL. HBsAg levels were measured at key time points: the start (SOT) and end (EOT) of the 1st treatment, 2nd (1st retreatment: retx_SOT, retx_EOT), and 3rd (2nd retreatment: retx2_SOT, retx2_EOT) treatments, as well as at the last follow-up, using the Elecsys HBsAg II Quantitative Assay (Roche). The annual HBsAg reduction velocity (log10 IU/mL/year) was calculated as the HBsAg log reduction divided by the treatment duration. The primary outcome was the proportion of patients achieving HBsAg <100 IU/mL by the end of follow-up.

Results: A total of 88 treatment-naïve HBeAg-negative CHB patients were recruited. The mean age at the first treatment was 54.5 ± 9.1 years; 86.4% were male, and 34.1% were cirrhotic. During the first treatment, 70 patients used Entecavir, 8 used Tenofovir, and 10 used other Nucs (LAM, LdT). For the second treatment, 65

patients used Entecavir, and 35 used Tenofovir. The median follow-up duration was 13.4 years (12.2–14.6). Sixty-six patients experienced relapse after the first retreatment, and 64 underwent further retreatment. Clinical relapse after repeated finite therapy was primarily observed in the first year and declined thereafter (1st, 2nd, 3rd, and 4th years from retx_EOT: 50.3%, 19%, 3.5%, and 2.6%, respectively). Median HBsAg levels (IU/mL) at key time points were as follows: SOT (1405 IU/mL), EOT (507 IU/mL), retx_SOT (953 IU/mL), retx_EOT (224 IU/mL), retx2_SOT (964 IU/mL), retx2_EOT (144 IU/mL), and last follow-up (76 IU/mL). Annual HBsAg reduction rates during the first, second, and third treatments were -0.091, -0.171, and -0.282 log10 IU/mL/year, respectively ($P < 0.001$). The proportion of patients achieving HBsAg <100 IU/mL increased progressively: 2.3% (SOT), 5.7% (EOT), 11.4% (retx_SOT), 29.6% (retx_EOT), and 53.4% (last follow-up). Three patients (two cirrhotic) developed HCC during follow-up, resulting in an annual HCC incidence of 0.33%. No liver-related mortality was observed.

Conclusions: Repeat finite therapy accelerates HBsAg reduction, significantly increases the proportion of patients achieving HBsAg <100 IU/mL, and maintains a low HCC incidence, making it a viable option for those failing to achieve a sustained response or functional cure after Nuc discontinuation.

⑥1

慢性腎臟病合併 C 型肝炎感染患者於抗病毒治療後，其肝臟相關之臨床危險因子分析

RISK FACTORS FOR LIVER-ASSOCIATED CLINICAL EVENTS IN CHRONIC KIDNEY DISEASE PATIENTS WITH CHRONIC HEPATITIS C INFECTION AFTER ANTIVIRAL TREATMENT

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Background: Hepatitis C virus (HCV)-infected individuals treated with direct-acting antivirals (DAAs) are at risk for liver-associated clinical events (LACE) after achieving sustain virological response (SVR). This study explored the risk factors for liver-associated clinical events in chronic kidney disease (CKD) patients with HCV infection receiving DAA therapy.

Aims: This study explored the risk factors for liver-associated clinical events in chronic kidney disease (CKD) patients with HCV infection receiving DAA therapy.

Methods: From March 2014 to December 2021, 738 patients with HCV-positive CKD who were regularly followed up at Kaohsiung Chang Gung Memorial Hospital for DAA treatment were included in the study.

Results: 738 patients with anti-HCV positive CKD patients were included in this study. Of these 738 patients, 696 patients who had achieved SVR without HCC before DAA treatment were analyzed. Univariate analysis showed that age (≥68.5 years), AFP (≥20 ng/ml), APRI ≥ 1.0, FIB-4 ≥ 3.25, with DM and liver cirrhosis (LC) were risk factors for the development of LACE. Multivariate analysis showed that age ≥ 68.5 (HR: 2.65, $p < 0.001$), AFP ≥ 20 (HR: 2.47, $p < 0.001$) and LC (HR: 8.60, $p < 0.001$) was an independent risk factor for the development of LACE.

Conclusions: In HCV-infected patients with CKD after DAA treatment, the age ≥ 68.5 years, AFP ≥20 and LC was an independent risk factor for the development of LACE even virus elimination.

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2015 至 2022 年 C 型肝炎相關的肝硬化及慢性肝病死亡率下降 43%：來自代表性哨兵醫院的估算
FORTY-THREE PERCENT DECREASE IN HCV-RELATED DEATHS FROM LIVER CIRRHOSIS AND CHRONIC LIVER DISEASES FROM 2015 TO 2022: A ESTIMATION BY A REPRESENTATIVE SENTINEL CENTER

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Background: The decrease in mortality related to Hepatitis C virus (HCV) is one of the WHO impact targets for the elimination of Hepatitis C. In Taiwan, cancer registration of liver cancer includes anti-HCV. However, there has been no national viral etiology registration for mortality cases of liver cirrhosis and chronic liver diseases (LC/CLD).
Aims: This sentinel center study was conducted to estimate the secular trends of HCV-specific mortality for LC/CLD.
Methods: The study period spanned from 2015 to 2022. According to ICD-10 codes K70, K73, and K74, the annual mortality numbers for LC/CLD were extracted from national biostatistics. Using Chang Gung Research Database (CGRD), cases that died from LC/CLD with available results for both HBsAg and anti-HCV tests were included in the analysis. Based on the proportions of HCV distributions from CGRD, the national viral etiology-specific case numbers were estimated using a direct standardized method.
Results: A total of 35,413 patients died from LC/CLD nationally, with 15,445 of them having medical records in CGRD, and 5,940 (16.8%) having results for both HBsAg and anti-HCV tests. The national case number was 4,878 in 2015, decreasing to 4,107 (-15.8%) in 2022. The proportion of anti-HCV decreased from 25.7% to 16.6% (-35.4%). Direct standardization showed that the estimated national case number for anti-HCV decreased from 1,424 to 811 (-43%).
Conclusions: Given the decrease in national patients dying from LC/CLD (-15.8%) and the reduction in the proportion of anti-HCV-positive cases in CGRD (-35.4%), we estimate that the number of anti-HCV-related LC/CLD cases decreased by 43% from 2015 to 2022.

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嘉義監獄受刑人 C 型肝炎篩檢及治療成效
CHRONIC HEPATITIS C ELIMINATION IN CHIAYI PRISONS: EFFECTIVENESS AND CHALLENGES OF DAA THERAPY IN HIGH-RISK POPULATIONS

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Background: Taiwan aims to eliminate hepatitis C virus (HCV). To achieve this goal, Taiwan's National Health Insurance began allowing second-round direct-acting antiviral (DAA) treatments in June 2021.
Aims: During the second large-scale HCV screening at Chiayi Prison, a decline in HCV RNA positivity was observed, though reinfection accounted for approximately 12%, particularly among people who inject drugs (PWID). This study analyzed the effectiveness and side effects of HCV treatment among incarcerated patients.
Methods: Incarcerated individuals at Chiayi Prison were recruited for anti-HCV antibody screening. Those with positive HCV ribonucleic acid (RNA) results received treatment with glecaprevir/pibrentasvir (GLE/PIB) at a specialized chronic hepatitis C (CHC) clinic within the prison. The primary endpoint was achieving a sustained virologic response 12 weeks after completing therapy (SVR12).
Results: As of October 31, 2024, 2,574 incarcerated individuals were invited for anti-HCV screening, with 2,139 (83.1%) participating after excluding cured or HCV RNA-negative cases. Anti-HCV positivity was 11.2% (239/2,139), and the viremic rate was 58.2% (139/239). The current study analyzed 82 patients who completed SVR12 testing by the end of December 2024, resulting in a 100% success rate. Of these, 95.1% were PWID, 12.2% experienced reinfection, 65.6% had hepatitis B virus (HBV) co-infection, and 20.7% co-used sedative-hypnotic drugs. The median FIB-4 score was 1.135 (0.825–1.568), with two patients having Child-Pugh class A cirrhosis. The median baseline HCV RNA level (log10) was 6.434 (5.754–6.683). Genotype 6 was the most common (50.0%), followed by GT 1a (29.3%) and GT 1b (11.0%).
Conclusions: PWID is a significant risk factor for HCV infection among incarcerated individuals. In Chiayi Prison, over 95% of the population consists of drug users, with reinfections primarily linked to drug use. The outcomes of HCV screening and treatment in Chiayi Prison can be applied to other correctional facilities or high-risk populations.

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提升慢性 C 型肝炎治癒後病患肝臟相關事件風險分層：納入 von Willebrand 因子預測因子

ENHANCED RISK STRATIFICATION FOR LIVER-RELATED EVENTS IN POST-HCV CURE PATIENTS: INCORPORATING VON WILLEBRAND FACTOR-BASED PREDICTOR

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Background: Von Willebrand factor (vWF) is a potential biomarker for endothelial dysfunction, portal hypertension, and liver fibrosis, all of which are associated with an increased risk of liver-related events (LREs). However, the role of circulating vWF levels in risk stratification for LREs in patients achieving viral eradication remains to be fully elucidated.

Aims: This study investigates the utility of incorporating von vWF-based predictors, along with other clinical features, to enhance LREs risk stratification in a cohort of patients with chronic hepatitis C (CHC).

Methods: This was a retrospective longitudinal cohort study conducted at a single medical center. The study population comprised 698 patients with CHC who achieved sustained virological response (SVR) to DAA (direct-acting antiviral) therapy between October 2016 and October 2024. Demographic data, medical history, liver stiffness (LS), spleen stiffness (SS), and laboratory values (natural logarithmized) including serum vWF, angiopoietin 2 and 1, were collected at baseline and at the time of SVR, defined as 12 weeks after the end of treatment. The primary outcome was the time to occurrence of incident LREs (including hepatocellular carcinoma) after achieving SVR. Cox proportional hazards regression analysis was employed to identify predictors of LREs. The discriminatory capability was assessed using Harrell's concordance statistic (c-statistic). Sensitivity analyses were performed to evaluate the robustness of the prediction models and the selected features. Kaplan-Meier analysis was also performed to visualize the significance of the predictors for clinical interpretability and utility.

Results: Of the 698 patients included in the study, 46 (6.6%) experienced LREs (median follow-up = 35.3 months). The median age of the patients was 59 (interquartile range 51–67) years, and 61.3% (n = 428) were male. In the multivariable Cox regression analysis, the following features were independently associated with an increased risk of LREs (n = 46): age, albumin (SVR), LS (SVR) (adjusted hazard ratio [aHR] 2.535, 95% confidence interval [CI] 1.435–4.479), and the vWF to platelet ratio (WFPR) at SVR (aHR 1.310, 95% CI 1.027–1.670, P = 0.030). The full model (n = 698) exhibited the c-statistics of 0.881 (95% CI 0.841–0.922, P < 0.001). Sensitivity analyses were initially stratified by compensated advanced chronic liver disease (cACLD) status (LS ≥ 1.59 m/s at SVR). In the subgroup (n = 157) with cACLD at SVR, the significant predictors at SVR for LREs (n = 35) comprised alpha-fetoprotein (AFP), albumin, bilirubin, and WFPR (c-statistics 0.701, 95% CI 0.596–0.792, P = 0.001, for WFPR). By contrast, in the subgroup (n = 541) without cACLD at SVR, the predictors at SVR for LRE prediction (LRE n = 11) included age, AFP, SS, and WFPR (c-statistics 0.703, 95% CI 0.575–0.830, P = 0.021, for WFPR). Time-stratified c-statistics of WFPR in the full cohort (n = 698) were 0.707 at 1 year, 0.798 at 2 years, 0.786 at 3 years, 0.790 at 4 years, and 0.785 at 5 years and 0.770 beyond 5 years (all P < 0.05). Kaplan-Meier analyses showed that WFPR at SVR (threshold: 2.67 maximizing the Youden index) effectively stratified patients (n = 698) into high- and low-risk groups for LREs (n = 46). Subgroup analysis also revealed significance (P = 0.003 and 0.002, respectively) of WFPR (thresholds 3.07 and 2.35, respectively) in both the subgroups with (n = 157) and without (n = 541) cACLD at SVR to predict LREs (n = 35 and n = 11, respectively). While WFPR showed moderate c-statistics (0.770, 95% CI 0.700–0.840, P < 0.001) compared to LS (0.868) in the full cohort (n = 698), it was comparable to SS in its predictive utility. Furthermore, WFPR significantly enhanced the c-statistics of SS (0.774) when combined in a prediction model (c-statistic 0.855, 95% CI 0.829–0.887, P < 0.001), with a statistically significant improvement of 0.081 (P = 0.031 by the DeLong test).

Conclusions: In conclusion, the vWF to platelet ratio at SVR can be utilized and included in risk stratification models for LREs in CHC patients after DAA therapy. The vWF platelet ratio enhances the predictive performance of existing non-invasive measures including SS. These findings may contribute to more accurate risk stratification and personalized post-SVR surveillance strategies in CHC.

主題：上消化道疾病（三）

⑮

荷蘭語版簡短心理健康問卷（ALIMETRY® 腸腦健康調查）在慢性胃十二指腸症狀患者中的驗證研究
VALIDATION OF THE DUTCH VERSION OF THE BRIEF MENTAL WELLBEING QUESTIONNAIRE (ALIMETRY® GUT-BRAIN WELLBEING SURVEY) FOR PATIENTS WITH CHRONIC GASTRODUODENAL SYMPTOMS

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Background: The mental well-being of patients with chronic gastroduodenal symptoms is becoming a growing concern due to its impact on symptom severity and treatment outcome. However, there remains a scarcity of effective tools for evaluating psychological aspects tailored to this specific population. Recently, a novel scale in English, Alimetry® Gut-Brain Wellbeing (AGBW) Survey, developed to evaluate psychological distress in patients with chronic gastroduodenal symptoms has been validated.
Aims: To validate the AGBW Survey in Dutch-speaking samples.
Methods: An internet-based, anonymous mental health survey was distributed to patients with DGBI or gastroparesis via email or neurogastroenterology clinics. The survey included the Dutch AGBW survey, consisting of 10 questions categorized into four related to depression, three related to stress, and three concerning anxiety, alongside a set of validated questionnaires, including Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Perceived Stress Scale-4 (PSS-4), Kessler Psychological Distress Scale (K-10), Big Five Inventory-2 (BFI-2), Emotion Regulation Questionnaire (ERQ), and Patient Assessment of Upper Gastrointestinal Disorders-Quality of Life (PAGI-QoL). We analyzed the psychometric data from these validated questionnaires and compared them to the results obtained from the AGBW survey to assess the reliability and validity.
Results: A total of 84 patients completed the survey (70.2% female, mean age= 41.8 ± 14.8 years). The AGBW Survey exhibited good validity and reliability. Regarding convergent validity, the subscale scores and total scores of the AGBW Survey displayed significant correlations with other measures of anxiety, depression, stress, and psychological distress (all $r > 0.5$, Figure 1). For divergent validity, there were no significant correlation between the AGBW total score and the scores of the BFI extraversion subscale, the ERQ cognitive reappraisal subscale, and the ERQ expressive suppression subscale. For concurrent validity, the AGBW total score was correlated with the PAGI-QoL (Figure 2). In terms of reliability, the Cronbach's alpha coefficients for depression subscale, stress subscale, anxiety subscale and total score were 0.86, 0.61, 0.83 and 0.90, respectively (values >0.7 for Cronbach's alpha are considered a good internal consistency). In addition, the corrected item-total correlations ranged from $r = 0.30–0.76$.
Conclusions: The Dutch AGBW Survey is a valuable and concise tool for evaluating the mental well-being of Dutch-speaking patients with chronic gastroduodenal symptoms.

⑯

巴瑞特氏食道症嚴重度與其高解析度食道壓力檢查數據之分析
ANALYSIS OF BARRETT'S ESOPHAGUS SEVERITY WITH HIGH RESOLUTION ESOPHAGEAL MANOMETRY PARAMETERS

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Background: Esophageal motility dysfunction was thought to be associated with gastroesophageal reflux disease (GERD). Barrett's esophagus was thought to be triggered by long-standing GERD but the relationship between Barrett's esophagus and esophageal motility dysfunction was still unclear.
Aims: This study was aimed to investigate the relationship between the severity of Barrett's esophagus and the result of their high resolution esophageal manometry (HRM) parameters.
Methods: We retrospectively reviewed data of refractory GERD patients who underwent HRM at our hospital. They were divided into three groups. Group 1: patients with refractory GERD without Barrett's esophagus. Group 2: patients with Barrett's esophagus but not eligible for radiofrequency ablation (RFA) under Taiwan National Health Insurance (NHI) policy. Group 3: patients with Barrett's esophagus eligible for RFA treatment under Taiwan NHI policy. Definition of refractory GERD was based on Taiwan NHI criteria for HRM. HRM data including patient characteristics, distal contractile integral (DCI), distal latency (DL) and integrated relaxation pressure (IRP) and Ineffective esophageal motility (IEM) were analysed and compared between these 3 groups using the Chi-square (χ^2) tests.
Results: Total 70 patients whose age were from 27 to 76 years old were enrolled and patients number were Group 1: 51, Group 2: 13, Group 3: 6 respectively. Severe Barrett's esophagus eligible for RFA had lowest DCI (DCI = 798.00, p = 0.829) and highest percentages of IEM (50%, p = 0.349).
Conclusions: We found severe Barrett's esophagus eligible for RFA had lowest DCI and highest percentages of IEM although they were not statistically significant. HRM data revealed a descending trend of DCI value from patients group with refractory GERD without Barrett's esophagus to patients group with refractory GERD and severe Barrett's esophagus.

⑰

功能性消化不良患者透過腹式呼吸可改善症狀，減輕心理困擾，並增強自律神經調節功能
DIAPHRAGMATIC BREATHING IMPROVES SYMPTOMS, REDUCES PSYCHOLOGICAL DISTRESS, AND ENHANCES AUTONOMIC REGULATION IN PATIENTS WITH FUNCTIONAL DYSPEPSIA

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Background: Disorders of gut-brain interactions (DGBIs), also known as functional gastrointestinal disorders, are defined by chronic or recurrent gastrointestinal symptoms without identifiable structural or biochemical abnormalities. Among the DGBIs defined by the Rome Foundation, functional dyspepsia (FD) and irritable bowel syndrome (IBS) are the most common and widely recognized conditions. DGBIs frequently overlap, leading to increased symptom severity. FD has also been linked toreduced vagal activity compared to healthy controls.
Aims: This study examined whether DB is effective in improving FD symptoms, psychological conditions, and heart rate variability (HRV) parameters.
Methods: Adults with FD diagnosed by Rome IV criteria underwent a stress autonomic nervous system (ANS) protocol with measurements at rest during a mental arithmetic test and recovery. Patient-reported outcomes (upper gastrointestinal symptoms, visceral sensitivity, stress, sleep, depression, and anxiety) were assessed using validated questionnaires. DB training was conducted after the first protocol and repeated at one and two weeks. Participants practiced DB twice daily for 5 minutes. Stress ANS protocols were reassessed at baseline, after one session, one week, and two weeks. Patient outcomes were evaluated at baseline, one week, and two weeks. Data were analyzed using generalized estimating equations.
Results: The study included 44 patients (median age 47, 56.8% female): 13 with PDS, 9 with EPS, and 22 with both. PDS patients exhibited lower parasympathetic activity than EPS patients (3.80 vs. 5.51, P = 0.010). Over time, DB decreased sympathetic activity (β = -0.97, P = 0.006) and increased parasympathetic activity during recovery (β =

0.27, P = 0.011). However, patients with EPS experienced smaller reductions in sympathetic activity (β = 2.31, P = 0.002). DB also improved gastrointestinal symptoms (β = -3.56, P = 0.001), visceral sensitivity (β = -7.04, P = 0.001), sleep (β = -1.12, P = 0.005), depression (β = -4.23, P < 0.001), and anxiety (β = -1.95, P = 0.018). However, PDS patients experienced less symptom improvement (β = 3.15, P = 0.02) but greater stress reduction (β = -1.5, P = 0.007). Notably, increased parasympathetic activity correlated with reduced gastrointestinal symptoms (r = -0.443, P = 0.043), depression (r = -0.349, P = 0.003), and anxiety (r = -0.314, P = 0.024).

Conclusions: DB, over time, improves symptoms and psychological conditions in FD and enhances parasympathetic activity while reducing sympathetic activity during a recovery period in stress ANS protocol. The association between increased parasympathetic activity and symptom relief further supports DB as a promising non-pharmacological therapy for FD, warranting further research into its long-term therapeutic outcome and underlying mechanisms.

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內視鏡黏膜阻抗測量可根據里昂共識 2.0 診斷或排除初治患者的胃食道逆流症

ENDOSCOPIC MUCOSAL IMPEDANCE MEASUREMENTS CAN IDENTIFY OR RULE OUT GERD IN TREATMENT-NAIVE PATIENTS IN ACCORDANCE WITH THE LYON CONSENSUS 2.0

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Background: Mucosal impedance (MI) assesses esophageal mucosal integrity during endoscopy, with low values indicating impaired integrity that may result from gastroesophageal reflux disease (GERD). The Lyon score, based on Lyon Consensus (LC), distinguishes GERD from inconclusive and non-GERD cases, but similar distinction using MI is lacking.

Aims: We evaluated the MI thresholds at index endoscopy that can predict presence and absence of conclusive GERD in treatment naïve symptomatic patients presenting for esophageal testing.

Methods: Patients with typical GERD symptoms and normal endoscopy underwent esophageal physiologic testing (pH-impedance monitoring, high resolution manometry) off acid-suppressive therapy. MI was measured during endoscopy using a balloon catheter with 20 sensors, reported as mean, median (interquartile range, IQR) and range. Analysis included acid exposure time (AET), reflux episodes, mean nocturnal baseline impedance (MNBI), hiatal hernia, and reflux-symptom association (RSA). Conclusive GERD was defined as presence of both AET >6.0% and MNBI <1500 Ω, while conclusive absence of GERD required AET <4.0, MNBI >2500 Ω and reflux episodes <40. MI was compared to MNBI using Pearson correlation. ROC analyses determined optimal MI thresholds for predicting or ruling out GERD, based on LC 2.0 criteria and Lyon score.

Results: In 45 symptomatic patients (median age 45.2 years; 62% female), MI correlated with MNBI (r = 0.504, p < 0.001), but MI values were significantly higher than MNBI (mean 4011 ± 1847 vs 2146 ± 899 Ω, median 4146 [IQR 2622-5106] vs 2134 [IQR 1427-2843] Ω and range 678.8-8206.5 vs 483–3996 Ω, all p < 0.0001). Using LC 2.0 criteria for conclusive absence of GERD, an MI threshold of 4142 Ω achieved 100% sensitivity and 73.3%

specificity with AUC of 0.83. Additionally, an MI threshold of 2622 Ω achieved 100% sensitivity, 85.0% specificity and AUC of 0.90 in predicting conclusive GERD. These MI thresholds had better performance characteristics compared to individual components (AET, MNBI) and Lyon score thresholds. When patients were classified into phenotypes based on the new MI thresholds of <2622 Ω for conclusive GERD, 2622–4142 Ω for inconclusive GERD, and >4142 Ω for absence of GERD, commonly used metrics from pH impedance monitoring demonstrated expected progression across phenotypes.

Conclusions: MI measured during index endoscopy can effectively segregate absence of GERD from conclusive presence of GERD when endoscopy is normal in treatment naïve symptomatic patients with suspected GERD. MI values are significantly different from MNBI from pH-impedance monitoring with different thresholds, and the two metrics cannot be directly compared or juxtapositioned. These findings support MI as a pragmatic tool during index endoscopy, especially to rule out GERD, and potentially to identify patients for GERD management.

⑥⑨

驗證喉部認知情感工具在咽喉逆流症狀患者中的適用性及其與症狀嚴重程度的相關性

VALIDATION OF THE LARYNGEAL COGNITIVE-AFFECTIVE TOOL (LCAT) IN PATIENTS WITH LARYNGOPHARYNGEAL SYMPTOMS AND ITS CORRELATION WITH SYMPTOM SEVERITY

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Background: The laryngeal cognitive-affective tool (LCAT) is a newly internationally validated questionnaire designed to enhance understanding of the complex psychosocial interplay among laryngeal-specific hypervigilance and symptom-specific anxiety, and their impact on symptom perception and burden in patients with chronic laryngopharyngeal symptoms (LPS). LCAT has been recently validated in Taiwanese population.

Aims: This study aimed to validate the LCAT in patients with LPS by assessing the differences in LCAT scores among healthy controls, patients with LPS, and patients with typical gastroesophageal reflux disease (GERD) symptoms, as well as examining the correlation between LCAT scores and LPS symptom severity on reflux symptom index (RSI).

Methods: Consecutive patients reporting laryngeal symptoms and/or typical GERD symptoms for more than 3 months were prospectively enrolled at a single center (Hualien Tzu Chi Hospital). Participants were characterized using the RSI, the GERD questionnaire (GERDQ), and the LCAT. Participants were categorized into four groups: healthy controls, patients with LPS, patients with typical GERD symptoms, and patients presenting with both LPS and typical GERD symptoms.

Results: A total of 66 participants were enrolled (mean age 50.7 years, range 20–75 years, 53% female), including 28 healthy controls, 12 patients with LPS, 13 with typical GERD symptoms, and 13 with both typical GERD symptoms and LPS. Patients with LPS and those with both GERD symptoms and LPS had higher LCAT scores than healthy controls and patients with typical GERD symptoms (21.2 and 31.1 vs. 8.3 and 6.5, respectively; $p < 0.001$). In addition, Pearson correlation showed a strong positive association between LCAT and RSI ($r = 0.786$, $p < 0.001$).

Conclusions: Patients with LPS exhibited higher LCAT scores compared with those without LPS. Moreover, the

LCAT score appears to be highly correlated with LPS severity on RSI. The LCAT has thus emerged as a valuable cognitive-affective measure for monitoring LPS. Future research should explore how LCAT scores can be used to predict therapeutic outcomes with various treatment modalities in patients with LPS.

⑦⓪

腦腸軸溝通障礙疾病共存對胃食道逆流症復發的影響

THE IMPACT OF COEXISTING DISORDERS OF GUT-BRAIN INTERACTION ON GASTROESOPHAGEAL REFLUX DISEASE RECURRENCE

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Background: Recurrence of gastroesophageal reflux disease (GERD) is frequently observed in patients after discontinuing proton pump inhibitors (PPIs). Disorders of gut-brain interaction, which often overlap with GERD, may influence the severity of GERD symptoms. However, it remains unclear whether these coexisting conditions increase the risk of GERD recurrence following the cessation of PPI therapy.

Aims: This study aimed to investigate the impact of overlapping disorders of gut-brain interaction, such as functional dyspepsia (FD) and irritable bowel syndrome (IBS), on the likelihood of GERD recurrence.

Methods: A total of 580 GERD patients were prospectively enrolled and completed a series of validated questionnaires prior to upper endoscopy. These included the GERD Questionnaire (GERDQ), reflux symptom index (RSI), Taiwanese depression questionnaire (TDQ), state-trait anxiety inventory (STAI), Pittsburgh sleep quality index (PSQI), and health-related quality of life (HRQoL) scale. All participants underwent PPI treatment and were followed longitudinally.

Results: Among the 330 patients who completed the study, 250 had GERD alone, and 80 had overlapping GERD and either FD or IBS. Patients with overlapping conditions exhibited significantly higher baseline scores on the GERDQ ($p = 0.001$) and RSI ($p = 0.002$) compared to those with GERD alone. Additionally, this group demonstrated higher psychosocial distress, reflected in elevated TDQ ($p = 0.001$) and STAI scores ($p < 0.001$), as well as poorer HRQoL scores ($p < 0.001$). GERD recurrence rates were higher in the overlapping group compared to the GERD-only group (40% vs. 23.6%, $p = 0.004$). Multivariate analysis identified overlapping conditions ($p = 0.024$) and higher baseline GERDQ scores ($p = 0.008$) as independent

predictors of GERD recurrence.
Conclusions: GERD patients with coexisting overlapping conditions and a higher baseline symptom burden are more likely to experience recurrence after stopping PPIs. This study highlights the importance of identifying and addressing these concurrent conditions as part of a comprehensive treatment strategy to effectively reduce GERD recurrence and improve disease management.

主題：下消化道疾病（二）

⑦①

即時電腦輔助系統用於比較水交換法與空氣充氣法在右側大腸腺瘤檢測率及每次大腸鏡檢腺瘤檢測率的隨機對照研究
A REAL-TIME COMPUTER-AIDED SYSTEM TO COMPARE RIGHT COLON ADENOMA DETECTION AND ADENOMA PER COLONOSCOPY RATES IN WATER EXCHANGE AND AIR INSUFFLATION – A RANDOMIZED CONTROLLED STUDY

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Background: A study analyzed randomized controlled trials (RCTs) using pre-recorded videos to compare water exchange (WE) with air insufflation, in conjunction with a computer-aided detection (CADe) algorithm. The findings indicated that CADe and WE effectively complemented each other's weaknesses (GIE, 2022;95:1198). Specifically, CADe improved polyp and adenoma detection rates (ADR) during water exchange procedures, while WE significantly enhanced the effectiveness of CADe. This synergistic effect not only improves diagnostic accuracy but also has the potential to reduce the incidence of interval colorectal cancers (ICC), which have been associated with low adenoma per colonoscopy (APC) and low ADR in the right colon. APC is defined as the total number of adenomas resected divided by the total number of colonoscopies performed, with a higher APC correlating to a reduced incidence of ICC (CGH, 2023;21:200-209; GIE 2024;99:787-95). The impacts of combining CADe with WE on enhancing overall ADR and APC were presented as an interim report at the 2024 Digestive Disease Week. Recruitment for the study has been completed.
Aims: The focus now shifts to examining the differences in right colon ADR and APC between WE and air insufflation when each is combined with CADe.
Methods: A CADe model was developed employing a

convolutional neural network with a transfer learning approach, specifically YOLOv4, to accurately identify colon polyps. The CADe algorithm achieved a notable mean average precision of 94.0% and an area under the receiver operating characteristic curve of 0.98. Sensitivity and specificity values were established at 0.96 and 0.97, respectively. The positive predictive value was determined to be 0.98, while the negative predictive value was 0.93. The algorithm underwent rigorous validation through a video analysis study. To evaluate its real-time applicability, 325 eligible patients were prospectively recruited and completed real-time CADe-assisted colonoscopies utilizing either water exchange (WE) or air insufflation methods. The resected polyps were subsequently examined by a pathologist who was blinded to the CADe results (ClinicalTrial.gov number NCT05448300).

Results: The real-time CADe colonoscopies included patients inserted with either WE (n = 165) or air insufflation (n = 160). Table 1. shows procedural data of the participants. Table 2. shows the right colon ADR was significantly higher in WE group (39.4%) compared with the air insufflation group (23.1%), P = 0.002. The right APC was significantly higher in WE group compared with the air insufflation group (0.82 versus 0.34, P < .0001), respectively.

Conclusions: This report indicates that the combination of WE improved the performance of CADe regarding right colon ADR and APC. The integration of CADe with WE has the potential to significantly reduce ICC. Long-term studies are necessary to validate this hypothesis.

⑦② 定義兒童大腸鏡中合理的盲腸到達時間：如何在完整檢查與過長檢查時間中取得平衡？ HOW LONG IS TOO LONG? DEFINING REASONABLE CECAL INTUBATION TIMES IN PEDIATRIC COLONOSCOPY TO BALANCE COMPLETE EXAMINATION AND PROLONGED PROCEDURE TIME

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Background: In recent years, colonoscopy for children has become increasingly common. The American Society for Gastrointestinal Endoscopy (ASGE) and the North American and European Societies of Pediatric Gastroenterology Hepatology and Nutrition (NASPGHAN and ESPGHAN) just released guidelines for pediatric colonoscopy. The quality indicators include 1. terminal ileal intubation unadjusted rate ≥85% 2. cecal intubation unadjusted rate ≥90% 3. adequate bowel preparation ≥80%. In adults, withdrawal time more than 6 minutes is the important indicator for adenoma detection rate. Currently, there are no recommendations for the appropriate procedure time for pediatric colonoscopy. Since pediatric colonoscopies are almost always performed under anesthesia, procedure time is important in minimizing sedation-related complications, which are the most common cause of complications in pediatric colonoscopy. Previous studies reported variable times, even in high-quality colonoscopies. Evaluating the benefits of a complete examination versus the risks of prolonged procedure time is a crucial issue.

Aims: Based on our experience, cecal intubation time (CIT) is the key step determining total procedure time, except when additional procedures, such as polypectomy, are performed. We aim to identify the factors that affect CIT and define a reasonable CIT for different populations.

Methods: We retrospectively evaluate all patients who underwent colonoscopy at our hospital between January 2022 and October 2024. All patients received the same bowel preparation. All colonoscopies were performed under general anesthesia by the same pediatric gastroenterologist, using the same scope. Data was collected on age, sex, height, weight, body mass index (BMI), surgical history, indications, bowel cleansing efficacy (using the Aronchick scale), diagnosis and pathology results, as well as cecal

intubation time.

Results: A total of 112 patients were analyzed. The cecal intubation rate was 97.3% (109/112), the terminal ileal intubation rate was 96.4% (108/112), and the adequate bowel preparation rate was 92.8% (104/112). There were no adverse events. The mean age was 9.4 years, ranging from 1 to 17 years. The most common indications were bloody stool (57.1%), abdominal pain (14.3%) and anemia (8.9%). Mean CIT was 12 minutes (2.8-56.6 minutes, SD 8.9 minutes), which was comparable to a recent study that suggests sub-10-minute ileal intubation is feasible. CIT was shorter in younger patients compared to older patients ($p = 0.016$). There was a significant difference ($p = 0.03$) in CIT between patients < 13 years (mean 10.6 minutes, SD 7.5 minutes) and those ≥ 13 years (mean 14.5 minutes, SD 10.7 minutes). Patients classified as having good (47.3%) and fair (24.1%) bowel cleansing according to the Aronchick scale had longer CIT compared to those classified as excellent (21.4%), with p values of 0.016 and 0.031, respectively. The results of the multivariate logistic regression analysis identified age ≥ 13 years, and poor or inadequate bowel cleansing as independent factors associated with CIT > 10 minutes [OR: 2.725 (1.027-7.23) $p = 0.044$; OR: 6.8 (1.122-42.161) $p = 0.037$].

Conclusions: In our study, older age and non-excellent bowel cleansing were found to prolong cecal intubation time. CIT exceeding 25.7 minutes (mean + 2 SD) in patients < 13 years and 35.8 minutes (mean + 2 SD) in patients ≥ 13 years may be considered prolonged and difficult colonoscopy. The benefit of a complete examination must be assessed based on the indication, potential diagnosis, and should outweigh the risks associated with prolonged procedure time.

⑦③

使用合併進階治療於治療發炎性腸道疾病：真實世界現狀與醫師態度之調查
REAL-WORLD USAGE AND ATTITUDE FOR ADVANCED COMBINED THERAPIES IN TREATING INFLAMMATORY BOWEL DISEASE

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Background: Advanced combination therapies (ACT) targeting distinct pathways show promise in breaking the therapeutic ceiling for inflammatory bowel disease.

Aims: This study addressed the gaps between current evidence and practice by exploring the real-world experiences and attitude toward ACT.

Methods: A cross-sectional online survey was conducted via QR code during meetings or email invitation. The survey covered participant demographics, experiences with ACT for ulcerative colitis (UC), Crohn's disease (CD), and knowledge of ACT.

Results: Among 234 participants from 20 countries, 51.7% had adopted ACT. Of these, 86% had treated UC, 66.9% CD, and 52.9% both. While 48.3% had no experience, 76.1% would try ACT if indicated. Refractory diseases were the most common indications (UC 44.1%, CD 48.7%). For ACT duration, 52.8% were time-oriented, favoring limited use within 6 months. No adverse events were reported in 59.5%. Of the events, infections (69.8%) were most common. Add-on strategy was the most adopted (UC 78.8%, CD 71.6%), particularly janus kinase inhibitor (JAKi) added on anti-integrin for UC (18.6%)

and anti-tumor necrosis factor alpha (anti-TNFα) added on anti-interleukin 12/23 (anti-IL12/23) for CD (14%). Concomitant strategy followed (UC 51%, CD 48.1%), while sequential strategy was the least used (UC 33%, CD 29.6%). Inexperienced physicians also preferred add-on use (87.2%), but prioritized goal-oriented use, targeting endoscopic (30.2%) and clinical (27.6%) remission.

Conclusions: In real-world practice, ACT was primarily used for refractory IBD with limited duration. Add-on use was the most adopted. Differences in treatment approaches reflet varying levels of physician experiences.

⑦④

超音波引導下消融治療於結直腸癌肝轉移之七年回顧：單一中心的成果與影響因子分析

A SEVEN-YEAR REVIEW OF ULTRASOUND-GUIDED ABLATIVE THERAPIES FOR COLORECTAL LIVER METASTASES: OUTCOMES AND INFLUENCING FACTORS FROM A SINGLE CENTER

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Background: Colorectal liver metastasis (CRLM) is generally considered a systemic disease, so the mainstay of treatment should be systemic therapies. Currently, it is believed that a multimodal approach, combining local ablative and systemic therapies, can improve tumor control and potentially prolong patient survival.

Aims: This study aimed to evaluate survival outcomes and influencing factors of CRLM patients treated with ultrasound-guided percutaneous ablative therapies.

Methods: A retrospective analysis of 56 patients treated with RFA (n = 40) or MWA (n = 16) was conducted at Taipei Medical University Hospital between January 2018 and December 2024. Kaplan-Meier survival analysis and group comparisons assessed overall survival and recurrence.

Results: A total of 56 patients were included in the analysis, with a median follow-up of 24.6 months. Kaplan-Meier survival analysis showed an overall survival (OS) rate of 86.60% at one year, 41.81% at three years, and 30.97% at five years, with a median OS of 30.03 months. There was no significant difference in survival between the RFA and MWA groups. Furthermore, the analysis of factors influencing recurrence revealed no statistically significant associations between recurrence and variables such as gender, age, BMI, tumor size, tumor proximity to vessels, cancer type, time from liver metastasis to procedure, treatment modality, or CEA levels. These findings suggest

that recurrence may be influenced by other factors not captured in this analysis.

Conclusions: Ultrasound-guided ablative therapies are effective and safe for CRLM, providing robust survival outcomes. Future multicenter studies are needed to explore local ablation method -specific differences.

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使用血液學檢驗協助改善發炎性腸道疾病之內視鏡活動性預測

ENHANCING INFLAMMATORY BOWEL DISEASE ENDOSCOPIC ACTIVITY PREDICTION BY USING BLOOD TESTS

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Background: Endoscopy is the gold standard for disease activity monitoring, and fecal calprotectin (FC) plays an important role in non-invasive tests. According to the patients' preference, endoscopy and stool examination are unpleasant, while serum biomarkers are more acceptable. Leucine-rich α-2-glycoprotein (LRG) is a new serum biomarker. In addition, C-reactive protein (CRP), albumin (Alb), and hemoglobin (Hb) are frequently applied in our daily work.

Aims: We aim to survey how to enhance disease monitoring by non-invasive blood tests.

Methods: This is a single-centered prospective study. Inflammatory bowel disease (IBD) patients receiving ileocolonoscopy at National Taiwan University Hospital from March 2022 to March 2024 were enrolled. Hb, Alb, CRP, serum LRG and fecal calprotectin were obtained within 1 month of endoscopy. Active endoscopic activity was defined as Mayo endoscopic score (MES) ≥2 for ulcerative colitis (UC) or simple endoscopic score for Crohn's disease (SES-CD) ≥6 for CD. The correlation between biomarkers and the predictive ability of biomarkers were analyzed by SAS 9.4.

Results: 203 patients (100 UC and 103 with CD) were enrolled. The range of serum LRG, CRP, Alb, and Hb were 4.6 to 40 ug/mL, 0.02 to 31.68 mg/dL, 3.6 to 5.2 g/dL and 7.1 to 16.5 g/dL, respectively. The area under curve (AUC) of CRP, LRG and FC for predicting active endoscopic findings were 0.61, 0.57 and 0.73 respectively. Among UC patients, 49 patients (49%) were in the active group. Serum LRG levels were positively correlated with CRP ($r = 0.376$, $p < 0.01$) and FC ($r = 0.201$, $p < 0.05$), while negatively correlated with Alb ($r = -0.358$, $p < 0.01$) and Hb ($r = -0.489$, $p < 0.01$). The AUC of CRP and LRG to predict endoscopic active lesions were 0.45 and 0.57. When using the combination, AUC of CRP + Hb + Alb + LRG (0.68) was significantly higher than CRP + Hb + Alb (0.53, p <

0.05), LRG + CRP + Alb (0.61) and CRP + Alb (0.49). The cut-off value of CRP and LRG was 1.0 mg/dL and 8.1 ug/mL. Among CD patients, 27 patients (26.2%) were with active endoscopic findings. Serum LRG levels were positively correlated with CRP ($r = 0.629$, $p < 0.01$) and FC ($r = 0.179$, $p = 0.07$), while negatively correlated with Alb ($r = -0.584$, $p < 0.01$) and Hb ($r = -0.495$, $p < 0.01$). The AUC of CRP and LRG to predict active endoscopic lesions were 0.70 and 0.61. The AUC of CRP + Hb + Alb + LRG was 0.71, higher than CRP + Hb + Alb (AUC 0.70, $p = 0.85$), LRG + CRP + Alb (AUC 0.67) and CRP + Alb (AUC 0.65) with the cut-off values of CRP as 0.08 mg/dL and LRG as 10.8 ug/mL.

Conclusions: LRG levels added on Alb, CRP, and Hb reveal the best prediction for endoscopic activity when using blood sample tests for the UC patients.

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3D 立體大腸鏡和 2D 標準大腸鏡對於大腸腺瘤偵測率之比較：一個多中心隨機分組臨床試驗

COMPARISON OF ADENOMA DETECTION RATE BETWEEN THREE-DIMENSIONAL AND STANDARD COLONOSCOPY: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Background: Improvement of adenoma detection rate (ADR) effectively reduces the subsequent incidence of colorectal cancer (CRC). Three-dimensional (3D) colonoscopy provided more anatomical details than standard two-dimensional (2D) colonoscopy and improved ADR in a simulation study. We aimed to compare the ADR between 2D and 3D colonoscopy.

Methods: In this multicenter randomized controlled trial, subjects aged ≥ 40 years who underwent colonoscopy for screening, surveillance, or symptoms were consecutively enrolled between February 2022 and June 2023 and randomized into 2D or 3D groups with a 1:1 ratio. The primary outcome was ADR. The secondary outcomes included the detection rates of flat adenoma, right-sided adenoma, proximal adenoma, sessile serrated lesion and advanced adenoma.

Results: Of the 348 participants recruited, 158 and 160 were allocated to 2D and 3D colonoscopy, respectively. The mucosa inspection time was comparable between the 3D (9.8 ± 2.6 minutes) and 2D (9.4 ± 3.1 minutes) groups ($p = .21$). The 3D group had significantly higher ADR (53.1% vs. 38.6%, difference (95% confidence interval, CI): 14.5% (3.7–25.4), $p = .0094$), as well as higher detection rates for flat adenoma (35.0% vs. 21.5%, difference: 13.5% (3.7–23.3), $p = .0076$), right-sided adenoma (26.3% vs. 15.2%, difference: 11.1% (2.2–19.9), $p = .015$), proximal adenoma (38.1% vs. 23.4%, difference: 14.7% (4.7–24.7), $p = .0045$) and adenoma sized 5–9 mm (45.0% vs. 31.0%, difference: 14.0% (3.4–24.5), $p = .010$). However, there was no difference in the detection rate of sessile serrated lesion and advanced adenoma.

Conclusions: 3D colonoscopy improved the detection of adenomas without significantly increasing the mucosa inspection time (ClinicalTrials.gov: NCT05153746).

主題：膽胰疾病（二）

⑦⑦

經胰管預切開技術在低檢查量環境下對於膽胰鏡檢查品質之影響
THE IMPACT OF TRANSPANCREATIC PRECUT SPHINCTEROTOMY ON THE QUALITY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN A LOW-VOLUME SETTING

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Background: Although quality improvement is crucial for ERCP, a low practice volume can pose challenges to achieving high-quality bile duct cannulation. Transpancreatic precut sphincterotomy (TPS) has been proven effective for advanced cannulation. However, existing data mainly come from skilled endoscopists in large medical centers. The impact of TPS on ERCP quality in a lower-volume setting deserves investigation.
Aims: The impact of TPS on ERCP quality in a lower-volume setting deserves investigation.
Methods: Our hospital performs approximately 200 ERCPs annually, with 1 expert endoscopist performing approximately half of them and 3 nonexpert endoscopists sharing the remaining cases. TPS was started and became our predominant advanced cannulation technique in April 2016. We retrospectively reviewed ERCP cases 3 years before and after the introduction of TPS. The primary endpoints of the study were the differences in 2 ERCP quality indicators, the bile duct cannulation rate and the incidence of post-ERCP pancreatitis (PEP).
Results: A total of 701 ERCP cases with naïve papilla were analyzed, with 350 patients treated before the introduction of TPS and 351 patients treated afterward. The successful cannulation rate was significantly improved (before, 87.4%; after, 92.3%, P = .032), whereas the incidence of PEP decreased, but not significantly (before, 4.0%; after, 2.8%; P = .402). All endoscopists benefited from using TPS, with nonexperts demonstrating a significantly higher improvement in the cannulation rate (before, 85.5%; after, 93.1%; P = .019).
Conclusions: TPS can effectively enhance the quality of ERCP irrespective of practice volume.

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ERCP 術中括約肌切開時短暫出血後，注射腎上腺素溶液以預防延遲性出血的療效：初步報告
EFFICACY OF PROPHYLACTIC EPINEPHRINE SOLUTION INJECTION IN PREVENTION OF DELAYED POST-SPHINCTEROTOMY BLEEDING IN PATIENTS WITH TRANSIENT BLEEDING DURING ERCP: A PRELIMINARY REPORT

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Background: Bleeding is the most frequently reported serious complication of endoscopic sphincterotomy, and the occurrence of any observed bleeding during the procedure is the risk factor of delayed post-EST bleeding. We use the endoscopic injection of epinephrine - most commonly used way, effective, and least expensive method for the management of immediately post-EST bleeding to prevent delayed post-EST bleeding.
Aims: To determine whether prophylactic epinephrine solution injection affects incidence of delayed post-EST bleeding in those patients with transient bleeding during ERCP.
Methods: This was a single blinded, two-arm parallel group, single center, randomized controlled study. From July 2021 to November 2024, a total of 6154 ERCPs were performed, of which 1988 patients had undergone endoscopic sphincterotomy (EST), and 160 consecutive patients were enrolled after excluding those who had previous EST, ampulla vater tumor, or underlying coagulopathy including thrombocytopenia, liver cirrhosis or chronic renal disease. Eligible patients who suffered transient bleeding more than 1 minute after sphincterotomy, were randomized to receive either epinephrine solution injection or not after whole procedure end. All patients were followed up for 30 days. The primary outcome was the proportion of patients with delayed post-EST bleeding.
Results: Altogether 160 patients (80 in the injection group and 80 in the non-injected group) who had undergone sphincterotomy with transient bleeding more than 1 minute were analyzed. Delayed bleeding was noted in four (5.0%) patients in the injected group and three (3.8%) patients in the non-injected group (P > 0.99). There were no significant differences in other outcomes, such as adverse effect

incidence including pancreatitis or cholangitis, a decrease in hemoglobin, or prolonged procedure time.
Conclusions: In the patient group of transient bleeding more than 1 minute after sphincterotomy, prophylatic epinephrine solution injection did not reduce the risk of delayed post-EST bleeding, though increased adverse effects were not found.

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部分覆膜金屬支架取代塑膠支架治療惡性肝外膽道狹窄：一醫學中心的臨床結果

PARTIALLY COVERED SELF-EXPANDABLE METAL STENTS REPLACE PLASTIC STENTS FOR MALIGNANT EXTRAHEPATIC BILIARY OBSTRUCTION: CLINICAL OUTCOMES OF A MEDICAL CENTER

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Background: Endoscopic biliary stenting has been well established as standard treatment of malignant biliary obstruction. Comparing with plastic stent, self-expandable metal stent (SEMS) has longer stent patency. However, few reports are published to compare primary SEMS placement and reintervention of SEMS to replace plastic stent.
Aims: The aim of this study was to assess the differences in stent patency, patient survival and complications between patients with primary metal stent placement and reintervention to replace previous plastic stent.
Methods: From Jan., 2010 to Dec., 2024, patients with malignant obstruction below the common hepatic duct (CHD) confluence undergoing biliary stenting with partially covered self-expandable metal stents (PCSEMS) were retrospectively analyzed. Malignancy was diagnosed based on clinical, laboratory, imaging, and pathological studies.
Results: A total of 427 patients undergoing biliary stenting with metal stents were identified from the database. Among those patients receiving uncovered SEMS (n = 101), fully covered (n = 43) SEMS and being lost to follow-up (n = 29) were excluded in the study. Finally, 254 patients (139 female and 115 male; median age 71.0 years) with PCSEMS for malignant obstruction below the CHD confluence were included. Malignancy included pancreatic cancer (n = 167, 66%), cholangiocarcinoma (n = 32, 13%), ampullary cancer (n = 30, 12%), metastatic cancer (n = 22, 8.7%), and gallbladder cancer (n = 3, 1.2%). Strictures were located at perihilar (n = 9, 3.5%) and distal (n = 245, 96.5%) extrahepatic duct respectively. Average length of stricture was 15.0 mm. All patients underwent endoscopic sphincterotomy before metal stent placement. One hundred and twenty-four (49%) patients received chemotherapy and/or radiotherapy. Fifty-nine (23%) patients underwent PTCD and/or PTGBD. PCSEMS was placed as a primary

intervention in 82 (32.3%) patients, and PCSEMS replacing plastic stent was performed in 172 (67.7%) patients. The overall stent patency and patient survival were 151.0 (0.0–1715.0) days and 165.0 (4.0–1715.0) days respectively. Patients undergoing reintervention were longer than primary intervention in stent patency (174.0 days vs 121.5 days; P = 0.010) and patient survival (188.5 days vs 130.5 days; P = 0.012). During the period of follow-up, stent complications occurred in 69 of 254 (27.2%) patients including cholecystitis (n = 6; 2.4%), pancreatitis (n = 5; 2.0%), stent migration (n = 5; 2.0%), liver abscess (n = 2; 0.8%), stent occlusion (n = 1; 0.4%), perforation (n = 1; 0.4%), and hemorrhage (n = 1; 0.4%). There was no significant difference between reintervention and primary intervention in early, late or overall complications of metal stents (P > 0.05).

Conclusions: For patients with malignant obstruction below the CHD confluence, primary metal stent placement and reintervention with PCSEMS showed comparable stent complications, although reintervention demonstrated longer stent patency and patient survival.

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積極與非積極靜脈輸液對急性胰臟炎臨床結果的比較：系統性回顧和統合分析

COMPARISON OF CLINICAL OUTCOMES BETWEEN AGGRESSIVE AND NON-AGGRESSIVE INTRAVENOUS HYDRATION FOR ACUTE PANCREATITIS: A SYSTEMIC REVIEW AND META-ANALYSIS

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Background: Current practice guidelines for optimal infusion rates during early intravenous hydration in patients with acute pancreatitis (AP) remain inconsistent.

Aims: This systematic review and meta-analysis aimed to compare treatment outcomes between aggressive and non-aggressive intravenous hydration in severe and non-severe AP.

Methods: This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We systematically searched PubMed, Embase and Cochrane Library for randomized controlled trials (RCTs) on November 23, 2022, and hand-searched the reference lists of included RCTs, relevant review articles and clinical guidelines. We included RCTs that compared clinical outcomes from aggressive and non-aggressive intravenous hydration in AP. Meta-analysis was performed using a random-effects model for participants with severe AP and non-severe AP. Our primary outcome was all-cause mortality, and several secondary outcomes included fluid-related complications, clinical improvement and APACHE II scores within 48 h.

Results: We included a total of 9 RCTs with 953 participants. The meta-analysis indicated that, compared to non-aggressive intravenous hydration, aggressive intravenous hydration significantly increased mortality risk in severe AP (pooled RR: 2.45, 95% CI: 1.37, 4.40), while the result in non-severe AP was inconclusive (pooled RR: 2.26, 95% CI: 0.54, 9.44). However, aggressive intravenous hydration significantly increased fluid-related complication risk in both severe (pooled RR: 2.22, 95% CI: 1.36, 3.63) and non-severe AP (pooled RR: 3.25, 95% CI: 1.53, 6.93). The meta-analysis indicated worse APACHE II scores (pooled mean difference: 3.31, 95% CI: 1.79, 4.84) in severe AP, and no increased likelihood of clinical improvement (pooled RR:1.20, 95% CI: 0.63, 2.29) in non-severe AP. Sensitivity analyses including only RCTs with

goal-directed fluid therapy after initial fluid resuscitation therapy yielded consistent results.
Conclusions: Aggressive intravenous hydration increased the mortality risk in severe AP, and fluid-related complication risk in both severe and non-severe AP. More conservative intravenous fluid resuscitation protocols for AP are suggested.

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內視鏡逆行胰膽管之膽汁菌種培養結果：探討惡性與良性膽道阻塞的微生物菌種差異
BILE CULTURE PATTERNS IN ERCP: EXPLORING THE MICROBIAL LANDSCAPE OF ACUTE MALIGNANT AND BENIGN OBSTRUCTION

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Background: Endoscopic retrograde cholangiopancreatography (ERCP) is a widely employed procedure for managing biliary obstructions, whether due to malignant or benign causes. Acute biliary obstruction presents significant clinical challenges, with bile cultures providing essential insights into microbial pathogens to guide antibiotic selection and therapeutic decisions.
Aims: This study aims to compare bile culture results between patients with acute malignant obstruction (MBO) and those with benign obstruction (BBO), focusing on microbial diversity, resistance patterns, and infection risk.
Methods: This single-center retrospective cohort study analyzed patients undergoing their first ERCP for acute biliary obstruction between January 1, 2024, and June 30, 2024. Patients were classified into two groups: MBO and BBO. Bile samples collected during ERCP were cultured for microbial identification and antibiotic susceptibility testing. Comparative analyses were performed to assess differences in microbial profiles between the groups.
Results: A total of 182 bile cultures were analyzed, comprising 138 from the BBO group and 44 from the MBO group. Among BBO patients, choledocholithiasis was the predominant cause (135/138, 98%), while pancreatic cancer was the most common indication in the MBO group (31/44, 63%). Overall, 120 cultures (66%) yielded positive results. Positive culture rates were significantly higher in the BBO group compared to the MBO group (69% vs. 57%, $p < 0.05$). Polymicrobial infections were more frequent in the BBO group (39% vs. 32%). Differences were also observed in monomicrobial cultures, with higher rates of Gram-positive bacteria in the BBO group (24% vs. 4%) and Gram-negative bacteria in the MBO group (31% vs. 56%). Candida was isolated in a small proportion of cases, with no significant difference between BBO (6%) and MBO (8%) groups.
Conclusions: Bile cultures obtained via ERCP demonstrate a high yield, with significant differences in microbial patterns between BBO and MBO groups. These findings underline the importance of tailoring antimicrobial strategies based on the underlying etiology of biliary obstruction.

主題：肝臟相關疾病

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經 X 光透視影像導引切片與經口膽道鏡導引切片在不明原因膽道狹窄診斷中之比較
COMPARISON OF FLUOROSCOPY-GUIDED FORCEPS BIOPSY AND PERORAL CHOLANGIOSCOPY-GUIDED FORCEPS BIOPSY FOR INDETERMINATE BILIARY STRICTURE

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Background: Endoscopic retrograde cholangiopancreatography (ERCP) with fluoroscopy-guided forceps biopsy (F-FB) is widely used to diagnose indeterminate biliary lesions. Recently, peroral cholangioscopy (POCS) with POCS-guided forceps biopsy (POCS-FB) has emerged as an alternative. However, the comparative effectiveness of F-FB and POCS-FB for diagnosing extrahepatic cholangiocarcinoma (ECC) remains unclear.
Aims: This study aims to evaluate the diagnostic accuracy and safety of F-FB and POCS-FB.
Methods: Patients who underwent F-FB or POCS-FB for the evaluation of indeterminate biliary lesions between January 2019 and November 2024 were retrospectively included. The diagnostic performance of F-FB and POCS-FB, including sensitivity, specificity, and accuracy, was compared based on pathological results. Adverse events related to both tissue acquisition techniques were also analyzed.
Results: A total of 21 patients with biliary diseases who underwent F-FB or POCS-FB were included. The sensitivity, specificity, and accuracy of F-FB were 72.5%, 100%, and 82.6%, respectively, while for POCS-FB, these values were 68.5%, 100%, and 80.5%. There were no significant differences in diagnostic performance between the two techniques. Similarly, the adverse event rates were comparable, with 3.0% for F-FB and 5.5% for POCS-FB (P = 0.346).
Conclusions: F-FB and POCS-FB demonstrate similar diagnostic performance for detecting malignancy in this study. POCS-FB may require more biopsy attempts and cholangioscopy image evaluations to make the accurate diagnosis.

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利用聲波輻射脈衝（ARFI）和 FIB-4 優化臨床照護中高風險 MASH 的篩檢
OPTIMIZING AT-RISK MASH SCREENING IN A INNOVATIVE CLINICAL CARE PATHWAY UTILIZING ARFI AND FIB-4

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Background: The spectrum of metabolic dysfunction-associated steatotic liver disease (MASLD) includes isolated steatosis, which may progress to metabolic dysfunction-associated steatohepatitis (MASH), fibrosis, cirrhosis, and hepatocellular carcinoma. Patients with significant fibrosis (fibrosis stage 2 or higher, [≥F2]) or advanced fibrosis (fibrosis stage 3 or higher, [≥F3]) face increased risks of morbidity and mortality. Early diagnosis of fibrosis and subsequent appropriate management can potentially prevent progression to cirrhosis and its complications. In 2021, liver stiffness measurement (LSM) using acoustic radiation force impulse (ARFI) elastography was found to be more cost-effective in Taiwan. Consequently, the clinical pathway was modified based on the AGA 2021 guideline by using FIB-4 > 1.3 or ARFI > 1.25 (according to Taiwanese data) in adults at risk (≥2 metabolic risk factors, type II diabetes mellitus, steatosis on imaging, or persistently elevated aminotransferases).
Aims: Our aim is to identify the best clinical care pathway for screening populations at risk for MASH. Specifically, we aim to evaluate the effectiveness of the modified clinical pathway in identifying at-risk MASH patients who are eligible for pharmacological treatment, thereby preventing progression to cirrhosis and its complications.
Methods: In 2021 in Taiwan, liver stiffness measurement (LSM) using acoustic radiation force impulse (ARFI) elastography was found to be more cost-effective. Thus, we modified the clinical pathway based on the AGA 2021 guideline by using FIB-4 > 1.3 or ARFI > 1.25 (according to Taiwanese data) in adults at risk (≥2 metabolic risk factors, type II diabetes mellitus, steatosis on imaging, or persistently elevated aminotransferases). This prospective study, conducted from 2021 to 2023, enrolled outpatients with indeterminate risk according to the modified clinical care pathway who were willing to receive a liver biopsy.

At-risk MASH was defined as MASH with SAF score ≥4 and significant fibrosis (≥F2), with SAF scoring at least 1 point in each category of steatosis, activity, and fibrosis on pathology. We used independent t-test, Mann-Whitney U test, Chi-square test, and Fisher's test to compare at-risk MASH and normal MASH. We also collected various parameters to predict MASLD or liver fibrosis, including NFS, APRI, FLI, HSI, VAI, and HOMA-IR. Patients with alcoholic hepatitis and autoimmune hepatitis were excluded.

Results: In our clinical care pathway, a total of 48 patients were included, with a median BMI of 30.0 (kg/m²). Five patients were HBV carriers and six patients were HCV carriers. Forty-seven patients had obesity; 22 patients had type II diabetes mellitus, 31 patients had diabetes mellitus, and 33 patients had dyslipidemia. The median ARFI was 1.98 and FIB-4 was 1.28. Forty-six (95.8%) patients were diagnosed with MASH proven by liver biopsy. Two patients were diagnosed with chronic inflammation of unknown etiology. Thirty-two (66.7%) patients were diagnosed with at-risk MASH. Compared to the normal MASH group, the glucose AC, insulin, and HOMA-IR were significantly higher in the at-risk MASH group ($P < 0.05$), and APRI was borderline significantly higher in the at-risk MASH group ($P = 0.07$). After excluding HBV and HCV carriers, glucose AC, insulin, HOMA-IR, and APRI remained significantly higher in the at-risk MASH group ($P < 0.05$). For diagnosis using HOMA-IR in our clinical pathway, the AUROC was 0.74, with cutoff values of 3.93 (sensitivity 0.72, specificity 0.75).

Conclusions: The modified clinical care pathway successfully identified patients with at-risk MASH, emphasizing the significance of glucose, insulin, HOMA-IR, and APRI as key markers for assessing fibrosis risk. Early detection and appropriate management are essential to prevent disease progression and improve patient outcomes. This pathway demonstrates the potential to reduce reliance on invasive liver biopsies in clinical practice.

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肥胖代謝功能障礙相關脂肪肝病短期生活改變後代謝組學和微生物群的變化
METABOLOMICS AND MICROBIOTA CHANGE AFTER SHORT-TERM LIFE MODIFICATION IN OBESE MASLD

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Background: The diagnosis of metabolic dysfunction-associated steatotic liver disease (MASLD) is based on radiological or pathological liver steatosis and fulfills one of the five cardiometabolic risks, which are 1. BMI ≥ 23 kg/m² or waist circumference >94 cm for men and >80 cm for women, 2. Fasting serum sugar >100 mg/dL or 2 hours post load sugar test >140 mg/dL or HbA1c >5.7%, 3. Blood pressure >130/85 mmHg, 4. Plasma triglycerides >150 mg/dL, 5. HDL-cholesterol >40 mg/dL for men and >50 mg/dL for women. Gut dysbiosis plays a key role in pathogenesis. Currently, the main management is based on life modification with exercise enhancement and caloric restriction to achieve body weight loss.

Aims: This study aims to explore the differences in clinical biochemical and metabolic indicators, blood metabolomics, and intestinal microbiota in obese with metabolic dysfunction-associated steatotic liver disease candidates before and after diet and exercise interventions.

Methods: Obese volunteers with a BMI ≥ of 27 were recruited from the gastrointestinal outpatient department. All subjects were informed of the research process and signed a subject consent form. Before and after the 8-week research plan, subjects will be required to measure their Anthropometric, blood biochemical tests, and serum metabolomics. To conduct pre and post-intervention intestinal microbiota analysis, all subjects must collect their feces on the 1st day and 8th week. In addition, all subjects must receive a diet and exercise plan tailored for them by nutritionists and sports experts. During the initial and end of the study, physicians will use transient elastography (TE) scans to assess liver fibrosis and liver fat distribution (CAP).

Results: 10 cases were recruited, with ages ranging from 42.20 ± 7.76 years old, male: female ratio 1:9. Anthropometrics such as weight, body mass index, Waist circumference, hip circumference, and body fat were significantly decreased. Clinical biochemical and metabolic

indicators such as AST, ALT, GGT, Creatinine, Total cholesterol, Triglyceride, High-density lipoprotein, Low-density lipoprotein, Uric Acid, HbA1c, Insulin, HOMA-IR, Hs-CRP were all reduced. No change was seen for transient elastography measurements, including liver stiffness of 5.11 ± 2.27 vs. 5.62 ± 2.31 (p = 0.400) and CAP 266.11 ± 84.29 vs. 291.67 ± 63.98 (p = 0.314). Liquid chromatography-mass spectrometry (LC-MS) to analyze six circulating fatty acids in plasma, including two short-chain fatty acids (propionate and butyrate) and four long-chain fatty acids (palmitic acid, stearic acid, palmitoleic acid, and oleic acid). Our study found that all six fatty acids showed a downward trend after the intervention. Two short-chain fatty acids (propionate and butyrate) and two long-chain fatty acids (palmitic and stearic acids) were decreased statistically significantly ($p < 0.05$). Stool microbiota sequencing showed Blautia (mean relative abundance 24.9%), Bifidobacterium (10.7%), and Streptococcus (7.4%) are the most dominant genera in our samples, with a decrease in Blautia relative abundance after the interventions. SCFA-producing genera Blautia correlates to butyrate and propionate, and Eubacterium correlates to butyrate concentrations. Bifidobacterium, Bacteroides, Lachnoclostridium, and Butyricoccus correlate negatively, and Dorea and Holdemanella correlate positively with LCFAs.

Conclusions: Although a prominent decrease in anthropometrics, biochemistry-reducing, liver stiffness, and CAP remained unchanged, and metabolomics analysis dictated a short-chain fatty acid (SCFA) and long-chain fatty acid (LCFA) decrease instead of an increase. Stool microbiota sequencing showed that the SCFA and LCFA-producing genera were more compatible with relative concentration. Anthropometry, clinical biochemistry, and metabolic indicators improve after diet and exercise interventions in MASLD patients—short-term life modification effectively modulates intestinal microbiota and metabolomics.

⑧⑤ 使用 Triglyceride-Glucose Index 評估肝臟脂肪浸潤程度之臨床可行性與診斷正確性研究 CLINICAL UTILITY AND DIAGNOSTIC ACCURACY OF TRIGLYCERIDE–GLUCOSE INDEX FOR EVALUATION OF HEPATIC STEATOSIS

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Background: Liver steatosis is a common entity in chronic liver diseases. One of the most important and a rapid-growing public health issue is metabolic dysfunction-associated steatotic liver disease (MASLD). MASLD is considered part of the metabolic syndrome spectrum with a closer relationship with insulin resistance and with an important correlation with extrahepatic diseases such as diabetes mellitus, chronic kidney disease, ischemic stroke and cardiovascular diseases. Thus, early identification for the risk of MASLD is important for public health and a simple and effective diagnostic tool would be useful to early detect and manage these subjects. The triglyceride–glucose (TyG) index has recently been proposed as a simple and low-cost surrogate marker of insulin resistance, and it has also recently been associated as a marker of MASLD.

Aims: To investigate the clinical utility of TyG index to predict the presence and degree of fatty liver based on the abdominal ultrasound findings. In addition, the diagnostic accuracy of TyG was examined by correlating with another commonly-used quantitative tool, controlled attenuation parameter (CAP) obtained by vibration controlled transient elastography (VCTE, FibroScan).

Methods: Between January 2024 to April 2024, a total of 200 patients who received both abdominal ultrasound and VCTE, with requirable blood tests results were included for analyses. The TyG index was calculated as Ln (fasting triglycerides [mg/dL] × fasting plasma glucose [mg/dL]/2). The degree of fatty liver by abdominal ultrasound was judged by typical imaging findings including increase in fine echoes of liver parenchyma, brighter than adjacent renal cortex, impaired visualization of intrahepatic vessels and diaphragm. CAP (dB/m) obtained by VCTE for hepatic steatosis assessment was recorded as reference. All statistical analyses were conducted using SPSS version 23.0 (SPSS Inc., Chicago, IL). Demographic and clinical

parameters were presented as means, standard deviations, or percentages as appropriate. Categorical variables were analyzed using the chi-squared test and continuous variables were analyzed using independent t-tests or one way ANOVA tests as appropriate. Linear correlation was used to evaluate the association between TyG and CAP. A statistically significant result was defined as $P < 0.05$.

Results: Mean age of enrolled patients was 52.9 ± 14.7 years and 105 (52.5%) of them was male. According the abdominal ultrasound findings, 82 (41.0%) of them had fatty liver. As compared with patients without fatty liver, fatty liver patients were elder ($P = 0.022$) and more frequently to have biochemical derangements including higher ALT ($P = 0.028$), fasting sugar ($P = 0.013$), HbA1c ($P = 0.002$), and triglyceride ($P < 0.001$). The TyG index was significantly higher for patient with fatty liver (4.70 ± 0.30 vs 4.41 ± 0.26, $P < 0.001$). Progressively elevation of TyG index was noted with the severity of fatty infiltration detected by ultrasound, from mild (4.60 ± 0.28), mild to moderate (4.66 ± 0.24) and reached to 4.92 ± 0.27 for patients with at least moderate fatty liver ($P < 0.001$). In addition, a significant correlation was found between TyG index and CAP (dB/m) obtained by VCTE (Pearson correlation coefficient gamma = 0.525, $P < 0.001$) regarding the assessment of steatosis.

Conclusions: Our study demonstrated that TyG index is a simple but useful tool to predict the presence and degree of liver steatosis. Clinicians can use this quantitative biomarker alone or in combination with CAP obtained by VCTE to assess the evolution of hepatic steatosis after therapeutic interventions.

⑧⑥

代謝功能障礙相關脂肪性肝病次族群患者之存活率與預後分析

SURVIVAL AND PROGNOSTIC FACTORS FOR SUBGROUP PATIENTS WITH METABOLIC-DYSFUNCTION ASSOCIATED FATTY LIVER DISEASE (MAFLD)

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Background: Metabolic-dysfunction associated fatty liver disease (MAFLD) has been demonstrated to be better than non-alcoholic fatty liver disease in identifying patients with adverse clinical events.

Aims: The purpose of this study was to determine the survival and prognostic factors of MAFLD patients underwent transient elastography (TE).

Methods: Between 2014 and 2019, patients underwent TE in this hospital were reviewed. Hepatic steatosis was defined as controlled attenuation parameter (CAP) >275 dB/m or combined CAP 248–275 dB/m with sonographic moderate fatty liver. Those patients with malignancy before TE were excluded. Patients with hepatic steatosis were stratified into subgroups according to positive criteria of MAFLD. The demographics and baseline clinical characteristics were recorded from medical records. All the patients were followed until death or the last visit. The survival of patient was determined by linking to the national health-related databases. We compared the survival among subgroups and determined the risk factors of mortality.

Results: The prevalence of MAFLD was 18.4%. A total of 1373 patients were enrolled for analysis, including 459 and 914 in group one (diabetes history under control or glycohemoglobin ≥6.5%) and two (body mass index ≥23.0 kg/m²). There were significantly higher liver stiffness (LS) and CAP values for patients in the group one. The median follow-up period was 4.5 years. There were 51 (3.7%) patients with mortality, including 30 (6.5%) and 21 (2.3%) in group 1 and 2. Group 2 patients had significantly better survival than group 1 in all patients ($p < 0.001$) and patients after propensity score matching ($p = 0.04$). There was sixteen patients died of malignancy without significant differences in the mortality due to malignancy development between two groups ($p = 0.387$). For all patients, older age, increased waist, abnormal albumin level, abnormal creatine level, increased liver stiffness, and group 1 patient were

the risk factors of mortality in multivariate analysis. While the risk factors of mortality were renal dysfunction (HR: 3.26) and abnormal alpha-fetoprotein level (HR: 4.71) for patients in group one, they were increased age (HR: 1.07), waist (HR: 1.07) and liver stiffness (HR: 1.06) for group two in multivariate analysis.

Conclusions: There were different survival and risk factors for subgroup patients with MAFLD. While renal dysfunction was the risk factor for MAFLD patients with diabetes, increased waist and liver stiffness were associated with mortality for overweight/obesity patients.

⑧⑦

IgG4 相關自體免疫性肝炎：病例報告及系統性回顧
IGG4-ASSOCIATED AUTOIMMUNE HEPATITIS: A CASE REPORT AND SYSTEMATIC REVIEW

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Background: IgG4-associated autoimmune hepatitis (IgG4-AIH) is increasingly recognized as a distinct diagnostic entity, characterized by the overlap of classic autoimmune hepatitis (AIH) features with IgG4-related disease (IgG4-RD) manifestations. IgG4-AIH challenges traditional diagnostic criteria by presenting unique features, including elevated serum IgG4 levels and significant infiltration of IgG4-positive plasma cells in the liver.

Aims: We aim to synthesize existing case reports and series to enhance the understanding of IgG4-AIH and provide clinicians with a concise overview to aid in its diagnosis and management.

Methods: We started with a detailed case vignette of a 70-year-old woman with suspected IgG4-AIH, which guided our systematic review in accordance with PRISMA guidelines. We conducted comprehensive literature searches in PubMed, Embase, and Web of Science up to January 26th, 2024. Studies on irrelevant topics, conference papers and animal research were excluded. A rigorous selection process was conducted by paired reviewers, with a third reviewer mediating any disagreements via panel discussion. Summary data were extracted from eligible studies.

Results: A total of 1,210 articles were identified, of which 31 studies (18 case reports and 13 case series) met inclusion criteria. Among the 262 AIH cases reported, 186 patients were diagnosed with IgG4-AIH. The demographic analysis revealed that 60% (156) of patients were female. The median age ranged from 44-67 years in case series and 40-73 years in case reports. Laboratory findings showed consistent elevation of serum IgG levels (1,750-6,614 mg/dL) with variable IgG4 levels. IgG4/high power field (HPF) ratios varied significantly, but many studies reported values ≥10. ALT levels were elevated in most cases. When documented, IAIHG scores typically ranged from 7 to 22, with most cases exceeding 15. Many patients

had concurrent IgG4-RD diagnoses either before or after diagnosis, with IgG4-related sclerosing cholangitis and autoimmune pancreatitis being the most common manifestations. Treatment primarily consisted of either glucocorticoid monotherapy or combination therapy with azathioprine. ALT normalization typically occurred within 1-3 months of treatment initiation.

Conclusions: IgG4-AIH is a distinct disease entity featuring a slight female predominance and an age range of 40-70 years. Patients demonstrate greater responsiveness to corticosteroid therapy compared to traditional AIH, often showing faster biochemical remission. Importantly, patients may also develop concurrent IgG4-RD in other organs. Recognizing this unique condition, primarily diagnosed by the presence of ≥10 IgG4/HPF, is crucial for optimizing patient management and improving outcomes.

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水果命名測驗：簡單可信用以篩檢東亞地區輕度肝性腦病變的工具

FRUIT NAMING TEST: A SIMPLE AND RELIABLE TOOL FOR SCREENING MINIMAL HEPATIC ENCEPHALOPATHY IN EAST ASIA

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Background: Minimal hepatic encephalopathy (MHE) is characterized by trivial neuropsychiatric symptoms without disorientation or asterixis and is a predictor of overt hepatic encephalopathy (OHE). Psychometric Hepatic Encephalopathy Score (PHES) is the golden standard in detecting MHE, but it is time-consuming and requires regional standardization. Animal Naming Test has been proven to facilitate rapid and reliable evaluation of MHE. People in East Asia are familiar with the Chinese Zodiac, a customary classification scheme that ascribes an animal to each year in a 12-year cycle. This may lead to potential bias when it comes to naming animals. We postulated that naming fruits instead of animals can reduce this bias.

Aims: (1) To determine the cutoff point of the Fruit Naming Test (FNT) for the detection of PHES-defined MHE. (2) To assess the prognostic value of the FNT in a group of Chinese patients with liver cirrhosis in Taiwan.

Methods: The patients with liver cirrhosis, diagnosed through liver biopsy or the presence of biochemical, ultrasonographic, or endoscopic features of portal hypertension, were enrolled and followed up from March 2013 to February 2023. Patients were instructed to list different types of fruits within 60 seconds and then underwent a PHES. Receiver operating characteristic (ROC) curve analysis was employed to determine the optimal cutoff value of FNT in differentiating MHE. The prognostic outcomes of OHE occurrence, all-cause mortality, and other cirrhotic complications (varices bleeding, spontaneous bacterial peritonitis, hepatorenal syndrome, and hepatocellular carcinoma) were determined. Sensitivity analysis was conducted according to the Child-Turcotte-Pugh (CTP) score and the Model for End-stage Liver Disease (MELD) score.

Results: Seventy-one cirrhotic patients were enrolled with

a median follow-up of 3,571 days. The median age of the participants was 62 (Interquartile range (IQR), 60–68). The most common liver cirrhosis etiology was virus-related (90%). Sixty-one (86%) patients had Child-Pugh class A. The median score of MELD was 6.1 (Interquartile range (IQR), 4.4–8.6). FNT of 10 was found to be the optimal cutoff with an Area-Under-Curve (AUC) value of 0.754 [95% CI: 0.611–0.896], having a sensitivity of 94.6% and a specificity of 33.3%. FNT was correlated with PHES (r = 0.45, p = 0.0001). The patients with FNT < 10 were associated with a higher risk of OHE compared to those with FNT ≥ 10 [multivariate Hazard Ratio (HR) = 3.05 (95% CI: 1.01–9.23, p = 0.04)]. Cirrhotic patients with FNT < 10 were associated with a higher risk of OHE in both CTP class A group (multivariate HR: 4.59 [95% CI: 1.24–17.03], p = 0.02) and MELD < 15 group (multivariate HR: 3.64 [95% CI: 1.16–11.43], p = 0.02), which sensitivity analysis confirms the usefulness of FNT in predicting OHE in patients with compensated cirrhosis. Besides OHE, the FNT can also predict the occurrence of other cirrhotic complications in patients with CTP class A.

Conclusions: In summary, fruit naming tests serve as simple and reliable tools for screening MHE in cirrhotic patients, particularly beneficial in East Asia, bearing a cultural reference to the Chinese Zodiac. FNT score < 10 indicates a higher risk of subsequent development of OHE. The significant difference in prognostic implications for overt HE is particularly pronounced in patients with compensated liver cirrhosis.

主題：肝腫瘤（二）

⑧⑨

晚期不可手術切除肝細胞癌於一線 Atezolizumab 合併 Bevacizumab 治療復發後二線藥物治療臨床結果分析

CLINICAL OUTCOMES OF SECOND-LINE THERAPIES FOLLOWING PROGRESSION ON FIRST-LINE ATEZOLIZUMAB PLUS BEVACIZUMAB IN PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA

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Background: Atezolizumab in combination with bevacizumab (Atezo + Beva) stands as the primary treatment option for unresectable hepatocellular carcinoma (uHCC) in the first-line setting currently. However, there is still a lack of data on the optimal sequential treatment following disease progression on Atezo + Beva.

Aims: This study tried to evaluate the clinical outcomes of patients with advanced HCC who received subsequent second-line systemic therapy for disease progression after Atezo + Beva.

Methods: From Sep. 2019 to Dec. 2024, patients who received Atezo + Beva for uHCC in the first-line setting with assessable image for response evaluation in Taipei Veteran General Hospital were retrospectively enrolled. The tumor responses were assessed with Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

Results: Of the 105 uHCC patients who received first-line atezolizumab plus bevacizumab (Atezo + Beva), 64 (61%) experienced disease progression. Among these, 39 patients (63.9%) received second-line treatment. Patients who received subsequent treatments demonstrated significantly improved median post-progression survival (PPS) compared to those who did not (17.9 months vs. 4.4 months; p = 0.005). Of the patients who underwent second-line treatments, 17 (43.6%) received lenvatinib plus pembrolizumab (Len + Pembro), 15 (38.5%) received lenvatinib monotherapy, and 7 (17.9%) received other therapies. The median progression-free survival (PFS) was significantly longer with Len + Pembro compared to lenvatinib monotherapy (5.9 months vs. 2.7 months; p = 0.039), although there was no significant difference in median PPS between the two groups (17.9 months vs. 14.1

months; p = 0.309). Furthermore, patients treated with Len + Pembro showed a numerically higher objective response rate (37.5% vs. 7.7%; p = 0.093) and disease control rate (81.3% vs. 46.2%; p = 0.064) compared to those treated with lenvatinib monotherapy.

Conclusions: Second-line therapies improve survival in uHCC following Atezo + Beva treatment. Len + Pembro demonstrates superior PFS compared to lenvatinib monotherapy, with response rates comparable to those seen in the first-line setting, highlighting its potential as an effective subsequent treatment after Atezo + Beva.

⑨⓪

質子幫浦抑制劑使用與肝切除術後肝細胞癌復發之間的關聯

THE ASSOCIATION BETWEEN PROTON-PUMP INHIBITOR USE AND RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER HEPATECTOMY

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Background: The association between long-term proton-pump inhibitors (PPIs) use and malignancies had long been discussed, but it still lacks consensus.

Aims: Our study investigated the association between PPI use and hepatocellular carcinoma (HCC) recurrence following curative surgery.

Methods: We retrospectively enrolled 6037 patients with HCC who underwent hepatectomy. Patients were divided into four groups according to their PPI usage. (non-users: <28 cumulative defined daily dose [cDDD]; short-term users: 28–89 cDDD; mid-term users: 90–179 cDDD, and long-term users: ≥180 cDDD, respectively). Recurrence-free survival (RFS) and overall survival (OS) were analyzed using Kaplan–Meier method and Cox proportional hazard models.

Results: Among the 6037 HCC patients, 2043 (33.84%) were PPI users. PPI users demonstrated better median RFS (3.10 years, interquartile range [IQR] 1.49–5.01) compared with non-users (2.73 years, IQR 1.20–4.74; with an adjusted hazard ratio [aHR] of 0.57, 95% confidence interval [CI] 0.44–0.74, P < 0.001). When considering the cumulative dosage of PPI, only long-term PPI users had significant lower risk of HCC recurrence than non-PPI group (adj-HR: 0.50; 95% CI: 0.35–0.70; P < 0.001). Moreover, the impact of long-term PPIs use on improving RFS was significant in most of the subgroup analysis, except in patients with advanced tumor stages, with non-cirrhosis, or with a history of chronic kidney disease. However, there were no significant differences in median OS between PPI users and non-users (4.23 years, IQR 2.73–5.86 vs 4.04 years, IQR 2.51–5.82, P = 0.369).

Conclusions: Long-term PPI use (≥180 cDDD) may be associated with a better RFS in HCC patients after hepatectomy.

⑨①

脂肪性肝病對肝細胞癌手術切除患者復發與存活的影響

IMPACT OF CONCURRENT STEATOTIC LIVER DISEASE ON RECURRENCE AND SURVIVAL IN HEPATOCELLULAR CARCINOMA PATIENTS FOLLOWING SURGICAL RESECTION

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Background: Despite growing recognition of the relationship between steatotic liver disease (SLD) and hepatocellular carcinoma (HCC), its impact of concurrent SLD on long-term outcomes of HCC remains poorly understood.
Aims: This study aimed to evaluate the influence of concurrent SLD on long-term survival outcomes in patients with HCC undergoing curative hepatectomy.
Methods: This retrospective study included patients diagnosed with HCC who underwent curative hepatectomy between January 2009 and December 2023. SLD was defined as non-tumor hepatic steatosis ≥5% based on pathological report. Kaplan-Meier analysis was used to compare recurrence-free survival (RFS) and overall survival (OS) between SLD and non-SLD groups. Laboratory data and HCC characteristics were recorded and analyzed by a Cox proportional hazards regression model to predict recurrence and all-cause mortality after hepatectomy.
Results: Of 2,159 eligible patients, 1,118 (51.8%) were diagnosed with concurrent SLD. Patients with concurrent SLD had a higher prevalence of diabetes, hypertension, body mass index (BMI) >23 kg/m², a lower proportion of AFP >10 ng/ml, and microvascular invasion compared to those without SLD. After a median follow-up of 59 months, patients with concurrent SLD exhibited a lower risk of recurrence (HR 0.848, 95% CI 0.729–0.987, p = 0.033) and mortality (HR 0.675, 95% CI 0.536–0.848, p = 0.001). Subgroup analyses revealed that SLD was associated with significant RFS benefits in non-B non-C (NBNC)-HCC (p < 0.001) and OS benefits in CHB-HCC and NBNC-HCC groups (p < 0.001).
Conclusions: Concurrent SLD is associated with improved recurrence and survival in patients with HCC following curative resection. These benefits are especially evident in NBNC and CHB subgroups, highlighting SLD as a potential prognostic marker for HCC outcomes.

⑨②

標靶治療與免疫治療對於主門靜脈栓塞之肝癌病人之療效比較

COMPARISON OF IMMUNE CHECKPOINT INHIBITORS VERSUS TARGET THERAPY FOR HEPATOCELLULAR CARCINOMA WITH MAJOR PORTAL VEIN THROMBOSIS

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Background: Hepatocellular carcinoma (HCC) with major portal vein invasion, including Vp3 and Vp4, indicates poor survival outcome and systemic therapy is the key treatment option for such condition. However, high-risk patients such as main portal vein thrombosis (Vp4) were mostly excluded from previous clinical trials, including REFLECT and Keynote 240. Whether these patients could be beneficial from tyrosine kinase inhibitors or immune checkpoint inhibitors and their responses to the thrombosed portal vein were unclear.
Aims: To evaluate patients receiving tyrosine kinase inhibitors or immune checkpoint inhibitors and their responses to the thrombosed portal vein.
Methods: One hundred and five consecutive HCC patients with vp3/ vp4 portal vein thrombosis received sorafenib or lenvatinib with or without immunotherapy in the first-line setting in Taipei Veteran General Hospital from Jan. 2018 to Sep. 2021 were retrospectively recruited. The tumor and portal vein specific response rates were assessed by an independent radiologist according to RECIST 1.1 criteria.
Results: Of them, 61 patients received sorafenib monotherapy, 20 received lenvatinib monotherapy, and 24 received lenvatinib plus pembrolizumab. Significantly better overall objective response rate (ORR: 29.5% vs. 8.2%, p = 0.004), disease control rate (DCR: 77.3% vs. 29.5%, p < 0.001), median PFS (5.8 vs. 2.2 months, p < 0.001) and median OS (12.2 vs. 6.3 months, p = 0.043) were observed in patients received lenvatinib-based treatment as compared with sorafenib treatment. The portal vein specific ORR (70% vs. 16.1%, p < 0.001) and DCR (95% vs. 61.3%, p = 0.007) were also significantly higher in the lenvatinib-based treatment subgroup. The findings were consistent in the 51 patients with main portal vein (Vp4) thrombosis. In multivariate analysis, extrahepatic

metastasis (HR = 1.799, p = 0.020) and lenvatinib-based treatment (HR = 0.491, p < 0.009) were significant factors associated with OS. However, a higher risk of hepatic encephalopathy (15.9% vs.3.3%, p = 0.033) was noted in lenvatinib-based treatment as compared with sorafenib treatment.

Conclusions: Lenvatinib-based treatment could provide better ORR, PFS, and OS for HCC patients with Vp3/Vp4 portal vein invasion. However, the risk of hepatic encephalopathy by lenvatinib treatment should be aware.

⑨③

免疫檢查點抑制劑治療浸潤型肝細胞癌的臨床結果

CLINICAL OUTCOMES OF IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH INFILTRATIVE TYPE HEPATOCELLULAR CARCINOMA

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Background: Infiltrative type HCC is an aggressive and challenging subtype characterized by a poor prognosis. Immune checkpoint inhibitors (ICIs) have revolutionized the systemic management of advanced HCC, but their efficacy in patients with infiltrative HCC remains unclear.

Aims: This study aimed to evaluate the clinical outcomes of first-line ICIs in patients with infiltrative HCC.

Methods: From May 2017 to October 2023, 167 unresectable HCC patients undergoing first-line ICIs treatment at Taipei Veterans General Hospital were prospectively enrolled. Infiltrative HCC was defined by a radiologist based on radiographic features. Baseline clinical demographic, tumor-specific parameters were recorded. Treatment response was assessed by modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria. Factors associated with progression-free survival (PFS) and overall survival (OS) were analyzed.

Results: Among the 167 patients, 26 had infiltrative HCC. Patients with infiltrative HCC were prevalent with portal vein (PV) invasion (92.3% vs 49.6%, p < 0.001) and up-to-11 out tumor burden (76.9% vs 46.1%, p = 0.015). Compared with non-infiltrative HCC, infiltrative HCC had a lower objective response rate (ORR) (19.2% vs. 32.7%, p = 0.348) and a shorter median OS (10.8 months vs. 16.4 months, p = 0.001). Multivariate analysis identified infiltrative HCC (HR = 2.320; p = 0.002), AST > 40 (HR = 2.993; p < 0.001), and viral etiology (HR = 0.487; p = 0.001) as independent predictors of OS. There were no specific factors associated with PFS. Among patients with infiltrative HCC, second-line treatment was associated with improved OS (14.0 vs. 8.9 months; p = 0.026).

Conclusions: Infiltrative HCC represents high tumor burden and vascular invasion, is less responsive to ICI, and has worse survivals. Early switching to second-line systemic therapy may improve survival.

⑨④

促發炎細胞激素驅動周邊 Foxp3 高表達調節型 T 細胞進入腫瘤部位：肝癌患者可靠且可近性高的預後生物標記

PROINFLAMMATORY CYTOKINES DRIVE PERIPHERAL FOXP3HIGH TREGS INTO TUMOR SITES: A RELIABLE AND ACCESSIBLE PROGNOSTIC BIOMARKER FOR HCC PATIENTS

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Background: Regulatory T cells (Tregs) play a critical role in hepatocellular carcinoma (HCC) progression, but systemic Treg depletion risks autoimmunity. Despite known Treg heterogeneity, no consensus exists on their functional subtypes.

Aims: This study aimed to classify Treg subpopulations using single-cell CITE-seq and validate their clinical and prognostic relevance in HCC patients.

Methods: Single-cell CITE-seq was conducted on 51,067 CD4+ T cells from eight HCC patients, analyzing samples from tumor, non-tumor, and peripheral blood. Validation involved 96 HCC patients and 53 healthy donors through flow cytometry, functional assays, and clinical data integration.

Results: Trajectory and TCR analyses identified a Foxp3high Treg subset in peripheral blood that preferentially migrates to tumor sites, acquiring a terminally differentiated, activated phenotype. Tumor-infiltrating Foxp3high Tregs exhibited elevated LAYN and tissue-resident memory (TRM) signatures and enhanced Foxp3 expression driven by proinflammatory cytokines in the tumor microenvironment. The CCL5/CCR5 axis mediated their recruitment from peripheral blood to tumors. A significant correlation was found between peripheral and intratumoral Foxp3high Tregs, supporting their potential as biomarkers. A predictive model using peripheral Foxp3high Tregs/CD4+ T cells >3.5% was developed, demonstrating robust prognostic performance for overall survival and early recurrence, with AUROCs exceeding 0.75 in both training and validation cohorts.

Conclusions: Peripheral Foxp3high Tregs migrate to tumors via the CCR5-CCL5 axis and mature under proinflammatory cytokines influence. Their proportion in blood correlates with tumor presence, making them a promising biomarker for predicting HCC outcomes.

壁報展示
第一部分：肝

P.01

以病患為中心的照護與慢性病毒性肝炎患者健康相關生活質量（HRQoL）之間的相關性：路徑分析
THE ASSOCIATION BETWEEN COMPREHENSIVE PATIENT-CENTERED CARE AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) FOR PATIENTS WITH CHRONIC VIRAL HEPATITIS: A PATHWAY ANALYSIS

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Background: Patient-centered care (PCC) is a crucial objective for enhancing healthcare in the 21st century. PCC has demonstrated effectiveness in caring for patients with chronic conditions. However, the process from PCC to patient outcomes has not been thoroughly studied, particularly for patients with chronic hepatitis.
Aims: To investigate the relationship between PCC and the outcomes of hepatitis patients and determine the key mediator in the connection between PCC and outcomes.
Methods: A cross-sectional study was conducted from October to December 2016 in four hospitals in northern Taiwan. Patients with chronic viral hepatitis were assessed for five PCC factors: autonomy support, goal setting, coordination of care, information/education/communication, and emotional support. Trust in the physician, patient adherence, and patient activation (PA) were selected as mediators, with health-related quality of life (HRQoL) as the patient outcome. Pathway analysis was applied to examine the correlation.
Results: In total, 496 chronic hepatitis patients were included in the study. The pathway analysis revealed that autonomy support ($\beta = 0.007$, $p = 0.011$), information/education/communication ($\beta = 0.009$, $p = 0.017$), and emotional support ($\beta = 0.001$, $p = 0.011$) correlated with better HRQoL. The effects of PCC factors are fully mediated by trust in physicians, patient adherence, and PA. Among them, PA is the key factor in the process of PCC.
Conclusions: For chronic viral hepatitis care, PCC should be introduced into clinical practice for better HRQoL, and PA is a key mediator.

P.02

屏東地區以核苷酸類似物治療慢性 B 型肝炎 e 抗原陰性患者停藥後其病毒與臨床復發率與預測因素分析
DISTINCT VIROLOGICAL AND CLINICAL RELAPSE RATES AND RISK PREDICTORS AFTER CESSATION OF TENOFOVIR AND ENTECAVIR THERAPY IN HEPATITIS B E ANTIGEN NEGATIVE PATIENTS PING-TUNG COUNTY EXPERIENCE

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Background: Nucleos(t)ide analogue (NUC) such as tenofovir, entecavir has been approved to be a first line therapy for treatment of chronic hepatitis B (CHB). Hepatitis B virus (HBV) relapse could occur after cessation of NUC due to waning of virus suppression. Studies have investigated the viral relapse (VR) rate and clinical relapse (CR) rate after tenofovir therapy. The cessation of tenofovir therapy had significantly earlier and higher virological and clinical relapse rates than that of entecavir therapy.
Aims: We aimed to determinate predictive factors associated with the durability after stopping NUC. We investigated and compared the CHB virological and clinical relapse rates between tenofovir and entecavir.
Methods: We retrospective enrolled CHB patients with HBeAg-negative who underwent tenofovir and entecavir therapy in Ping-Tung County. By APASL guideline, the timing of NUC cessation was undetectable HBV DNA on 3 occasions 6 months apart and treatment more than 2 years. After cessation of NUC therapy, we followed ALT levels at 3, 6, 9, 12 months. Serum HBV DNA levels were checked if patients showed a two upper limit of normal ALT level. VR was defined as reappearance of HBV DNA > 2000 IU/mL from undetectable status. CR stands for the elevation of alanine aminotransferase (ALT) more than two times upper limits of normal (UNL) in addition to the presence of VR.
Results: Of 93 consecutive patients enrolled, 44 were in tenofovir group and 49 were in entecavir group. The

follow-up and treatment period for each patient was calculated as 8.34 ± 4.45 years and 2.49 ± 0.50 years. The male 69.9% was predominant. The mean age was 59.8 ± 12.12 years. The baseline mean HBV DNA level was 5.22 ± 1.47 (log10 IU/mL). The total bilirubin level was 2.96 ± 4.07 mg/dl. The ALT (IU/L) (ULN x times) was 9.84 ± 13.68. No significant differences were found in age, sex, base ALT level, total bilirubin, and serum HBV DNA between these two groups. The cumulative rates of VR and CR were 30.1%, 36.6%, 37.6%; 18.3%, 30.1%, 32.3%, at 1-year, 3-year, and 5-year, respectively. The cumulative 1-year virological relapse rate was significant higher in patients with tenofovir than those with entecavir (19.4% vs. 10.8%, P = 0.031). At 3 months after cessation, no patient had HBV VR and CR in entecavir group. Patient with tenofovir group had significant earlier VR times than those in entecavir group in the first 12 months after cessation (17.1% vs. 0%, 31.4% vs. 2.9%, 0.0% vs. 14.3%, 2.9% vs. 11.4%, 5.7% vs. 14.3%, at 3 months, 3-6 months, 6-9 months, 9-12 months, >12 months, respectively P < 0.001). No significant difference was obtained in clinical relapse times between those groups (P = 0.069). Patients in tenofovir group had earlier times of VR and CR than entecavir group during the first 6 months after cessation therapy (48.6% vs. 5.7%, P < 0.001 in VR; 25% vs. 6.3%, P = 0.040 in CR). Base on Cox proportional hazard model, factors with times at 6 months were associated with virological relapse (HR: 3.426; 95% CI: 1.172-10.015; P = 0.024).

Conclusions: Twelve months after cessation of NUC therapy, patients in tenofovir group had a higher cumulative virological relapse rate than those in entecavir group. Patients with HBeAg-negative who discontinued tenofovir had significantly higher earlier times and virological and clinical relapse rates than those who discontinued entecavir. Close monitoring of liver function and HBV DNA levels may be necessary, especially within 6 months after cessation of tenofovir therapy.

P.03

抗病毒治療對 B 型肝炎相關肝細胞癌術後早期復發的影響

THE IMPACT OF ANTIVIRAL THERAPY ON EARLY POSTOPERATIVE RECURRENCE OF HEPATITIS B VIRUS-RELATED HEPATOCELLULAR CARCINOMA

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Background: Antiviral therapy has been shown to reduce recurrence of hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC). While studies from Taiwan using the National Health Insurance Research Database have demonstrated long-term benefits, its effect on early recurrence using hospital-based data remains unclear.

Aims: To evaluate the impact of antiviral therapy on early postoperative recurrence of HBV-related HCC in a single-center retrospective cohort.

Methods: This retrospective study included 70 HBV carriers who underwent curative resection for HCC at Chang Gung Memorial Hospital. HCC cases were identified using ICD diagnostic codes, and clinical data were extracted from electronic medical records. Patients were divided into antiviral therapy (n = 46) and non-therapy (n = 24) groups. Baseline characteristics, including age, tumor size, ICG retention, and cirrhosis, were compared using independent t-tests for continuous variables and Chi-square tests for categorical variables. The primary outcome was early recurrence, defined as recurrence within one year.

Results: Baseline characteristics were similar between groups, including age (59.65 ± 7.47 vs. 62.92 ± 8.11, p = 0.519), tumor size (31.22 ± 18.37 mm vs. 36.29 ± 20.97 mm, p = 0.373), and cirrhosis prevalence (58.7% vs. 50%, p = 0.487). Early recurrence rates were lower in the antiviral therapy group (43.5% vs. 62.5%), but the difference was not statistically significant (p = 0.131).

Conclusions: This hospital-based study suggests that antiviral therapy may reduce early recurrence of HBV-related HCC, consistent with prior population-based findings. However, the small sample size limits statistical power. Future research will enroll larger number of cases and conduct subgroup analysis to better define the clinical benefits of antiviral therapy.

P.04

Sofosbuvir/Velpatasvir/Voxilaprevir 對於治療失敗的 C 型肝炎病人的治療成效：Real-World 回顧性研究
REAL-WORLD EFFECTIVENESS OF SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR IN PREVIOUS TREATMENT FAILURE HCV PATIENTS

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Background: Chronic hepatitis C infection can lead to severe liver complications, including cirrhosis and hepatocellular carcinoma. The progression from chronic infection to these life-threatening conditions highlights the importance of early detection and treatment. Fortunately, current antiviral therapies with direct-acting antiviral agents (DAAs) for hepatitis C are highly effective, achieving cure rates exceeding 95% in many trials. However, a subset of patients may experience treatment failure, potentially due to factors such as viral resistance or non-adherence. These individuals may require additional rescue therapies.

Aims: We aimed to assess the efficacy of rescue therapy with Vosevi(Sofosbuvir, Velpatasvir, and Voxilaprevir) for previous treatment of HCV patients in real world data.

Methods: This study is a retrospective cohort analysis conducted from November 1, 2021, to November 1, 2024 in Chi Mei Hospital, Liouying. The inclusion criteria for this study comprised adults over 18 years of age who experienced treatment failure after Direct Acting Antiviral (DAA) therapy for Hepatitis C Virus (HCV). Patients were excluded if they had HCV reinfection or did not complete the full course of treatment. The primary outcomes assessed were End of Treatment Response (ETR), Sustained Virological Response (SVR) at 12 weeks post-treatment, defined as HCV RNA levels lower than 12 IU/mL, and liver recovery based on improvement in liver function following anti-viral administration and SVR. Additional retrospective analyses were conducted to enhance the study's findings.

Results: A total of 17 patients completed a 12-week treatment course of sofosbuvir/velpatasvir/voxilaprevir. The demographic baseline is presented in Table 1. The mean age of participants was 57.9 years (range: 37-78), with 10 males (58.8%). The distribution of HCV genotypes was as follows: 1a (0%), 1b (23.5%), 2 (47.1%), 3 (11.8%), and 6 (17.6%). Notably, among the patients with Genotype 3, there were two individuals, one of whom was confirmed to be an intravenous drug user (IDU). This highlights a significantly high proportion of Genotype 3 patients compared to the general population, suggesting a potentially elevated relapse rate in this group. Among the cohort, 4 patients (23.5%) had cirrhosis, and the mean HCV RNA level at baseline was 5.8 ± 1.5 log10 IU/ml. The mean ALT level before treatment was 135 ± 118 U/L. Previous DAA regimens included NS5A plus NS5B inhibitors in 6 patients (35.3%) and NS5A plus NS3 inhibitors in 11 patients (64.7%). Additionally, 4 patients (23.5%) had diabetes mellitus, and 2 (11.8%) had hypertension. At baseline, no patients had HCV RNA levels below 12 IU/ml. By week 4, none of them achieved this target, which increased to 94.1% (16 out of 17) at 12 weeks, indicating an End of Treatment Response (ETR). However, 2 patients were not evaluated for Sustained Virologic Response at 12 weeks (SVR12) due to incomplete follow-up, and 2 others were lost to follow-up. This resulted in an Intention-to-Treat (ITT) SVR12 rate of 70.6% (12 patients) and a Per-Protocol (PP) SVR12 rate of 92.3% (12 out of 13). In this study, liver function tests showed a decrease in mean AST levels from 50.4 IU/L at baseline to 23.6 IU/L at Week 24, and mean ALT levels decreased from 80.8 IU/L to 22.1 IU/L over the same period. Mean total bilirubin levels remained stable, averaging 0.9 mg/dL across all time points. Additionally, mean albumin levels were consistent, ranging from 4.2 to 4.4 g/dL, while INR levels remained stable at 1.0. Platelet levels showed a slight increase from 157.0 x 10^9/L at Week 4 to 184.9 x 10^9/L at Week 24. A paired t-test assessed changes over a two-year follow-up period in patients treated with the sofosbuvir/velpatasvir/voxilaprevir regimen. Significant findings included a reduction in mean AST levels from 41.9 U/L pre-treatment to 24.3 U/L post-treatment ($t = -3.8$, $P = 0.004$), indicating improved hepatic function. Mean ALT levels also decreased significantly from 74.3 U/L to 25.5 U/L ($t = -2.7$, $P = 0.023$). Mean total bilirubin (Bil-T) levels decreased from 0.9 mg/dL to 0.7 mg/dL; however, this change was not statistically significant ($t = 1.4$, $P = 0.201$). Mean platelet counts increased slightly from 177.3 x 10^9/L to 187.1 x 10^9/L ($t = 0.5$, $P = 0.660$), indicating stable platelet levels. Additionally, the FIB-4 score improved significantly from 2.5 to 1.9 ($t = -2.5$, $P = 0.042$), suggesting a reduction in liver fibrosis. Overall, these results demonstrate that the sofosbuvir/velpatasvir/voxilaprevir regimen effectively achieved SVR and improved liver enzyme levels and fibrosis after two years of follow-up in this cohort of patients with chronic hepatitis C.

Conclusions: Sofosbuvir/Velpatasvir/Voxilaprevir demonstrates a high success rate in patients with prior treatment failure for hepatitis C, as evidenced by real-world data. It effectively reduces liver inflammation and fibrosis over a two-year follow-up, establishing it as a rescue therapeutic option for these challenging cases. Notably, in the sole case of treatment failure, the patient was HCV genotype 2, young, had a low viral load, normal kidney function, no liver cirrhosis, exhibited good medication adherence, and had previously received a complete course of NS5A plus NS3 inhibitor therapy. This suggests that the treatment failure may be attributable to resistance-associated substitutions, underscoring the need for further research in this area.

P.05

C 型肝炎病毒根除患者發生肝癌之相關因子－萬芳醫院及基隆醫院經驗
THE RISK FACTOR OF HEPATOCELLULAR CARCINOMA DEVELOPMENT IN THE POST HEPATITIS C VIRUS ELIMINATION – THE EXPERIENCES OF WAN-FANG AND KEELUNG HOSPITAL

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Background: Hepatitis C virus infection is a important cause of hepatic fibrosis, cirrhosis, and development of HCC. The achievement of an SVR can reduce the risk of hepatocarcinogenesis; however, a substantial population still develops HCC after an SVR, which suggests that surveillance for the early detection of HCC should be continued after an SVR, as recommended in clinical practice guidelines.
Aims: This study aimed to reveal the difference between medical center and regional hospital about patient's characteristics and medical care. In addition, we tried to explore the predictive factor of HCC development after achievement of an SVR in individual patients.
Methods: From Jan 2018 to Jun 2022, 389 cases of Wan Fang hospital and 241 cases of Keelung hospital with SVR after DAA treatment were collected. Excluding criteria were loss following (n = 231) or following up less than 2 years after SVR (n = 107), and still active tumor stage before SVR (n = 6). Finally 179 cases (46.0%) of Wan Fang hospital and 107 (44.4%) cases of Keelung hospital were included for analysis.
Results: The 286 cases cohort included 138 men and 148 women with a median age of 62 ± 12 years old at entry and a 39.92 ± 14.54 months follow-up. 27 cases (9.4%) of HBV co-infection and 45 cases (15.7%) of liver cirrhosis were noted. Total 16 cases had treated HCC without obvious residual lesion before SVR, 15 cases (94%) in Wan Fang hospital. At last, total 28 cases (9.8%) had new HCC in following up, including 20 de-novo type and 8 recurred type. Under multivariate logistic regression models, sex (OR: 4.14, 95% CI: 1.41–12.13, P = 0.01), liver cirrhosis (OR: 7.36, 95% CI: 2.43–22.23, P < 0.001) and history of treated HCC before DAA treatment (OR: 5.77, 95% CI: 1.13–29.38, P = 0.035) were the significant factors for new HCC development in our study population.

Conclusions: Because high rate of loss follow up (231/630, 36.2%), the 9.8% incidence rate of new HCC in our study group may be overestimated. But we still keep attention to follow the patients after SVR, especially male gender, liver cirrhosis and pre-treated HCC.

P.06

異丙酚 - 普洛福（Propofol）誘導的急性肝炎－一案例報告
PROPOFOL-INDUCED ACUTE HEPATITIS: A CASE REPORT

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Background: Propofol (2,6-diisopropylphenol, Propofol) is a short-acting intravenous anesthetic suitable for induction or maintenance of general anesthesia, sedation during surgical procedures, and can be used alone or in combination with local anesthetic or general anesthetic. Adverse effects of propofol infusion: There are few published case reports of an association between propofol infusion and acute liver injury. A systematic review from the published literature in PubMed showed that approximately 20 cases of propofol-induced hepatitis were reported. These include: 1. Incidence: Extremely rare, with an estimated incidence of <0.1% propofol administration 2. Demographics: No clear age or gender preference 3. Risk factors: Pre-existing liver disease, multiple exposures to propofol, and concomitant hepatotoxic medications.
Aims: An abnormally elevated liver enzyme was found on the fourth day after surgery for acute appendicitis.
Methods: A 63-year-old man with acute appendicitis was found to have an abnormally elevated liver index on the fourth day after surgery, the AST (GOT) 1123 U/L, the ALT (GPT) 1004 U/L, He was referred to gastroenterology for further diagnosis and treatment. The patient did not have any fever or physical symptoms before hospitalization, he denied drinking, had chronic hepatitis B with cirrhosis in the past, long-term treatment with antiviral drugs (TAF), was diagnosed with hepatocellular carcinoma (liver cancer) in 2010, and after one surgery and two radiofrequency ablation treatments, liver cancer progressed to stage III in 2019 (T4N0M0, stage IIB). Continued use of targeted and immunological drug treatment (Lpilimumab, Nivolmuab, Cyramaza, Lenvima), The AST and ALT indices were maintained at about 2X normal values (Figure 1), and the anesthetic medication during surgery was fentanyl 100 mg, Cisatracurium 10 mg and Popofol Cet 4.1 (ug/ml) (total 10.3 cc).
Results: On the fourth postoperative day, the liver index was abnormally elevated, the AST is 1123 U/L (13–39 U/L), the ALT is 1004 U/L (7–52 U/L), the total bilirubin is 1.69 mg/dL (0.30–1.00 mg/dL, the direct bilirubin is 0.67

mg/ dL (0.03–0.18 mg/dL), the GGT is 130 U/L (9–64 U/L), the alkaline phosphatase is 194 U/L (34–104 U/L), the ultrasonography showed, cirrhosis of liver with mild ascites, no evidence IHD dilatated. We further serum study, HBV DNA < 10 IU/ml, CMV IgM Ab: 0.23 (<0.85) nonreactive, EB virus VCA IgM 0.5 (<0.8) nonreactive. The patient received Glycyrrhizin 200 mg/day and Supportive care, on day 7: AST 86 U/L, ALT 146 U/L, final follow-up: AST 79 U/L, ALT 95 U/L, same as previous data before admission.

Conclusions: Inhibition of mitochondrial function has been proposed as a potential mechanism by which propofol may lead to hepatocyte free fatty acid accumulation, hepatic steatosis, and acute liver injury. Genetic studies have identified differences in propofol metabolism and have suggested that this is a factor in rare cases of propofol-induced liver damage. A case report describes the use of pharmacological lymphocyte stimulation assays as a potential tool to identify patients with propofol-induced liver injury. Past literature has reported that steroids and N-acetylcysteine therapy are effective, mainly due to improved serum aminotransferase activity with treatment with N-acetylcysteine, a free radical scavenger. In this case, the liver index was effectively improved after 7 days, and the jaundice index did not continue to rise, indicating that it was also an effective medication, but the acute hepatitis caused the patient's ascites to produce and showed that the liver's compensatory function deteriorated. Because the patient had developed ascites and the liver index improved significantly in 7 days, no liver biopsy was performed. In this case, three anesthetic drugs, Fentanyl, Cisatracurium, and Popofol Cet 4.1 (ug/ml), were used, and the former two had no records of acute liver injury from past literature, so they were consistent with the diagnosis of propofol-propofol-induced acute hepatitis. Propofol-induced hepatitis, although rare, represents a major adverse effect that clinicians should be aware of. This case highlights the importance of: 1. Preoperative liver function assessment 2. Careful monitoring of high-risk patients 3. Timely identification and treatment of liver complications 4. Considering the use of alternative anesthetics in patients with liver disease, further research is needed to better understand the risk factors and prevention strategies for propofol-induced hepatitis.

P.07

台灣東北部社區醫學世代研究 (NTCMRC) 中探討環境荷爾蒙暴露對肝功能的性別特異性之影響

EXPLORING THE SEX-SPECIFIC EFFECTS OF XENOESTROGEN EXPOSURE ON LIVER FUNCTION: INSIGHTS FROM THE NORTHEASTERN TAIWAN COMMUNITY MEDICINE RESEARCH COHORT (NTCMRC)

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Background: Phthalates are synthetic chemicals added to consumer products to enhance flexibility and durability. Xenoestrogens (XEs), a type of endocrine disruptor, mimic estrogen by binding to its receptors, potentially disrupting physiological processes and hormonal balance. While previous studies suggest that XE exposure may negatively impact liver function, the specific mechanisms and precise effects on hepatic health remain unclear.

Aims: This study investigated the relationship between xenoestrogen exposure and liver function, focusing on associations between urinary XE metabolites and key hepatic biomarkers. The study also aimed to examine sex-specific differences in how XE exposure affects liver function.

Methods: This retrospective study analyzed data from the Northeastern Taiwan Community Medicine Research Cohort (NTCMRC), including 120 participants divided into high and low XE exposure groups. Participants were recruited from northern Taiwan and assessed using a questionnaire on lifestyle and dietary habits.

Results: The results revealed significant sex-specific differences in liver function and XE exposure. Males showed higher levels of AST, ALT, and GGT compared to females and had a higher prevalence of smoking, alcohol use, and betel nut chewing. Multivariable regression revealed that urinary Triclosan levels were negatively associated with AST and ALT in the overall sample and the male subgroup. Similarly, Triclocarban levels were negatively associated with GGT in both groups. In females, univariate analysis identified a significant negative association between urinary Monoisononyl

Phthalate (MiNP) levels and AST/ALT, a relationship not observed in males. These findings indicate a potential sex-specific vulnerability to certain xenoestrogens. However, the study's small sample size limits the generalizability of these results, necessitating further research.

Conclusions: This study identified significant negative associations between urinary Triclosan and Triclocarban levels and liver biomarkers, particularly in males, suggesting a potential risk for liver dysfunction. In females, MiNP showed sex-specific associations with liver biomarkers, underscoring the need for further research on differential susceptibility. Future studies with larger and more diverse populations are needed to confirm these findings and elucidate the underlying mechanisms.

P.08

肝血管肉瘤：單一醫學中心 18 年經驗再回顧
PRIMARY HEPATIC ANGIOSARCOMA: A REVISED 18 YEAR-EXPERIENCE AT ONE MEDICAL CENTER

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Background: Primary hepatic angiosarcoma (PHA) is a rare, highly aggressive liver tumor. It is often misdiagnosed due to its vague clinical manifestations and nonspecific imaging findings. The rapid progression of PHA results in poor prognosis, and while surgical resection offers the best chance for survival, systemic treatments are largely ineffective.

Aims: This study retrospectively reviews the clinical presentation of PHA at Mackay Memorial Hospital.

Methods: We reviewed PHA diagnoses from June 2006 to September 2024, with confirmation from a pathologist. Patient demographics, tumor characteristics, and survival data were collected. Survival analysis was performed using Kaplan-Meier (K-M) curves in SPSS version 25.

Results: A total of 17 patients were included in the study (10 males, 7 females), with a median age of 73 ± 10.2 years (IQR). The most common initial symptoms were gastrointestinal discomfort, including abdominal pain/fullness (47%), poor appetite (12%), and weight loss (12%). Only 18% of patients had a history of chronic hepatitis B or C. Laboratory findings showed anemia (88%), hypoalbuminemia (52%), hyperbilirubinemia (47%), elevated transaminases (35%), and increased FIB-4 index (70%). Imaging studies commonly misdiagnosed PHA as hepatocellular carcinoma (41%), metastatic cancer (41%), or cholangiocarcinoma (35%). Only two cases were initially suspected to be angiosarcoma (12%). Initial treatments for PHA included best the supportive care (n = 11), transarterial embolization or chemoembolization (n = 2), radiation therapy (n = 1), chemotherapy (n = 2), and surgery (n = 3). The median survival time was 73 ± 89.2 days (IQR). Only one patient survived beyond one year, following two successful R0 liver resections for a recurrent solitary tumor. We compared the survival rates of PHA at our hospital between 2006–2013 and 2014–2024, and found no significant difference.

Conclusions: Based on our research, PHA remains a rare and highly fatal tumor, often initially misdiagnosed as other malignancies. Clinicians should consider the possibility of PHA before pathological confirmation. After diagnosis, the majority of patients receive palliative care. Over the last ten years, outcomes for PHA treatment at our hospital have remained unchanged.

P.09

非選擇性乙型阻斷劑與肝性腦病的關聯：系統性回顧與統合分析
THE ASSOCIATION OF NSBB AND HEPATIC ENCEPHALOPATHY: A SYSTEMIC REVIEW AND META-ANALYSIS

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Background: Liver disease causes over two million deaths annually, with cirrhosis being a major contributor, which leads to portal hypertension and complications such as ascites, varices, and hepatic encephalopathy (HE). Non-selective beta-blockers (NSBBs) are effective for managing portal hypertension, but their role in the development of HE is debated.
Aims: To assess NSBBs' impact on HE risks, offering insights into their safety and optimal use in cirrhotic patients.
Methods: We searched PubMed, Web of Science, ScienceDirect and Cochrane Library databases for studies that compared NSBB versus endoscopic band ligation (EBL), endoscopic injection sclerotherapy (EIS) or placebo in prevention of esophageal varices bleeding (EVB). Pooled odds ratio (OR) was determined using a random effects model. The pooled ORs of incidence of HE or death due to HE in the NSBB group compared with the control group comprised the outcomes. Subgroup analyses based on preserved liver function were performed.
Results: Eleven studies with a total of 1457 patients were extracted. NSBB did not increase the risk of HE compared with EBL, EIS or placebo (OR: 1.13, 95% CI = 0.73-1.75). In subgroup analysis, NSBB did not increase the risk of HE compared with EBL, EIS or placebo even in patients with decompensated liver cirrhosis (OR: 1.05, 95% CI = 0.66-1.66). There were no differences in the incidence of hepatocellular carcinoma or EVB with or without NSBB.
Conclusions: NSBB did not increase the incidence of HE, even in patients with decompensated liver cirrhosis. Further prospective study focus on carvedilol should be conducted to investigate the possible pros and cons.

P.10

以 Fibrosis-4 Index 及瞬時振動彈性成像技術評估代謝功能障礙相關脂肪性肝病之纖維化程度並不一致
DISCORDANCE BETWEEN FIBROSIS-4 INDEX AND VIBRATION CONTROLLED TRANSIENT ELASTOGRAPHY FOR FIBROSIS STAGE ASSESSMENT FOR PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a rapidly growing chronic liver disease, affecting over 38.0% of the global population, and rising to a prevalence of 90.0% in morbidly obese individuals. MASLD is considered part of the metabolic syndrome spectrum with a closer relationship with insulin resistance and with an important correlation with extrahepatic diseases such as diabetes mellitus, chronic kidney disease, ischemic stroke and cardiovascular diseases. For patients with MASLD, fibrosis stage is the most important prognostic factor for the long-term outcomes. MASLD patients with advanced fibrosis were more likely to develop cirrhotic complications and hepatocellular carcinoma. Fibrosis-4 index (FIB-4) was a commonly used non-invasive risk score to stratify fibrosis stage, however, previous studies have shown discordance between FIB-4 and other evaluation tools.
Aims: To investigate the clinical utility of FIB-4 to stratify the fibrosis stage for patients with MASLD. Liver stiffness measurement (LSM in kPa) obtained by vibration controlled transient elastography (VCTE, FibroScan) served as the validation tool.
Methods: Between January 2024 to April 2024, a total of 82 patients who received abdominal ultrasound which showed hepatic steatosis fulfilled MASLD diagnostic criteria with available blood tests and FibroScan results were enrolled. FIB-4 was calculated by the following formula: FIB-4 = Age (years) × AST (IU/L)/[platelet count ($\times 10^9$/L) × √ALT (IU/L)]. Study subjects were divided into low risk, indeterminate risk, and high risk based on the following FIB-4 cutoffs: low risk <1.3, high risk >2.67,

and indeterminate risk (1.3–2.67). The LSM on FibroScan served as the validation tool for outcome measurement. Subjects are considered to be low risk for clinically significant fibrosis with LSM <8 kPa, as highlighted in the AGA and AASLD practice guidance, and high risk for clinically significant fibrosis with LSM >12 kPa. Demographic and clinical parameters were presented as means, standard deviations, or percentages as appropriate. Categorical variables were analyzed using the chi-squared test and continuous variables were analyzed using independent t-tests or one way ANOVA tests as appropriate. A statistically significant result was defined as $P < 0.05$.

Results: Mean age of enrolled patients was 55.6 ± 12.2 years and 51 (62.2%) of them was male. The mean value of hematology and biochemistries tests results for study subjects were as follows: Hgb: 14.5 ± 1.3 g/dL, PLT: 247.8 ± 56.2 x1000/cumm, ALT: 28.5 ± 17.3 U/L, AST: 22.5 ± 7.8 U/L, TG: 134.9 ± 85.8 mg/dL, HDL: 59.2 ± 57.9 mg/dL, fasting sugar: 106.6 ± 28.0 mg/dL, and HbA1c: 6.03 ± 0.86%. Of the 62 subjects classified as low risk for advanced liver fibrosis based on the FIB-4 <1.3 cutoff, only 5 subjects (8.1%) were not low risk because they had LSM ≥8 kPa on FibroScan, indicating high negative predictive value. A total of 18 subjects were classified as indeterminate by FIB-4, however, 17 subjects (94.4%) were classified as low risk by FibroScan, with an LSM <8 kPa. Misclassification of fibrosis stage was found for all two patients with FIB-4 >2.67, but with an LSM <12 kPa. As compared with patient ≤60 y/o, elder patients were more likely to have the probability of fibrosis misclassification by FIB-4 (39.5% vs 20.5%, $P = 0.059$).

Conclusions: Our study demonstrated that for patients with MASLD, the best way for clinical utility of FIB-4 is to rule out advanced fibrosis. Validated by FibroScan, more than 90% patients with FIB-4 <1.3 had LSM <8 kPa. However, misclassification of fibrosis stage was quite common toward overestimation for patients with FIB-4 intermediate and high risk. Secondary fibrosis risk assessment for confirmation by blood-based, imaging or histology tools were strongly recommended.

P.11

腸道賀爾蒙在肝硬化的角色
THE RULE OF GUT HORMONES IN LIVER CIRRHOSIS

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Background: The pathophysiological alterations of gut hormones in cirrhotic patients remain poorly understood. Research focusing on multiple gut hormones in this population is scarce, and relevant domestic data are limited.

Aims: This study aimed to investigate differences in plasma gut hormone levels between cirrhotic patients and healthy individuals and to explore associations between these hormone levels and cirrhosis-associated complications.

Methods: Thirty-one healthy people and 145 cirrhotic patients were retrospectively enrolled. Differences in hormone levels between the cirrhotic group and the healthy control group were assessed. One-year cirrhosis-associated clinical events were recorded.

Results: The average age of cirrhotic patients was 59.6 ± 10.4 years, with 77.2% male. Hepatitis B was the most common cause of cirrhosis (38.6%), and most patients had mild disease (Child–Pugh A: 45.5%). The most frequent complication was bacterial infections (16.3%). The glucagon-like peptide-1 (GLP-1) levels in cirrhotic patients were significantly elevated (17,857.84 ± 53969.4 pg/ml) as compared to those in healthy individuals (743.06 ± 231.53 pg/ml $p < 0.01$). The cholecystokinin (CCK) levels in the cirrhotic group were higher than those in the healthy group (0.85 ± 0.81 vs. 0.53 ± 0.24 pg/ml, $p < 0.01$), while the serotonin levels were significantly lower in the cirrhotic group than in the healthy group (62.92 ± 55.41 vs. 182.47 ± 130.31 ng/ml, $p < 0.01$). The ghrelin levels increased in the cirrhotic group than in the healthy group (6.65 ± 29.71 vs. 0.28 ± 0.69 ng/ml, $p = 0.011$). In patients with cirrhosis, the GLP-1 levels were lower in those with mortality than survivors (15,947.10 ± 26882.75 pg/ml vs. 18,763.11 ± 58053.51 pg/ml, $p = 0.015$), higher in hepatic encephalopathy (HE) than those without HE (47,882.42 ± 92568.83 pg/ml vs. 15,421.18 ± 51323.37 pg/ml, $p = 0.016$) and higher in those with infections than those without infections (40,030.84 ± 91685.53 pg/ml vs. 14,424.49 ± 46937.57 pg/ml, $p = 0.005$). The CCK levels were lower in cirrhotic patients with HE than those without HE (0.63 ± 0.76 pg/ml vs. 0.82 ± 0.77 pg/ml, $p = 0.031$), and the

serotonin levels were reduced in cirrhotic patients with spontaneous bacterial peritonitis (SBP) than those without SBP (27.19 ± 24.22 ng/ml vs. 63.68 ± 55.61 ng/ml, p = 0.025).

Conclusions: Gut hormones differ significantly in cirrhotic patients compared to healthy individuals with specific hormone levels linked to cirrhosis-related complications. These findings highlight potential roles of gut hormones in disease progression and complications, warranting further research for validation.

P.12

中量飲酒對於代謝性脂肪肝之影響
IMPACT OF MODERATE ALCOHOL INTAKE ON METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: The consumption of alcohol exceeding 140 grams per week for women and 210 grams per week for men is defined as increased alcohol intake and is excluded from the diagnosis of metabolic dysfunction-associated steatotic liver disease (MASLD). The impact of moderate alcohol consumption below the cut-off values on MASLD remains unclear.

Aims: Evaluate the impact of moderate alcohol consumption (below the cut-off values) on MASLD.

Methods: Participants from Taiwan Biobank database after exclusion those with positive for HBsAg, anti-HCV, and former drinkers were selected. MASLD was diagnosed if having hepatic steatosis on ultrasound plus at least one of cardiometabolic criteria. Moderate alcohol intake was defined as continuous drinkers with alcohol consumption below 210 grams for men and 140 grams for women weekly. The fibrosis 4 (FIB-4) score was used to assess the severity of liver fibrosis, and carotid plaques on duplex ultrasound were employed to diagnose atherosclerosis. MASLD patients were divided into two groups: one group abstaining from alcohol completely or social drinking and the other group consuming moderate alcohol.

Results: In a total of 18,160 (mean age 55.28 ± 10.41; 33.2% males) participants, there were 7,316 (40.3%) MASLD patients. Of them, 417 (5.7%) participants had moderate alcohol intake, but no drinking in 6899 participants The participants with MASLD with moderate alcohol intake were younger and male predominant. After propensity score matching for age and gender, it was observed that patients in the moderate alcohol intake group had higher triglyceride, HDL, and uric acid levels, but lower LDL levels. The levels of GGT, FLI, and FIB-4 were all higher. Additionally, the proportion of carotid artery plaques was also higher than those with no/social alcohol intake.

Conclusions: Moderate alcohol intake increases the risk of liver injury and atherosclerotic in MASLD patients, suggesting MASLD patients should refrain from alcohol intake.

P.13

脂肪肝對接受賀爾蒙藥物治療乳癌患者的影響
IMPACT OF FATTY LIVER IN BREAST CANCER PATIENTS WITH ENDOCRINE THERAPY

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Background: Breast cancer is the most frequently diagnosed malignancy among women worldwide and one of the common causes of cancer related mortality. Fatty liver disease is one of the most common chronic liver diseases. It is also a frequent finding of ultrasonogram in breast cancer patients. Endocrine therapy (ET) including selective estrogen receptor modulator (SERM) and aromatase inhibitor (AI) is an important adjuvant systemic therapy for breast cancer. However, long term ET can lead to adverse effects including fatty liver disease.
Aims: The aim of this study was to investigate the impact of fatty liver disease in breast cancer patients with ET, including clinicopathologic factors and survival.
Methods: From January 2001 to December 2022,1092 patients were diagnosed with tissue-proven breast cancer at the Cheng-Chin general hospital Chung-Gang branch with follow up till December 2024. Among them,911 patients were found to have receive ET (BET). They were classified as patients with fatty liver group (BET+F, N0.458) and patients without fatty liver group (BET-F, No.453). Patients were evaluated on the basis of age, BMI, clinical variables, coexistence of viral hepatitis, survival time and stage. Data were statistically analyzed using the chi-squared test & student's t-test. Analysis of survival was performed using the Kaplan-Meier method.
Results: Demographic data including average age, clinical laboratory data, coexistence of viral hepatitis, stage of the disease are summarized in table 1 and table 2. The breast cancer with fatty liver group (BET+F) was found to be older, have higher BMI, HbA1C, triglyceride, GOT, GPT, ALKP, Hb, levels and white blood cell, platelet counts. The presence of fatty liver disease in breast cancer patients with ET did not influence the prognosis.
Conclusions: The presence of fatty liver had no significant impact on survival of breast cancer patients with endocrine therapy.

P.14

肝功能異常及代謝症候群發生率之探討
HEPATIC TRANSAMINASES AND INCIDENCE OF METABOLIC SYNDROME

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Background: Plasma hepatic aspartate and alanine transaminases (AST and ALT) may reflect the severity of nonalcoholic fatty liver disease (NAFLD), a metabolic disorder, while the association of hepatic transaminases and risk of metabolic syndrome (MetS) has not been confirmed previously among young adults.
Aims: We used the data collected from health check to evaluate the association of hepatic transaminases and the risk of metabolic syndrome.
Methods: There were 2,890 military men and women, with ages of 18–39 years, free of baseline MetS in Taiwan in 2014. Incident MetS were followed in the annual military health examinations from baseline till the end of 2020. The definition of MetS was made according to the International Diabetes Federation criteria. Plasma AST and ALT concentrations were checked at baseline. Multivariable Cox regression model with adjustments for sex, age, each component of MetS, body mass index, substance use status and physical activity at baseline were performed to determine the associations. Subgroup analyses were performed according to sex and each MetS component.
Results: During a median follow-up of 5.8 years, 673 incident MetS (23.3%) developed. There were an association of ALT and AST levels (each 10 U/L increase) with incident MetS [hazard ratios (HRs) and 95% confidence intervals (CIs): 1.05 (1.01–1.09) and 1.11 (1.04–1.19), respectively]. In subgroup analyses, the risk of incident MetS with ALT and AST levels was significantly greater in women [HRs: 1.75 (1.07–2.87) and 2.14 (1.35–3.41), respectively] and in those without central obesity [HRs: 1.07 (1.02–1.11) and 1.14 (1.06–1.23), respectively] than their counterparts (p-values for interaction by sex: 0.06 and 0.001, respectively; and by central obesity: 0.04 and

0.07, respectively).
Conclusions: Plasma hepatic transaminases levels were positively associated with incident MetS among young adults. The individual role of central obesity and sex on the association of ALT and AST with incident MetS should be further clarified.

P.15

使用超音波評估腹部脂肪層厚度與兒童脂肪肝之關聯性分析
USING ULTRASOUND TO ASSESS ABDOMINAL FAT LAYER THICKNESS FOR EVALUATING FATTY LIVER DISEASE IN CHILDREN

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Background: Reports from the World Health Organization indicate that the rapid increase in overweight and obesity is a significant health issue affecting both adults and children. Obesity is considered one of the key factors contributing to the development of fatty liver disease. An increase in body fat can further exacerbate this condition. However, the commonly used measure, body mass index (BMI), does not provide a direct indication of body composition. Abdominal obesity is well-known to be associated with a higher risk of metabolic and cardiovascular comorbidity in adults. Additionally, studies have suggested that visceral fat is moderately correlated with insulin resistance in children.
Aims: In our study, we aim to investigate the relationship between abdominal fat layers and non-alcoholic fatty liver disease in children. Additionally, we intend to identify the threshold value of fat layer thickness that can predict the presence of fatty liver disease.
Methods: We conducted a retrospective study of pediatric patients who underwent abdominal sonogram examinations at Mackay Children's Hospital from May 2024 to September 2024. We included cases where the thickness of the intra-abdominal fat layers could be clearly identified. Patients under 1-year-old and above 18-year-old were excluded. Body weight (BW) and height (BH) were obtained from medical records. The waist circumference (WC) was measured at the midpoint between the lateral iliac crest and the lowest rib; the hip circumference (HC) was the maximum length around the hip. The abdominal fat layer thickness was obtained by one finger span (approximately 2 cm) above the umbilicus at the transverse view. The subcutaneous fat thickness (SFT) was defined as the maximum length from the skin-fat interface to the linea alba; the visceral fat thickness (VFT) was measured from the linea alba to the anterior wall of the aorta at the same view.
Results: A total of 97 boys and 69 girls were enrolled in our study. Among the patients, 32 boys and 9 girls were diagnosed with fatty liver disease. Due to physiological

differences, males and females were analyzed separately. Statistically significant differences in SFT and VFT were observed between patients with and without fatty liver in both genders. Additionally, SFT and VFT were positively correlated with BW, BMI, WC and HC as indicated by Pearson correlation analysis in both genders. Notably, SFT showed a higher correlation coefficient than VFT. Receiver Operating Characteristic (ROC) curve analysis was performed on fat layer thickness and fatty liver disease. The highest Youden index for SFT was 1.075 cm in males (AUC 0.924, sensitivity 1.0) and 0.88 cm in females (AUC 0.893, sensitivity 1.0). For VFT, the highest Youden index was 3.845 cm in males (AUC 0.907, sensitivity 0.813) and 3.555 cm in females (AUC 0.809, sensitivity 0.889).

Conclusions: Sonographic evaluation of abdominal subcutaneous and visceral fat thickness is useful for assessing fatty liver disease in children. Additionally, BMI, weight, waist circumference and hip circumference change are more sensitive indicators of subcutaneous fat thickness than visceral fat thickness.

P.16

一個簡單的模式可以預測肝細胞癌病患接受手術切除發生早期復發
A SIMPLE MODEL TO PREDICT EARLY RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER RESECTION

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Background: Multiple studies have reported models for predicting early recurrence of hepatocellular carcinoma (HCC) after liver resection (LR). However, these models are too complex to use in daily practice.

Aims: We aimed to develop a simple model.

Methods: We enrolled 1133 patients with newly diagnosed HCC undergoing LR. The Kaplan − Meier method and log-rank test were used for survival analysis and Cox proportional hazards analysis to identify prognostic factors associated with early recurrence (i.e., recurrence within two years after LR).

Results: Early recurrence was identified in 403 (35.1%) patients. In multivariate analysis, alpha-fetoprotein (AFP) 20–399 vs. < 20 ng/ml (HR = 1.282 [95% confidence interval = 1.002–1.639]; p = 0.048); AFP ≥ 400 vs. < 20 ng/ml (HR = 1.755 [1.382–2.229]; p < 0.001); 7th edition American Joint Committee on Cancer (AJCC) stage 2 vs. 1 (HR = 1.958 [1.505–2.547]; p < 0.001); AJCC stage 3 vs. 1 (HR = 4.099 [3.043–5.520]; p < 0.001); and pathology-defined cirrhosis (HR = 1.46 [1.200–1.775]; p < 0.001) were associated with early recurrence. We constructed a predictive model with these variables, which provided three risk strata for recurrence-free survival (RFS): low risk, intermediate risk, and high risk, with two-year RFS of 79%, 57%, and 35%, respectively (p < 0.001).

Conclusions: We developed a simple model to predict early recurrence risk for patients undergoing LR for HCC.

P.17

肝癌接受熱消融治療後符合及超出米蘭標準之復發後存活分析
LONG-TERM OUTCOMES OF RECURRENCE WITHIN AND BEYOND MILAN CRITERIA FOLLOWING THERMAL ABLATION FOR HEPATOCELLULAR CARCINOMA

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Background: Recurrence rates following thermal ablation for hepatocellular carcinoma (HCC) remain high, but the patterns of recurrence and post-recurrence outcomes are not well characterized.
Aims: This study aimed to investigate the recurrence patterns and long-term post-recurrence survival (PRS) in patients with HCC after thermal ablation.
Methods: A retrospective analysis was conducted on 824 patients who underwent thermal ablation for HCC between 2007 and 2023. Recurrence patterns and factors influencing PRS in patients with recurrence within and beyond the Milan criteria were evaluated.
Results: During a median follow up of 54.5 month, 536 patients experienced HCC recurrence. Among them, 83.8% and 16.2% had recurrence within and beyond Milan criteria, respectively. For patients with recurrence within Milan criteria, early recurrence, recurrent tumor size, AFP, ALBI grade, and FIB-4 score were independent predictors of PRS. In patients with recurrence beyond Milan criteria, diabetes mellitus, macrovascular invasion, AFP, ALBI grade, and FIB-4 score independently predicted PRS. Based on PRS predictors, a risk model stratified patients with recurrence within Milan criteria into four risk groups, with median PRS of 103.7, 65, 48.7 and 28.6 months, respectively ($p < 0.001$). For recurrence beyond Milan criteria, a separate risk model classified patients into three risk groups, showing median PRS of 70.1, 24.7, and 8.1 months, along with probabilities of downstaging to Milan criteria of 70.4%, 39.3%, and 3.4%, respectively ($p < 0.001$).
Conclusions: PRS in patients with recurrent HCC after thermal ablation is significantly influenced by recurrence patterns, tumor characteristics, and liver function reserve. These findings may guide post-recurrence treatment strategies, optimize the timing of referral for salvage liver transplantation, and inform the design future clinical trials.

P.18

將 Up7-ALBI Score 用來評估在無法手術切除的肝癌病患中使用 Lenvatinib 的預後
USING THE UP7-ALBI SCORE TO PREDICT OUTCOMES IN HEPATOCELLULAR CARCINOMA TREATED WITH LENVATINIB

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Background: Lenvatinib is effective for unresectable hepatocellular carcinoma (HCC), but current prognostic models lack integration of tumor burden and liver function.
Aims: This study aimed to investigate the combined utility of the Up-to-7 criteria and ALBI grade for survival prediction in HCC patients treated with lenvatinib.
Methods: This multi-center, retrospective study analyzed 205 patients with unresectable HCC treated with lenvatinib. Tumor burden was assessed using the Up-to-7 criteria, and liver function via ALBI grade. Cox proportional hazards models identified independent predictors of progression-free survival (PFS) and overall survival (OS). These predictors were incorporated into a novel scoring system, the Up7-ALBI score, which stratified patients into prognostic groups.
Results: The overall response rate was 13.2% by RECIST 1.1 criteria, with higher response in patients without metastases and within the Up-to-7 criteria. The median PFS and OS were 7.3 and 12.2 months, respectively. Univariate analysis showed that tumors beyond the Up-to-7 criteria ($p < 0.05$), serum alanine aminotransferase levels > 40 U/L ($p < 0.01$), the presence of main portal vein thrombosis ($p < 0.01$), and albumin-bilirubin (ALBI) grade 2-3 ($p < 0.01$)

were significantly associated with poorer OS. I Multivariate analysis identified the Up-to-7 criteria (HR: 1.61, 95% CI: 1.00–2.57) and ALBI grade 2–3 (HR: 1.62, 95% CI: 1.06–2.47) as independent predictors of OS. The Up7-ALBI score stratified patients into three groups with significantly different OS (median OS: 30.8 vs. 14.4 vs. 9.3 months, $p < 0.01$).

Conclusions: The Up7-ALBI score, which integrates tumor burden and liver function, effectively predicts survival outcomes in patients with unresectable HCC treated with lenvatinib. However, further studies are needed to validate its applicability across different stages of HCC or with other systemic therapies.

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接受 Lenvatinib 治療且在 RECIST 1.1 與 mRECIST 標準間存在不一致反應的 HCC 患者之治療結果

OUTCOME OF HCC PATIENTS RECEIVING LENVATINIB WITH DISCORDANT RESPONSES BETWEEN RECIST 1.1 AND MRECIST CRITERIA

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Background: RECIST 1.1 is the standard for assessing systemic therapy in hepatocellular carcinoma (HCC), while mRECIST is designed for evaluating locoregional therapy responses. Lenvatinib shows higher response rates with mRECIST compared to RECIST 1.1.

Aims: The aim of this study was to investigate the prognostic impact of discordant responses between these criteria.

Methods: This retrospective, multi-center study reviewed 151 HCC patients treated with lenvatinib from January 2017 to July 2022. Patients were divided into four groups based on treatment response: group 1 (PR/mCR + mPR), group 2 (SD/mCR + mPR), group 3 (SD/mSD), and group 4 (PD/mPD). The outcomes among groups and predictive performance and agreement between both criteria were compared.

Results: The overall response rate was 8.6% by RECIST1.1 and 44.4% by mRECIST, with a disease control rate of 85.4% for both criteria. Median progression-free survival was 8.3 months, and median overall survival was 11.5 months. Group 1 had the longest progression-free survival (21.9 months), followed by groups 2, 3, and 4 (8.6, 7.8, and 5.2 months, respectively; $p = 0.007$). Overall survival

was longest in group 1 (39.1 months), followed by groups 3, 2, and 4 (16.0, 12.4, and 8.3 months; p = 0.001). Inverse probability of treatment weighting showed no significant difference between groups 2 and 3 in progression risk (hazard ratio = 1.46, p = 0.31) and mortality (hazard ratio = 0.75, p = 0.45). Kappa value was 0.402 (p < 0.001) between two criteria, and RECIST 1.1 criteria yielded a lower value of AIC (752.6) compared to the mRECIST criteria (753.5).
Conclusions: This study highlights discordance between RECIST 1.1 and mRECIST criteria in assessing lenvatinib efficacy in HCC, while RECIST 1.1 criteria providing a better prognostic value.

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利用機器學習與決策樹模型，顯示 PIVKA-II 和 AFP 在肝細胞癌患者中的預後價值
MACHINE LEARNING-BASED DECISION-TREE MODEL DEMONSTRATING THE PROGNOSTIC VALUE OF PIVKA-II AND AFP IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Background: Protein induced by Vitamin K absence or antagonists-II (PIVKA-II) and alpha-fetoprotein (AFP) are two widely used tumor markers for the surveillance and diagnosis of hepatocellular carcinoma (HCC). However, their prognostic value remains unclear.
Aims: The study aimed to evaluate the prognostic ability of PIVKA-II and AFP for HCC patients, and to develop a machine learning-based decision-tree model to predict patient outcomes.
Methods: The study retrospectively enrolled 598 consecutive treatment-naïve HCC patients diagnosed from 2020 to 2023. Patients were categorized into four groups based on their serum PIVKA-II (cut-off value 1500 mAU/mL) and AFP (cut-off value 20 ng/mL) levels at diagnosis. The cohort was randomly divided into a training cohort (n = 418) and a validation cohort (n = 180). A Cox proportional hazards model was used to identify independent risk factors for overall survival (OS). A machine learning-based decision-tree analysis was then performed on the training cohort to develop a model predicting OS, which was subsequently validated in the validation cohort.
Results: The four groups showed significant differences in tumor characteristics, including tumor stage, size, number of tumors, presence of extra-hepatic metastasis and vascular invasion, as well as liver functional reserve. After a median follow-up of 16.0 months (interquartile range 5.0–22.0), 141 patients had died, with a 3-year OS rate of 63.0%. The 3-year OS rates for the four groups (high AFP & high PIVKA-II, high AFP & low PIVKA-II, low AFP & high PIVKA-II, low AFP & low PIVKA-II) were 31.7%, 67.3%, 51.6%, and 70.0%, respectively (p < 0.001). Multivariate analysis revealed higher serum AFP levels, high PIVKA-II levels, lower serum albumin level, higher

serum creatinine level, higher serum alkaline phosphatase levels, larger prothrombin time international normalized ratio (PT INR), presence of vascular invasion, and non-curative treatment as independent risk factors for poor OS in the training set. The machine learning-based decision-tree model included AFP, PIVKA-II, vascular invasion, serum creatinine level, PT INR, and treatment modalities as important factors, demonstrating an accuracy rate of 79.4% (95% CI: 72.8%–85.1%) in predicting OS in the validation cohort.

Conclusions: The machine learning-based decision-tree model, utilizing both serum PIVKA-II and AFP levels, accurately predicted the outcomes of HCC patients.

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以 PNI 來預測肝細胞患者接受 Lenvatinib 的預後

PROGNOSTIC NUTRITION INDEX PREDICTS THE PROGNOSIS OF HEPATOCELLULAR CARCINOMA PATIENTS TREATED WITH LENVATINIB

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Background: The prognostic nutritional index (PNI) is considered prognostic factors for patients with hepatocellular carcinoma (HCC); however, its association with the efficacy of lenvatinib on advanced HCC has been less investigated.

Aims: This study was conducted to evaluate the prognostic role of PNI for patients with advanced HCC received first-line lenvatinib.

Methods: From Sep 2019 to Dec 2022, 261 patients with unresectable HCC treated with lenvatinib as first-line systemic therapy in our institute were evaluated. The PNI was calculated as follows: 10 x serum albumin level (g/dL) + 0.005 x serum lymphocyte count (number/mm^3) with the cut-off as 45 based on previous studies. Patients were divided into the low-PNI (<45) and the high-PNI (≥45) groups.

Results: This study enrolled 226 patients, including 76 patients in the low-PNI group, and 150 in the high-PNI group, respectively. Compared with the low-PNI group, the high-PNI group showed better progression-free survival (7.5 vs 4.5 months, $p = 0.011$) and overall survival (18.6 vs 9.1 months, $p < 0.001$) Additionally, patients with high PNI had lower occurrence of treatment related adverse events than those with low PNI. Furthermore, multivariate analysis revealed that high PNI was associated with improved prognosis (Hazard ratio: 0.60, 95% confidence interval: 0.39-0.94, $p = 0.027$) after adjusting post-treatment, and Child-Pugh class.

Conclusions: The PNI might be useful in predicting the prognosis of advanced HCC patients with first-line lenvatinib treatment.

P.22

腫瘤負荷評分對不同身體功能狀態肝細胞癌患者的預後影響之差異

DIFFERENTIAL PROGNOSTIC IMPACT OF TUMOR BURDEN SCORE ON HEPATOCELLULAR CARCINOMA PATIENTS WITH VARIABLE PHYSICAL PERFORMANCE STATUS

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Background: Performance status (PS) plays a crucial role in prognostic prediction for patients with hepatocellular carcinoma (HCC). The extent of tumor burden is also a major survival determinant. Recently, tumor burden score (TBS) was proposed to evaluate the extent of tumor involvement, but the interaction between TBS and PS has not been evaluated.

Aims: We aimed to assess the prognostic role of TBS in HCC patients with variable PS.

Methods: A large cohort of 4185 treatment-naïve HCC patients were retrospectively analyzed. The multivariate Cox proportional hazards model was used to determine the independent predictors associated with survival.

Results: Patients with poorer PS had significantly higher TBS at baseline. In the Cox model, older age, lower serum albumin level, higher serum bilirubin, creatinine and α-fetoprotein (AFP) levels, presence of ascites, presence of vascular invasion, PS 1–2, PS 3–4, and medium TBS and high TBS were independently associated with increased mortality in the entire cohort ($p < 0.001$). In subgroup analysis stratified by PS, TBS was able to predict long-term survival in patients with PS 0 in the multivariate model. For patients with PS 1–2, the trend was significant only in those with high TBS ($p < 0.001$); in patients with PS 3–4, TBS was not significantly associated with survival ($p > 0.05$).

Conclusions: TBS is a feasible prognostic marker for HCC and can well discriminate long-term survival in patients with good PS. Our findings demonstrate that TBS has a differential prognostic impact on HCC and may play a distinct role in outcome prediction for patients with variable PS.

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免疫療法和 Lenvatinib 作為一線全身性治療肝功能受損肝細胞癌患者的結果比較：一醫學中心經驗

COMPARATIVE OUTCOMES OF FIRST-LINE SYSTEMIC THERAPY WITH IMMUNOTHERAPIES AND LENVATINIB FOR HEPATOCELLULAR CARCINOMA PATIENTS WITH IMPAIRED LIVER FUNCTION: A MEDICAL-CENTER EXPERIENCE

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Background: Hepatocellular carcinoma (HCC) is a major cause of cancer-related mortality worldwide. All first-line treatments approved for advanced HCC, including immunotherapies (IOs) and tyrosine kinase inhibitors (TKIs), have primarily been studied in patients with Child-Pugh class A cirrhosis. However, information regarding the efficacy and clinical outcomes of these therapies in patients with impaired liver function remains limited.

Aims: This study aims to compare the outcomes of immunotherapies and lenvatinib in hepatocellular carcinoma patients with impaired liver function.

Methods: This retrospective study evaluated the clinical outcomes of first-line systemic treatments, including IOs such as atezolizumab with bevacizumab, nivolumab, and pembrolizumab, as well as lenvatinib, in patients with impaired liver function categorized by albumin-bilirubin (ALBI) grade and modified ALBI (mALBI) grades. Data were collected retrospectively from the electronic medical records of patients who received these therapies between May 2018 and April 2024 at Mackay Memorial Hospital. Clinical characteristics, overall survival (OS), and progression-free survival (PFS) were compared among patients with impaired liver function.

Results: A total of 98 HCC patients with ALBI grade 2 were included, comprising 27 patients treated with IOs and 71 patients treated with lenvatinib. Kaplan-Meier survival analysis revealed no significant differences in OS or PFS between the IO group and the lenvatinib group; however, the IO group exhibited a trend toward longer OS and PFS. In subgroup analysis, 40 HCC patients with mALBI grade

2a, consisting of 10 patients receiving IOs and 30 patients receiving lenvatinib, the IO group had a trend toward longer OS and PFS. In patients with mALBI grade 2b (n = 17 in the IO group, n = 41 in the lenvatinib group), the IO group exhibited a trend of OS but shorter PFS. The baseline characteristics for each cohort are presented in the tables, along with the survival curve figures.

Conclusions: This study found no differences in OS and PFS between HCC patients receiving IOs and lenvatinib with impaired liver function across the ALBI grade 2, mALBI grade 2a, and 2b subgroups. These findings warrant further investigation in larger, prospective studies.

P.24

代謝相關脂肪肝病對 Lenvatinib 治療肝細胞癌療效的影響：一醫學中心的回顧性研究
IMPACT OF METABOLIC-ASSOCIATED STEATOTIC LIVER DISEASE ON LENVATINIB EFFICACY IN HEPATOCELLULAR CARCINOMA: A RETROSPECTIVE STUDY FROM ONE MEDICAL CENTER

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Background: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related deaths worldwide. Recently, metabolic-associated steatotic liver disease (MASLD) has emerged as a significant underlying cause of HCC. Lenvatinib, an oral receptor tyrosine kinase inhibitor (TKI), is recognized as a first-line treatment for advanced HCC. However, the effect of MASLD on the therapeutic response to Lenvatinib remains poorly understood, creating a critical gap in optimizing treatment strategies for this patient population.

Aims: This study aims to present real-world experiences regarding the impact of MASLD on the efficacy of Lenvatinib in patients with HCC at a single medical center.

Methods: This retrospective study focused on patients with HCC who received Lenvatinib as a first-line treatment at MacKay Memorial Hospital from May 30, 2020, to April 30, 2024. HCC patients classified into the MASLD and non-MASLD groups were enrolled according to the EASL-EASD-EASO Clinical Practice Guidelines. An HSI (Hepatic Steatosis Index) score of 30 or higher indicates a steatotic liver disease. Treatment outcomes, including overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and disease control rate (DCR), were evaluated and compared between the two groups.

Results: A total of 118 HCC patients were enrolled in the study, with 61 assigned to the MASLD group and 57 to the non-MASLD group. The two patient groups exhibited no significant differences regarding sex, age, viral infection, AFP level, PIVKA II level, and BCLC stage. HCC patients with MASLD exhibited significantly longer overall survival compared to those without MASLD (OS: 20.2

months vs. 10.5 months, p = 0.006). HCC patients with MASLD showed no statistical significance in PFS (11.2 vs. 10.1 months, p = 0.453), ORR (23.6% vs. 18%, p = 0.632), and DCR (50.9% vs. 50%, p > 0.999) compared to those without MASLD.

Conclusions: This study highlights that HCC patients with MASLD experience more prolonged overall survival than those without MASLD when treated with Lenvatinib. Further prospective research is needed to elucidate the underlying mechanisms and refine therapeutic strategies for this growing patient population.

P.25

比較是否罹患 MASLD 對無法手術切除之肝細胞癌患者，接受一線免疫治療的影響

COMPARISON OF OUTCOMES IN PATIENTS WITH AND WITHOUT METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE UNDERGOING IMMUNOTHERAPY-BASED FIRST-LINE SYSTEMIC THERAPY FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma (HCC) represents a major global health challenge with a high mortality rate, particularly in cases where the tumor is unresectable. While first-line treatments using immunotherapy, particularly the combination of Atezolizumab and Bevacizumab (A+B) along with other immune checkpoint inhibitors (ICIs), have been well studied in unresectable HCC, the effectiveness outcomes in patients with and without metabolic dysfunction-associated steatotic liver disease (MASLD) still lack comprehensive data.

Aims: This study aims to present real-world experiences utilizing immunotherapy-based first-line systemic therapy for unresectable HCC in patients with and without Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in a single medical center.

Methods: In this retrospective study, we reviewed the medical records in MacKay Memorial Hospital from Jan. 1st, 2020, to Nov. 30th, 2024. Patients with unresectable HCC who received immunotherapy as first-line systemic therapy were enrolled. The definition of MASLD is based on EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease. Steatotic liver disease is defined by the HSI (Hepatic Steatosis Index) score, which is derived from a regression model/formula using ultrasound as the reference modality, using “BMI, diabetes, ALT to AST ratio”. Cut-off scores of < 30 for ruling out steatosis. Mann-Whitney U test, Fisher exact test, and Kaplan-Meier method were applied for the analysis of clinical characteristics, overall

survival (OS), progression-free survival (PFS), objective response rate (ORR), and disease control rate (DCR) between patients with MASLD and non-MASLD.

Results: Patients with unresectable HCC who received immunotherapy as first-line systemic therapy (n = 52) were enrolled and divided into two groups: the MASLD group (n = 21) and the non-MASLD group (n = 17). The mean age was 69.57 ± 12.07 years, and 57% of patients were male. Among these patients (Table 1), no significant differences were found in the two groups regarding sex, age, HBV, HCV, FIB-4, BCLC stage, total bilirubin level, and extra-hepatic spread number. Radiological best overall responses are detailed in Table 2. The two groups had no significant difference in DCR, PFS, and OS (Table 2, Figure 1), but statistical significance was noted in PR and ORR.

Conclusions: Our real-world data revealed no significant difference in overall survival and progression-free survival between patients with and without MASLD who received immunotherapy as first-line systemic therapy. However, those diagnosed with MASLD had a better partial response to first-line immunotherapy. Additional prospective studies are required to reach a conclusive verdict.

P.26

針對罹患酒精性肝炎、B 型肝炎、C 型肝炎的肝硬化病人後續產生肝細胞癌的發生率之比較

COMPARISON OF THE CUMULATIVE INCIDENCE OF HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS WITH ALCOHOLIC HEPATITIS, HEPATITIS B, AND HEPATITIS C

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Background: HCC stands out as the primary form of liver cancer and ranks as the third most common cause of cancer-related mortality worldwide. HBV and HCV infections, along with heavy alcohol consumption, are well-established risk factors for the development of HCC.

Aims: Our study compare the cumulative incidence of HCC attributable to alcohol-related liver disease (ALD), HBV-related cirrhosis, and HCV-related infections, and aim to clarify the clinical characteristics of them.

Methods: A total of 14,073 patients with liver cirrohsis were retrieved from the National Health Insurance Research Database (NHIRD); they were separated into 3 groups, with underlying cirrhosis related to either alcohol, HBV or HCV, and matched in 1:1:1 ratio, with eventually 1470 patients in each group. The cumulated incidence of hepatocellular carcinoma, the univariate and multivariate anaylsis in each group were then calculated during study period.

Results: After statistical matching, patients with alcoholic liver cirrhosis have significantly higher comorbidity rates, such as cerebrovascular disease, acute coronary syndrome, heart failure, peptic ulcer and liver decompensation, compared to patients with HBV-LC and HCV-LC. Although the slope is lower compared to HBV-LC and HCV-LC group, the trend of cumulative incidence for HCC in ALC group still shows an upward trajectory, indicating alcoholic cirrhosis to be an important independent risk factor for the development of HCC.

Conclusions: Alcoholic liver cirrhosis significantly increases the risk of HCC through a combination of metabolic, genetic, and inflammatory mechanisms. Addressing heavy alcohol consumption and its associated risk factors is essential to reduce the global burden of alcohol-associated cirrhosis and HCC. Our study highlights the relationship between alcoholic liver cirrhosis and the development of HCC, emphasizing the need for comprehensive strategies to manage and mitigate this public health issue.

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血清甲胎蛋白濃度的遽降可以預測肝癌患者對於免疫治療的反應
PLUMMETED SERUM ALPHA-FETOPROTEIN CONCENTRATIONS PREDICT THE RESPONSES OF IMMUNOTHERAPY IN HEPATOCELLULAR CARCINOMA PATIENTS

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Background: Hepatocellular carcinoma (HCC) is the sixth most common malignancy and the fourth leading cause of cancer-related deaths worldwide. Immune checkpoint inhibitors have shown promise in treating advanced HCC and has been recommended as first line treatment in systemic treatment of HCC; however, objective response rate (ORR) remains suboptimal. Therefore, identifying effective biomarkers to predict treatment efficacy is crucial.
Aims: To investigate possible biomarkers to predict the efficacy of immunotherapy in subjects with HCC as early as possible.
Methods: A total of 59 subjects with HCC receiving immunotherapy was prospectively enrolled in the present study, and treated with at least one dose of immune checkpoint inhibitor (ICI) therapy, including pembrolizumab, nivolumab, or atezolizumab plus bevacizumab. In addition, subjects without completed follow-up tumor marker records after ICIs therapy and elevated baseline alpha-fetoprotein (AFP ≤ 25 ng/ml) were excluded. The serum levels of AFP were measured after 1, 2, 3, 6 and 8 weeks of ICIs therapy. We evaluated the radiologic responses of the tumors by modified Response Evaluation Criteria in Solid tumors (mRECIST). There are finally 27 subjects perform analysis. AFP reduction was calculated by the proportion between serum level after treatment and baseline. Receiver operating characteristic (ROC) curves were plotted to compare the performance of AFP reduction for predicting therapeutic response.
Results: Baseline characteristics between responder (complete response and partial response) and non-responder (stable disease and progress disease) groups showed no statistically significances in age, body weight, performance status score, BCLC stage, Clip stage and Child–Pugh class. The area under the receiver operating characteristic curve (AUROC) for AFP reduction at 1st week was 0.533 (95% CI, 0.304–0.762, p = 0.771); 2nd week was 0.577 (95% CI, 0.350–0.804, p = 0.497); 3rd week was 0.687 (95% CI, 0.474–0.900, p = 0.099); 6th week was 0.703 (95% CI, 0.503–0.904, p = 0.073); 8th week was 0.709 (95% CI, 0.511–0.906, p = 0.065).
Conclusions: Our study revealed that the AUROC for AFP reduction reach to an acceptable predictive value as soon as the 3rd week after treatment. Early monitoring of AFP reductions during ICIs therapy could guide clinical physician in assessing treatment efficacy.

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二甲雙胍對不可切除肝細胞癌免疫療法療效的影響
IMPACT OF METFORMIN ON THE EFFICACY OF IMMUNOTHERAPY IN UNRESECTABLE HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality. Immune checkpoint inhibitors (ICIs), particularly atezolizumab and bevacizumab, are the standard first-line treatment for unresectable HCC; however, their efficacy may be reduced in patients with type 2 diabetes mellitus (T2DM) and non-alcoholic steatohepatitis (NASH) due to immune dysregulation and impaired CD8+ T-cell function. While preclinical studies indicate metformin, an antidiabetic agent, exhibits immunomodulatory effects to synergize with ICIs, its impact on unresectable HCC outcomes was still obscure.

Aims: To evaluate the possible effects of metformin in patients with unresectable HCC receiving atezolizumab and bevacizumab.

Methods: A total of 66 diabetic patients with unresectable HCC who were treated with atezolizumab and bevacizumab was retrospectively enrolled. Clinical and radiological parameters associated with therapeutic response were assessed to evaluate progression-free survival (PFS), and overall survival (OS) using Kaplan-Meier analysis. Independent predictors of treatment outcomes were identified through multivariate analysis employing the Cox proportional hazards model.

Results: Kaplan-Meier analysis revealed a significant difference in PFS between patients receiving metformin and those treated with other antidiabetic therapies (median PFS: 11.9 vs. 6.3 months, p = 0.02). OS was also significantly longer in the metformin group compared to other therapies (median OS: 47.4 vs. 12.5 months, p = 0.008). After adjusting for age, gender, performance status, liver disease etiology, Child-Pugh classification, cancer of the liver Italian program (CLIP) score, presence of macrovascular invasion or extrahepatic spread, and concurrent therapies with immunotherapy, metformin use remained a significant independent predictor of PFS (HR 0.48; 95% CI 0.23–0.99; p = 0.050) and OS (HR 0.36; 95% CI 0.14–0.93; p = 0.036).

Conclusions: Our clinical evaluation demonstrated a significant association between metformin use and improved survival outcomes in diabetic patients with unresectable HCC treated with atezolizumab and bevacizumab.

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經皮腫瘤消融術治療小型肝癌的療效
THE EFFICACY OF PERCUTANEOUS TUMOR ABLATION FOR SMALL HEPATOCELLULAR CARCINOMA

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Background: Percutaneous tumor ablation, including radiofrequency ablation (RFA) and percutaneous ethanol injection therapy (PEIT), which play an important role in the treatment of hepatocellular carcinoma (HCC). Previous studies demonstrate that RFA have better survival benefit than PEIT, however, the efficacy of RFA and PEIT for small HCC were not well discussed.

Aims: This study aims to evaluate the effectiveness of RFA and PEIT in treating small HCC lesions ≤1.5 cm, analyzing the outcomes based on different treatment modalities.

Methods: The medical records of patients diagnosed with HCC who underwent RFA or PEIT as first-line treatment and had tumor sizes less than 1.5 cm at MacKay Memorial Hospital between January 1, 2009, and December 31, 2023, were retrospectively reviewed. Exclusion criteria included cases of HCC classified as BCLC stage C or D. These patients were divided based on the first percutaneous tumor ablation treatment modality into two groups: RFA and PEIT. The clinical characteristics of patients in different treatment groups were compared using the Mann-whitney U test and Fisher exact test. Survival analysis was calculated by using the Kaplan-Meier method. Time to progression (TTP) was measured from the date of treatment until the first documented tumor progression in imaging studies according to the modified response evaluation criteria in solid tumors (mRECIST) by independent radiologic assessment.

Results: Sixty-one patients diagnosed with HCC were enrolled in this study. The RFA group (n = 42, 68.85%) and the PEIT group (n = 19, 31.15%). Patient characteristics were summarized in Table 1. In this study, the median TTP and the overall survival (OS) were 25.48 (95% CI, 11.66–39.30) and 115.00 (95% CI, 86.29–143.71) months in small HCC patients. The median TTP was 44.68 months (95% CI, 27.72–61.64) and 5.62 months (95% CI, 1.94–9.30), for RFA group and PEIT group, respectively. The mean OS was 96.53 (95% CI, 79.51–113.54) and 78.54 (95% CI, 56.36–100.71) months, for RFA group and PEIT group, respectively. Kaplan-Meier analysis showed that PEIT was similar to RFA in OS in patients with small HCC ($p = 0.236$). (Fig. 2) and RFA have better outcome than PEIT of TTP in patients ($p = 0.001$) (Fig. 3).

Conclusions: This real-world data suggests that RFA may have a longer TTP compared to PEIT in patients with small HCC. However, OS appears to be similar between the two groups. The potential efficacy of rescue second-line therapies following PEIT may contribute to comparable OS in patients with small HCC.

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經皮腫瘤消融術在治療老年人肝癌的臨床應用
THE CLINICAL UTILITY OF PERCUTANEOUS TUMOR ABLATION FOR ELDERLY HCC PATIENTS

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Background: Elderly patients with hepatocellular carcinoma (HCC) face a heightened risk of the disease and often have increased surgical risk. Percutaneous tumor ablation, including radiofrequency ablation (RFA) and percutaneous ethanol injection therapy (PEIT), can be considered alternative treatment options for these individuals. While previous studies suggest RFA may be more effective than PEIT in the general HCC population, the optimal percutaneous tumor ablation approach for elderly patients with significant comorbidities remains uncertain.

Aims: This study aims to evaluate the treatment outcomes of percutaneous tumor ablation for HCC in elderly patients.

Methods: A retrospective review of medical records was conducted at MacKay Memorial Hospital, a tertiary referral center in Taiwan, from January 1, 2009, to December 31, 2023. Inclusion criteria included patients diagnosed with HCC who underwent RFA or PEIT as the initial treatment and were aged 65 years or older. Exclusion criteria included HCC patients with BCLC stage C or D and those who had undergone prior surgery or embolization therapy before percutaneous tumor ablation.

Results: A total of 194 patients newly diagnosed with HCC were enrolled in this study. These patients were divided into two groups based on initial treatment modality; the RFA group (n = 168, 86.6%) and the PEIT group (n = 26, 14.4%). During a median follow-up period of 40.00 months (range, 2–125 months), 41 (24.4%) patients in the RFA group and 14 (53.9%) patients in the PEI group died. In the study subjects, the 1-, 3-, and 5-year cumulative probabilities of overall survival (OS) rates were 99.0%, 82.9%, 66.5%, respectively. In the RFA group and the PEIT group were 99.4%, 89.9%, 79.8% and 92.3%, 73.1%, 61.5%, respectively. In this study, the median OS were 91.0 (95% CI, 70.4–111.6) months in all elderly HCC patients. The median OS was 117 months (95% CI, 68.7–165.3), 75 months (95% CI, 39.78–110.22) for RFA group and PEIT group, respectively. The survival rate of RFA was significantly higher than the PEIT group (p = 0.030). In univariate Cox regression analysis, the treatment modality, Child–Pugh score, age and FIB-4 score were significant risk factors for OS. PEIT, higher Child–Pugh score, old age and FIB-4 score >3.25 were associated with poor survival. In multivariate Cox regression analysis, PEI, higher Child–Pugh score and FIB-4 score >3.25 were associated with poor survival.

Conclusions: In this real-world study, RFA demonstrated superior OS compared to PEIT in elderly patients with HCC.

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射頻消融術與經皮酒精注射治療大於 1.5 公分肝細胞癌的存活獲益比較
SURVIVAL BENEFIT COMPARISON OF RADIOFREQUENCY ABLATION VERSUS PERCUTANEOUS ETHANOL INJECTION FOR HEPATOCELLULAR CARCINOMA TUMORS LARGER THAN 1.5 CM

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Background: While radiofrequency ablation (RFA) generally demonstrates superior survival outcomes compared to percutaneous ethanol injection therapy (PEIT) in the treatment of hepatocellular carcinoma (HCC), previous studies have suggested that PEIT may be a viable treatment option for small HCCs. However, previous studies have not established a definitive size threshold for HCCs that are unsuitable for treatment with PEIT.

Aims: Our study aims to emphasize the treatment outcome of percutaneous tumor ablation methods for HCC patients with tumor size larger than 1.5 cm.

Methods: A retrospective study was conducted at MacKay Memorial Hospital from January 1, 2009, to December 31, 2023. Inclusion criteria included patients diagnosed with HCC with a maximum tumor dimension greater than 1.5 cm on imaging studies (computed tomography or magnetic resonance imaging) who underwent either RFA or PEIT as the first-line treatment. Exclusion criteria included patients with: 1) BCLC stage C or D HCC, 2) a history of prior surgery or embolization therapy before percutaneous tumor ablation, and 3) a maximum tumor dimension less than 1.5 cm." Survival analysis was calculated by using the Kaplan-Meier method. Time to progression (TTP) was measured from the date of treatment until the first documented tumor progression in imaging studies by independent radiologic assessment.

Results: A total of 250 patients newly diagnosed with HCC were enrolled in this study. Based on the initial treatment modality, patients were categorized into two groups: the RFA group (n = 224, 89.6%) and the PEIT group (n = 26, 10.4%). No significant differences were observed between the two groups in terms of age, gender, etiology, FIB-4 score, alpha-fetoprotein (AFP) levels, and tumor size and number. However, the mean Child-Pugh score was significantly higher in the PEIT group. In this study, the median overall survival (OS) and the TTP were 99.0 months (95% CI, 76.95–121.05) and 29.4 (95% CI, 20.9–37.9) months in HCC patients with tumor larger than 1.5 cm. The median OS was 117 months (95% CI, 98.10–135.90), 51 months (95% CI, 7.5–94.5), for RFA group and PEIT group, respectively. The median TTP was 30.6 months (95% CI, 23.7–37.6), 11.7 months (95% CI, 0–35.2), for RFA group and PEIT group, respectively. The RFA group demonstrated significantly longer OS compared to the PEIT group ($p < 0.001$). Similarly, RFA was associated with a significantly longer TTP than PEIT in the enrolled patients ($p = 0.035$).

Conclusions: This retrospective study suggests that RFA may be the preferred treatment option for HCC larger than 1.5 cm, while PEIT may be less suitable for these larger lesions.

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一醫學中心真實臨床經驗：免疫治療與 Lenvatinib 作為 BCLC B 期不可切除肝細胞癌的一線全身治療比較

A SINGLE-CENTER REAL-WORLD EXPERIENCE: LENVATINIB VERSUS IMMUNOTHERAPY AS FIRST-LINE SYSTEMIC TREATMENT FOR BARCELONA CLINIC LIVER CANCER (BCLC) STAGE B UNRESECTABLE HEPATOCELLULAR CARCINOMA

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Background: Currently, immunotherapy, particularly the combination of atezolizumab and bevacizumab, is widely used as a first-line systemic treatment for unresectable hepatocellular carcinoma (HCC) due to its superior survival outcomes compared to, sorafenib, a multiple tyrosine kinase inhibitors (TKIs). However, for patients with Barcelona Clinic Liver Cancer (BCLC) stage B unresectable hepatocellular carcinoma, it remains unclear whether immunotherapy as a first-line treatment offers better outcomes, particularly when compared to lenvatinib, a TKIs.

Aims: This study aims to compare Lenvatinib and immunotherapy as first-line treatments for patients with unresectable HCC at BCLC stage B.

Methods: In this retrospective study, we reviewed the medical records of patients with unresectable HCC in MacKay Memorial Hospital from Jan. 1st, 2020, to Jul. 31st, 2023. Patients with BCLC stage B HCC who received either immunotherapy-based treatment or lenvatinib as first-line systemic therapy were enrolled in the study. Clinical characteristics, progression-free survival (PFS), and overall survival (OS) were compared between patients who received immunotherapy and those who received lenvatinib as first-line systemic therapy.

Results: The patients with BCLC stage B unresectable HCC (n = 31) were enrolled and divided into two groups: the lenvatinib group (n = 21) and the immunotherapy group (n = 10). The mean age was 65.9 ± 12.9 years and 65% of patients were male. Among these patients (Table 1), no significant differences were found in the two groups regarding age, sex, liver cirrhosis, total-bilirubin level, and extra-hepatic spread number. However, there were significant differences in alcoholism ($p < 0.05$). There was no significant difference in overall survival and progression-free survival curves between the lenvatinib and the immunotherapy groups ($p = 0.669$ and 0.806). The median OS in the lenvatinib and the immunotherapy groups was 20.3 months and 27.1 months, respectively. The median PFS of the lenvatinib and the immunotherapy groups was 10.1 months and 3.5 months, respectively.

Conclusions: Our real-world data showed no significant difference in treatment response and survival between the patients with BCLC stage B unresectable HCC treated with lenvatinib or immunotherapy as first-line systemic therapy. Further prospective studies are needed to draw definitive conclusions.

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B 肝與 C 肝肝癌手術後之預後比較
THE COMPARISON OF POST-OPERATIVE OUTCOME BETWEEN HEPATITIS B AND HEPATITIS C-RELATED HEPATOCELLULAR CARCINOMA

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Background: The survival outcome of HBV and HCV-related HCC (hepatocellular carcinoma) patients who received curative hepatectomy showed variable results in previous studies. However, most of the studies were conducted before introducing DAA (direct-acting antiviral) therapy for HCV patients. With the application of DAA for HCV patients, it remains unclear about the outcome of HBV and HCV-related HCC patients after curative hepatectomy.
Aims: To compare the postoperative outcome between HBV and HCV related HCC.
Methods: This prospective study enrolled HCC patients with positive HBsAg and anti-HCV who received curative hepatectomy from July 2015 to September 2024. Cox regression analysis was applied for independent predictors of HCC recurrence. The Kaplan-Meier method with the log-rank test was used to compare cumulative incidences of HCC recurrence and overall survival between HBV and HCV patients. A propensity score matching (PSM) at a 1:1 ratio was applied to adjust confounders between HBV and HCV patients such as age, sex, cirrhotic status, preoperative ALT levels and TNM clinical stage at first curative operation.
Results: There were 122 HBV patients and 55 HCV patients enrolling into the study with mean age of 63 years, 79% of male, 35% of cirrhosis, 85% of ALBI grade I, 60% of TNM stage I, and 57% having microvascular invasion. Among HBV patients, 95% were HBeAg negative, median HBV DNA level at operative date was 2.78 log10 IU/mL, and 43% received nucleos(t)ide analogue (Nuc) before curative surgery. While for HCV patients, 93% had undetectable HCV RNA and 62% had received DAA therapy before curative surgery. During the median follow-up of 3.4 years, a total of 58 patients (45 HBV, 13 HCV) had HCC recurrence. Multivariate Cox regression identified TNM stage ≥ II (adjusted hazard ratio (aHR):2.648 (95% CI: 1.571-4.463), $p < 0.001$) was the only independent predictor of HCC occurrence. Of note, HCV patient was less likely to encounter HCC recurrence compared to HBV patients but the statistical difference did not reach significance (crude hazard ratio: 0.681 (0.367-1.264), $p = 0.223$) Before PSM, HBV-HCC patients had a higher 4-yr recurrent rate compared to HCV-HCC patients. (41% vs. 24%, $p = 0.073$). The 4-yr overall survival (OS) was similar (91% vs 87%, $p = 0.294$). After PSM (55 HBV and 55 HCV patients), the HBV-HCC patients still had a higher 4-yr recurrence rate than HCV-HCC patients (51% vs 24%, $p = 0.012$). Similarily, the 4-yr OS was still comparable in both groups (90% vs 87%, $p = 0.473$).
Conclusions: Despite propensity score matching to adjust clinical and tumor factors between HBV and HCV-HCC patients, HBV-HCC still shows higher recurrence rates after curative resection. However, the OS remains comparable in both groups. These findings emphasize the distinct recurrence risk in HBV-HCC patients, suggesting the need for tailored management strategies in this population.

第二部分：消化道及膽胰疾病

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台灣食道弛緩不能的流行病學與臨床實踐型態：一項全國性人口為基礎的世代研究
EPIDEMIOLOGY AND PRACTICE PATTERNS OF ACHALASIA IN TAIWAN: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Background: Achalasia is a rare gastrointestinal motility disease manifested by impaired esophageal peristalsis and lower esophageal sphincter relaxation. Data on its epidemiology and outcomes in Taiwan are limited.
Aims: This study aimed to assess the incidence, characteristics, and clinical management of achalasia patients in Taiwan.
Methods: Patients newly diagnosed with achalasia from 2001 to 2013 were recruited from the Taiwan National Health Insurance Research Database. The study obtained data on the patients' age, gender, urbanization, socioeconomic status, area of residence, diagnostic methods, and interventional management. The incidence, diagnostic modalities, treatment methods, malignancy and mortality outcome were analyzed.
Results: A total of 206 new achalasia cases were identified. The mean annual incidence in Taiwan was 1.64 (95% confidence interval 1.22–2.05) per 100,000 persons. The mean age at diagnosis was 51.8 years old. The age-specific incidence of achalasia peaked in patients aged between 70–80 years old and above 80 years old. For achalasia diagnosis, endoscopy, CT scan, barium studies, and manometry were performed in 123 (59.71%), 97 (47.09%), 49 (23.79%), and 11 (5.34%) patients, respectively. During long-term follow-up, 7 patients (3.39%) developed esophageal cancer, and 39 patients (18.93%) died. The median survival was 10.65 years after achalasia diagnosis with a 10-year survival rate of 76.22%.
Conclusions: This is the first population-based epidemiologic study of achalasia in Taiwan, revealing the incidence of achalasia before the high-resolution manometry era. Clinicians should be vigilant for esophageal cancer development and mortality during long-term follow-up. There is also room for enhancing the utilization of various diagnostic tools for achalasia.

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胃中食物滯留程度及病患特性之關聯
ASSOCIATION BETWEEN THE DEGREE OF GASTRIC FOOD RETENTION AND PATIENT CHARACTERISTICS

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Background: Retained gastric food contents are frequently observed in patients undergoing upper endoscopy. Some studies have shown that patients with certain characteristics or underlying medical conditions are associated with retained gastric food during endoscopic examination.
Aims: In this study, we aim to correlate the prevalence and degree of food retention on upper endoscopy with patient characteristics and underlying medical histories.
Methods: Eighty-two patients with retained food residue in the stomach and another eighty-two patients without it during upper endoscopy were included to analyze correlations using t-tests, chi-square tests, and ANOVA.
Results: No statistical significance was observed in the prevalence or degree of food retention during upper endoscopy in relation to patient characteristics and underlying medical histories. Nonetheless, possible trends toward significance were still observed in patients with a history of cancer, GERD, chronic kidney disease, or those using GLP-1 receptor agonists.
Conclusions: Our study indicates that the presence or degree of gastric food retention is not significantly associated with specific patient characteristics or underlying medical conditions, despite certain limitations.

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上消化道內視鏡檢查的成本：單一醫學中心的分析
THE COST OF AN ESOPHAGOGASTRODUODENOSCOPY: A SINGLE CENTER ANALYSIS

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Background: Recent studies have demonstrated that esophagogastroduodenoscopy (EGD) is a cost-effective method for early upper gastrointestinal cancer screening, particularly in Asian countries with higher incidence rates. 1,2 The cost of EGD varies from different countries. For instance, the average cost of an EGD is approximately USD 2,750 in the United States and ¥13,000 in Japan. 3,4 In Taiwan, the current reimbursement for EGD is set at NT$ 1,575 by the National Health Insurance Administration. However, advancements in medical technology, rising inflation, and increased material and labor costs have significantly escalated overall medical expenses. These trends underscore the importance of reassessing and potentially revising the cost structure for EGD to ensure sustainability and accessibility.

Aims: This study evaluates the cost of an esophagogastroduodenoscopy (EGD) for adult patients at a single hospital center.

Methods: The cost calculations were based on a detailed assessment of labor, capital investments, cleansing and disinfection, medications, personal protective equipment (PPE), and consumables required for unsedated EGD in adult patients at Cathay General Hospital. Hospital records from 2021 to 2023 showed an average annual volume of 2,800 procedures, equating to approximately 11 procedures per working day over a 52-week, 5-day work year. Labor costs were categorized into patient preparation, physician and technician fees, and nurse attendant cleaning fees. Patient preparation included tasks such as appointment booking, registration, procedure explanation, and general counseling, each taking approximately 3 minutes, with costs calculated based on hospital salaries. The physician's fee was set at 30% of the health insurance reimbursement rate, while technician and cleaning fees were based on daily salaries divided by 11 procedures per day. Capital expenditure covered two endoscopic video processors, eight endoscopes, one storage cabinet, and three washer-disinfectors, with an estimated lifespan supporting 28,000 procedures over 10 years. Additional costs for computers and large-screen displays were also accounted for over the same period. Medication costs were calculated per patient using a fixed dose. Cleaning and disinfection costs were determined by dividing the total two-week expenditure by 110 procedures. PPE and consumables included fixed costs per patient and costs averaged over two weeks for certain items.

Results: Table 1 shows the breakdown of the cost per procedure, based on a volume of 2,800 procedures per year. The total cost per EGD is NT$ 1,887. This includes a labor cost of NT$ 909.9, capital investment of NT$ 537.3, cleaning and disinfection cost of NT$ 242, medication cost of NT$ 36, PPE cost of NT$ 13.7, and consumables cost of NT$ 147.6. Figure 1 illustrates the percentage distribution of various cost categories, with labor costs (48%), capital expenditures (28%), and cleaning and disinfection costs (13%) as the largest contributors, respectively.

Conclusions: The total cost of performing an EGD is NT$ 1,887 for an unsedated adult patient in a single hospital center. Among them, the physician fee is calculated based on 30% of the current health insurance reimbursement rate. The total cost would be higher if adjusted to reflect actual current expenses. In conclusion, the findings based on this single center indicate that the actual cost of EGD has significantly exceeded the reimbursement provided by the health insurance system. Further research is needed to support the development of updated reimbursement and healthcare policies in the future.

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台灣藜對右旋糖酐硫酸鈉所導致的小鼠慢性結腸炎的預防功效
PREVENTIVE EFFECT OF DJULIS ON DEXTRAN SULFATE SODIUM-INDUCED CHRONIC COLITIS IN MICE

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Background: Djulis is a grain crop native to Taiwan that has previously been shown to reduce inflammation. Based on these effects, its effects and potential benefits for individuals with inflammatory bowel disease (IBD) is of interest. This study used mice and induced chronic colitis in mice with dextran sodium sulfate (DSS). We evaluated whether djulis consumption could reduce symptoms in the mice.
Aims: To evaluate the efficacy of djulis as a treatment option for patients with IBD.
Methods: A total of 40 mice were randomly divided into 5 groups: blank group (B), control group (C), low-dose group (L), medium-dose group (M), and high-dose group (H). Body weight and disease activity index (DAI) were recorded throughout the study. Groups C, L, M, and H were administered 2% DSS on days 1 to 5 and 10 to 15 to induce chronic colitis. Group L, M and H were administered 5%, 10% and 15% djulis respectively. Mice were sacrificed at the end of the study, and serum and colon samples were collected for analysis.
Results: The DAI scores of groups L, M, and H were significantly lower than those of group C, indicating that the use of Djulis did improve the condition. Moreover, the DAI score of group H on day 18 was significantly lower than that of group L. Mice that consumed djulis (groups L, M and H) showed restoration of colon length, with group H having the most obvious effect.
Conclusions: Djulis alleviates chronic colitis in mice by reducing inflammation. Future research is needed to prove the usefulness of djulis as a dietary treatment for people with inflammatory bowel disease.

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台灣醫師對於 IBD 病人的內視鏡追蹤策略選擇：一個匿名問卷調查
THE CHOICE OF ENDOSCOPIC SURVEILLANCE STRATEGIES FOR IBD PATIENTS AMONG TAIWANESE PHYSICIANS: AN ANONYMOUS QUESTIONNAIRE SURVEY

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Background: Chronic inflammation caused by inflammatory bowel disease (IBD) increases the risk of patients developing colorectal cancer or dysplasia. Guidelines recommend that patients with IBD undergo regular colonoscopic surveillance based on factors such as the degree of inflammation, family history, and comorbidities. Previous studies have shown that chromoendoscopy has a higher detection rate for colorectal cancer screening, and most guidelines also recommend chromoendoscopy as the preferred endoscopic technique for colorectal cancer surveillance.
Aims: This questionnaire aims to understand the strategies used by physicians in Taiwan for colorectal neoplasia (CRN) screening in IBD patients.
Methods: The questionnaire will be distributed using an anonymous online survey at gastroenterology-related conferences and social media groups. It will include questions on the respondents' hospital level, career duration, number of IBD patients under their care, and the ratio of biologics use. The survey will investigate their IBD surveillance strategies, such as the choice of endoscopic techniques, whether they use image-enhanced endoscopy (IEE), biopsy strategies, and non-invasive tools. The results will be analyzed to determine if there are differences in the selection of endoscopic techniques based on the variance in physician characteristics.
Results: A total of 53 physicians from Taiwan completed the survey. Of these, 39 (73.6%) were from tertiary-level hospitals, 37 (69.8%) had been practicing for over 10 years, 18 (34.0%) were caring for more than 50 IBD patients, and 11 (20.8%) had more than 30% of their IBD patients on biologics. Regarding the choice of endoscopic techniques, 25 (47.2%) used high-definition white light endoscopy (HD-WLE), 17 (32.1%) used standard-definition WLE, 11 (20.8%) used virtual chromoendoscopy, and none

used chromoendoscopy. A total of 41 (77.4%) physicians used IEE (including virtual chromoendoscopy or WLE used in combination with IEE at inflammatory sites) for surveillance. The use of IEE was significantly associated with the number of IBD patients under care ($p = 0.018$), but there was no significant correlation with other physician characteristics. The reasons for selecting endoscopic techniques were as follows: 28 (52.8%) chose techniques for time efficiency, 20 (37.7%) based their choice on evidence-based medicine, and 5 (9.4%) were limited by the availability of endoscopic techniques. Besides, a total of 46 (86.8%) physicians adopted the target biopsy strategy.

Conclusions: The proportion of Taiwanese physicians using chromoendoscopy for IBD surveillance is relatively low. Additionally, physicians who care for a greater number of IBD patients are more likely to use IEE as a surveillance tool.

P.39

18F-FDG PET/CT 在大腸息肉檢測中的角色：一項回顧性研究
EVALUATION OF 18F-FDG PET/CT IN THE DETECTION OF COLORECTAL POLYPS: A RETROSPECTIVE STUDY

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Background: Positron Emission Tomography (FDG-PET) is widely used for screening distant metastases in tumors and often detects incidental glucose uptake abnormalities, including colorectal lesions. Colorectal polyps, as common intestinal lesions, are typically asymptomatic, making early detection challenging. Currently, the primary method for detecting colorectal polyps is the fecal occult blood test (FOBT). However, FOBT has limitations, including false positives and false negatives, and cannot differentiate between various types of intestinal lesions.

Aims: This study aims to investigate whether FDG-PET can serve as an effective tool for screening colorectal lesions and to evaluate its potential in early detection of such lesions.

Methods: This retrospective study evaluated the efficacy of 18F-FDG PET/CT in screening for colorectal polyps. We reviewed the medical records of 32,346 individuals who underwent whole-body 18F-FDG PET/CT scans at Changhua Christian Hospital between November 2014 and October 2024. These patients were primarily individuals with known or suspected malignancies. Among them, 64 non-colorectal cancer patients showed abnormal glucose uptake in the colorectal region on FDG-PET images. These patients were further referred for colonoscopy, and the identified lesions were sent for histopathological examination to determine the diagnostic accuracy of FDG-PET for colorectal polyps and tumors. Clinical indications for FDG-PET were meticulously documented, and a detailed review of clinical records was performed for each positive case. For these cases, colonoscopy results and pathology reports were examined to confirm the final clinical diagnosis. The correlation between standardized uptake values (SUV) on FDG-PET images and the malignancy of subsequent pathological findings was analyzed. Additionally, the interval between FDG-PET scans and colonoscopies was examined to assess its impact on diagnostic outcomes.

Results: Among the 64 patients, 32 underwent

colonoscopy. Of these, 23 patients (71.8%) had at least one corresponding lesion identified in pathology reports, while no lesions were found in 9 patients. Pathological findings in the 23 patients revealed 6 cases (26.0%) of malignant tumors, 15 cases (65.2%) of tubular adenomas and tubulovillous adenomas, and 2 cases (8.6%) of hyperplastic polyps. Statistical analysis showed no significant difference in SUV values between patients with positive and negative findings on FDG-PET ($p = 0.53411 > 0.05$). Patients later diagnosed with colorectal cancer had intervals between PET and colonoscopy ranging from 2 weeks to 7 years, with an average of 34.75 months. For patients with benign adenomas, the interval ranged from less than 1 week to 1.5 years, with an average of 4.44 months. Although there was a trend toward longer intervals in patients diagnosed with tumors, the difference was not statistically significant ($p = 0.15976 > 0.05$).

Conclusions: The presence of localized 18F-FDG uptake and its intensity observed in FDG-PET/CT cannot rule out the possibility of malignant tumors or adenomas, necessitating confirmation through colonoscopy. Although the interval between PET and colonoscopy was not significantly associated with lesion type, the data indicate that patients with tumors often experienced longer intervals. Therefore, it is recommended to perform colonoscopy promptly when suspicious colorectal lesions are detected on 18F-FDG PET/CT.

P.40

回顧性分析大腸直腸癌患者的五年存活率與復發情況

A RETROSPECTIVE ANALYSIS OF FIVE-YEAR SURVIVAL RATES AND RECURRENCE IN COLORECTAL CANCER PATIENTS

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Background: According to the latest data from the Taiwan Cancer Registry, colorectal cancer (CRC) has been the most prevalent cancer for 14 consecutive years, with a new case diagnosed every thirty minutes.

Aims: This retrospective study aimed to analyze the five-year survival rates and recurrence patterns of CRC patients from 2015 to 2023.

Methods: The study involved a cohort of patients diagnosed with CRC at Tainan Municipal Hospital, managed by Show Chwan Medical Care Corporation, within a specified time frame. The clinical outcomes of these patients were monitored over a minimum period of five years. Key variables were systematically reviewed, including tumor stage at diagnosis, treatment modalities (such as surgery, chemotherapy, and radiation), and recurrence patterns. The 5-year overall survival (OS) rate and disease-free survival (DFS) rate were calculated to evaluate the effectiveness of current treatment protocols. Furthermore, the study analyzed recurrence rates and identified factors associated with an increased risk of relapse, including advanced stage at diagnosis, histological subtype, and response to initial treatment.

Results: The findings indicate that early-stage detection and personalized treatment strategies are crucial for improving survival rates. Furthermore, the study highlights the importance of regular follow-up and surveillance in reducing recurrence rates and enhancing long-term outcomes for CRC patients.

Conclusions: This analysis provides valuable insights into trends in survival and recurrence, contributing to the refinement of clinical practices and establishing a foundation for future research to improve the prognosis for CRC patients.

P.41

建立大腸直腸癌復發預測的模型：區域教學醫院的經驗
CONSTRUCTING A COLORECTAL CANCER RECURRENCE PREDICTION MODEL: A STUDY OF RISK FACTORS BASED ON DATA FROM 2015-2023

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Background: According to the latest data from the Taiwan Cancer Registry, colorectal cancer (CRC) has been the most prevalent cancer for 14 consecutive years, with a new case diagnosed every thirty minutes.
Aims: This study aimed to develop a predictive model for colorectal cancer recurrence based on risk factors identified from data collected between 2015 and 2023.
Methods: A cohort of CRC patients diagnosed at Tainan Municipal Hospital, managed by Show Chwan Medical Care Corporation, was retrospectively analyzed to identify key factors influencing recurrence. The study collected demographic, clinical, and pathological data, including age, gender, tumor stage, histological type, surgical margins, lymph node involvement, and adjuvant therapies. Statistical methods, including logistic regression and machine learning algorithms, were employed to evaluate the relationship between these variables and the likelihood of cancer recurrence. The objective was to develop a reliable risk prediction model to identify high-risk patients who may benefit from more intensive monitoring and tailored treatment strategies.
Results: Early-stage tumors and negative surgical margins were linked to a reduced risk of recurrence, while advanced stages, lymph node involvement, and certain histological subtypes were associated with an increased likelihood of recurrence.
Conclusions: The predictive model exhibited significant accuracy, offering clinicians a valuable tool for predicting recurrence and enhancing post-treatment surveillance. This study underscores the importance of personalized follow-up care, enabling timely interventions to improve patient outcomes. By identifying the most relevant risk factors and incorporating them into a practical model, this research advances the management and prognosis of CRC patients.

P.42

台灣發炎性腸炎生物製劑使用的挑戰：一個醫學中心健保給付審核現況研究
CHALLENGES IN ACCESSING BIOLOGICS FOR INFLAMMATORY BOWEL DISEASE IN TAIWAN: A STUDY OF NHI REIMBURSEMENT REJECTIONS IN A MEDICAL CENTER

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Background: Advanced therapy is an emerging treatment for inflammatory bowel disease (IBD), but its clinical application is limited by cost. In Taiwan, applying for biologics under the National Health Insurance (NHI) system requires strict criteria. Adult patients must hold a catastrophic illness card for IBD and have failed at least six months of conventional therapy before initiating advanced therapy. For ulcerative colitis (UC), a Mayo score ≥9 with an endoscopic subscore ≥2 are required. For Crohn's disease (CD), one of the following conditions must be met: (1) Crohn's Disease Activity Index (CDAI) ≥300, (2) non-healing post-surgical fistula with CDAI ≥100, or (3) two surgeries within a year with CDAI ≥100. Biologic therapy initiation requires a response by week 8, followed by reassessment at week 24. After a 54-week treatment course, a 3-month drug holiday is mandatory before reapplying for biologic therapy, with relapse criteria mirroring the initial conditions. These restrictions create significant challenges for biologic therapy in Taiwan.
Aims: This study aims to investigate the challenges and reimbursement situation of advanced therapy for IBD in Taiwan.
Methods: This study analyzed NHI biologic drug reimbursement applications submitted between November 1, 2012, and November 30, 2024. The number of rejected applications and the reasons for rejection were summarized.
Results: A total of 1,665 NHI biologic applications were reviewed, with 358 (21.5%) rejected (CD: 263/1,157, 22.7%; UC: 95/508, 18.7%). The rejection rate decreased from 25.9% in 2018 to 15.5% in 2024. Common rejection reasons were insufficient use of conventional therapy (52.5%), insufficient drug holiday (23.5%), and incomplete data (11.5%). Rejection reasons varied significantly between CD and UC ($p = 0.019$). CD patients had higher rejection rates due to insufficient drug holidays.

Conclusions: In Taiwan, biologic therapy for IBD requires six months of conventional therapy and a three-month drug holiday before reapplication. CD patients experience higher rejection rates than UC patients, primarily due to insufficient drug holidays, although rejection rates have decreased over time.

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比較換水大腸鏡與傳統充氣法大腸鏡的腺瘤發現率：真實世界回顧性研究
A RETROSPECTIVE REAL-WORLD STUDY COMPARING ADENOMA DETECTION RATES BETWEEN WATER EXCHANGE AND AIR INSUFFLATION

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Background: Randomized controlled trials have consistently shown that water exchange (WE) achieves the highest adenoma detection rate (ADR). However, large-scale real-world evidence is lacking. This study aims to assess the effectiveness of WE in improving ADR compared to air insufflation in a real-world setting.
Aims: This study aims to assess the effectiveness of WE in improving ADR compared to air insufflation in a real-world setting.
Methods: This retrospective study was conducted at a regional hospital in Taiwan between January 2019 and October 2024. Colonoscopies utilizing WE and air insufflation techniques were analyzed. A total of 6,080 procedures performed by three endoscopists were included. Logistic regression was used to identify factors associated with ADR.
Results: Among the 6,080 colonoscopies, 3,363 were performed using WE, and 2,717 with air insufflation. Despite differences in baseline characteristics such as younger age, less sedation, higher use of PEG preparation, and more OB-positive cases in the WE group, ADR was significantly higher with WE compared to air insufflation (58.0% vs. 43.0%, $P < 0.001$). The WE method also showed superior outcomes in polyp detection, bowel preparation quality, and overall procedure efficacy but required longer insertion and withdrawal times. Multivariate logistic regression identified WE as an independent predictor of ADR (OR: 1.378, 95% CI: 1.159–1.637, $p < 0.001$). Other predictors included older age (OR: 1.651, 95% CI: 1.235–2.207, $p = 0.001$), smoking (OR: 1.816, 95% CI: 1.095–3.010, $p = 0.021$), effective bowel preparation using PEG (OR: 0.999, 95% CI: 0.999–1.000, $p = 0.002$), and withdrawal times ≥6 minutes (OR: 5.892, 95% CI: 1.967–17.645, $p = 0.002$).
Conclusions: This study highlights the significantly higher ADR achieved with WE compared to air insufflation, even in a real-world setting. The findings emphasize the potential of WE in reducing interval colorectal cancers. Further studies are warranted to explore the long-term clinical impact of these results.

P.44

探討 50 歲以下無症狀之年輕成人糞便免疫化學檢測的陽性率
TO INVESTIAGE THE POSITIVE RATE OF FECAL IMMUNOCHEMICAL TESTS IN ADULTS UNDER 50 YEARS OLD

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亞東紀念醫院肝膽胃腸科

Background: The incidence of colorectal cancer (CRC) in adults under 50 has been increasing, potentially due to dietary and lifestyle changes, genetic predispositions, and environmental factors. The fecal immunochemical test (FIT) has proven to be an effective screening tool for CRC in individuals over 50, with positivity rates in Taiwanese adults in this age group ranging from 3.8% to 11.1%. However, little is known about FIT positivity rates in asymptomatic younger adults under 50.
Aims: This study aimed to determine the prevalence of positive FIT results in asymptomatic adults under 50 years old.
Methods: We conducted a retrospective study at a tertiary hospital, analyzing FIT results from asymptomatic individuals under 50 years old between May and December 2017.
Results: A total of 4,618 asymptomatic patients from the Far Eastern Memorial Hospital Health Management Center underwent FIT during the study period. Of these, 283 (6.1%) had positive FIT results, while 4,335 had negative results. The relationship between FIT results and patient factors, such as age and gender, was analyzed. A statistically significant association was observed between FIT positivity and age (P = 0.02), while no significant association with gender was identified.
Conclusions: The FIT positivity rate among asymptomatic adults under 50 was comparable to that of individuals aged 50 or older. Further investigation is needed to assess the relationship between positive FIT results and the detection of neoplastic colonic polyps or CRC via colonoscopy in this population. These findings may provide additional support for initiating CRC screening at a younger age.

P.45

在患有發炎性腸道疾病的婦女中，年齡較疾病活性具有對抗穆氏管荷爾蒙更高的影響力
AGE IS MORE IMPORTANT THAN DISEASE ACTIVITY IN AFFECTING ANTI-MüLLERIAN HORMONE LEVEL IN WOMAN WITH INFLAMMATORY BOWEL DISEASE

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Background: Anti-müllerian hormone (AMH) is widely used as a non-invasive surrogate marker for ovarian reserve. Previous research into the relationship between AMH and inflammatory bowel disease (IBD) yielded inconsistent results. The correlation between serum inflammatory cytokines and AMH has not been evaluated.
Aims: This study aims to provide insights from the Asian population and to determine how different factors (including inflammatory cytokines) influence the AMH levels in ulcerative colitis (UC) and Crohn's disease (CD) patients.
Methods: Female IBD patients of reproductive age (from 18 to 49 years old) who were under proactive therapeutic drug monitoring and tight control were enrolled in this longitudinal study. The enrollment spanned from November 2016 to January 2024. Serum samples were tested for AMH and inflammatory cytokines, including interleukin (IL)-1β, IL-6, IL-10 and TNF-α. Fecal calprotectin tests and serum tests were within 3 months. All statistical analysis was conducted with IBM SPSS Statistics version 22.
Results: A total of 119 tests were performed in 37 IBD patients (47 tests in 16 UC patients and 72 tests in 21 CD patients). The mean follow-up period was 31.4 months. The mean AMH level was higher in CD patients (CD 3.9 ng/mL, UC 1.8 ng/mL, $p < 0.001$) while the mean age was also younger in CD patients (CD 30.8 years old, UC 37.6 years old, $p < 0.001$). Using univariate analysis, the factors influencing AMH in IBD patients were age, type of IBD, abdominal surgery, body-mass index (BMI), hemoglobin and albumin levels; BMI and type of IBD remained significant in multivariate analysis. The mean of the AMH was lower in the younger group (18–34 years old, 4.3 ng/mL) than the elder group (35–49 years old, 1.5 ng/mL) ($p < 0.001$). As AMH < 2 ng/mL indicates a low

ovarian reserve, we only analyzed the factors influencing AMH in the younger population. Using univariate analysis, the contributors for AMH level in young CD patients included perianal involvement, disease location, abdominal surgery, IL-6, hemoglobin, and albumin levels, while the contributors for AMH level in young UC patients were age, white blood cell level, and disease duration. Perianal involvement ($p = 0.001$) was the significant factor affecting AMH level in young CD patients while disease duration ($p = 0.028$) was the significant factor affecting AMH level in young UC patients by multivariate analysis. There was a trend that AMH levels were lower in patients with active IBD compared to those with inactive IBD, including the clinical, biochemical, and endoscopic aspect.

Conclusions: Age is the main predictor of AMH levels in Asian IBD patients just like the general population. IL-6 is negatively correlated with AMH levels in young CD patients. Controlling disease activity is especially important in young IBD patients in order to prevent lower AMH levels.

P.46

比較年輕早發性大腸息肉與 50 歲以上的大腸息肉患者的息肉特徵

COMPARE THE CHARACTERISTICS OF YOUNG ONSET COLONIC ADENOMA (YOA) WITH PATIENTS ELDER 50 YEARS

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Background: While overall rates of colorectal cancer (CRC) have declined in individuals above 50 years of age, the incidence of CRC in young adults (CRCYAs) are increasing from time to time. Besides, previous reports have shown thst CRCYAs had worse prognosis due to higher proportion of advanced stage tumors. Therefore, try to early detection of young onset adenoma (YOA), and removal of these precursor lesions is vital to prevent CRCYAs.

Aims: Our aim of this study is try to evaluate the special characteristics and possible risk factors of YOA.

Methods: Patients who underwent colonoscopic polypectomy from Jan. 2020 to Mar. 2020 in our hospital were recruited in this retrospective study. We compare the characteristics of neoplastic polyps in YOA group (age before 50 years, N = 52) and elder group (age > 50, N = 235).

Results: 287 patients with 490 neoplastic adenomas (83 in YOA group and 407 in elder group) were detected in this study. The average polyp number or size showed no significantly difference in two group. YOA group had similar prevalences of advance adenoma compare to elder group (18.1% vs. 15.5%, $p = 0.523$); However, the rate of adenocarcinoma was higher in elderly group (9.4% vs. 3.8%). About the distribution, YOAs are more likely at left side colon compare to elderly (66.3% vs. 45.9%, $p < 0.001$). About the morphology of neoplastic lesions, the ulcerative polyps were more common seen in elder group (4.2% vs. 2.4%, $p < 0.001$).

Conclusions: CRCs are still more common among elder individuals. However, the rate of advanced adenoma are comparable in YOA group and elder group. YOAs are more likely at left side colon. Early screening and subsequent distal endoscopic surveillance, especially distal colon, might modify risk of CRCYAs. More research is needed to understand the prevalence, risk factors of YOAs.

P.47

血漿中微量元素對於發炎性大腸疾病患者疾病活躍度的影響
IMPACT OF SERUM MICROELEMENT LEVELS ON DISEASE ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic gastrointestinal inflammation. Emerging research indicates that microelements, such as selenium and zinc, play essential roles in immune regulation and inflammatory processes.
Aims: This study aims to explore the relationship between serum microelement levels and disease activity in patients with IBD.
Methods: A total of 146 participants were enrolled in this study, including 36 healthy controls, 60 patients with CD, and 50 with UC. Blood samples were collected and analyzed for microelement levels after informed consent was obtained. Clinical and endoscopic data were also recorded. The study was conducted at Tri-Service General Hospital and approved by the Institutional Review Board (IRB), protocol number A202305042. Statistical analyses were performed using SPSS 20.0.
Results: In patients with IBD, lower serum levels of iron, zinc, and selenium were associated with increased disease activity (P = 0.020, 0.068, and 0.017, respectively), particularly in those with Crohn's disease. Conversely, higher serum copper levels were inversely correlated with disease activity in IBD patients (P = 0.001). Additionally, the serum copper/zinc and copper/selenium ratios were significantly linked to disease activity in IBD patients (P = 0.001 and 0.004, respectively), with the copper/selenium ratio showing a notable association with disease activity specifically in Crohn's disease patients (P = 0.007).
Conclusions: Altered microelement levels were observed in patients with IBD, with reduced serum selenium and zinc levels correlating with increased disease activity. Elevated copper levels were also linked to disease severity. This study also indicates that the serum copper/zinc and copper/selenium ratios are significantly associated with disease activity in patients with IBD, with a stronger association observed in patients with CD.

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胸腔膽汁積液：罕見經皮穿肝引流術併發症
BILOTHORAX: RARE COMPLICATION OF PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE (PTBD) OVER A 10-YEAR PERIOD

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Background: Bilothorax is defined as the accumulation of bile in the pleural cavity. Although bilothorax has various causes, PTBD-related bilothorax is rare, with only four cases reported between 1971 and 2023 out of 23 bilothorax cases identified using "bilious pleural effusion" as a search term (ACG Case Reports Journal, 2024; 11). A review of 115 cases using the terms "bilothorax," "cholethorax," or "thoracobilia" found PTBD-related bilothorax accounted for 23.47% (27 cases) [Pulmonary Medicine, 2024]. Despite this, PTBD-related bilothorax remains uncommon. The removal of small 7 Fr or 8.5 Fr pigtail catheters can lead to severe hemothorax due to the grapple-hook mechanism [Chest 2023 Procedures Case Report Posters 6, Emerg Med J. 2007;24]. Bilothorax can cause severe inflammation, empyema formation, and rapid clinical deterioration. Immediate evaluation and prompt treatment are warranted [Egyptian J Radiology and Nuclear Medicine 2022].
Aims: To report our PTBD-related bilothorax cases and highlight conditions under which a high index of suspicion for bilothorax should be maintained. A proposed measure for managing new-onset asymptomatic pleural effusion post-PTBD may theoretically reduce the severity of bilothorax during PTBD pig-tail catheter removal due to the grapple-hook mechanism.
Methods: From October 2014 to September 2024, data on percutaneous transhepatic cholangio-drainage (PTCD) and percutaneous transhepatic gallbladder drainage (PTGBD) performed on inpatients over a 10-year period were retrieved from the hospital database for analysis. Inclusion Criteria: Adult patients >18 years old. PTBD cases with pleural effusion. Exclusion Criteria: Pleural effusions due to heart failure, low albumin levels, organ inflammation, pneumonia, and those without pleural fluid analysis were excluded by reviewing the inpatient admission records. The diagnostic criterion for bilothorax was defined as a pleural effusion fluid-to-serum bilirubin ratio greater than 1 [Pleura. 2017;4:21–31].
Results: A total of 222 PTBD cases were identified,

including 154 male and 68 female patients, with a mean age of 62.7 years (range 26–98). Among these, 30 cases presented with pleural effusion, and bilothorax was confirmed in 2 cases after excluding 15 cases of PTBD with pleural effusion that were performed for non-biliary drainage purposes, as well as pleural effusion due to heart failure, low albumin levels, organ inflammation, pneumonia, and cases without pleural fluid analysis upon reviewing the inpatient records. The incidence of bilothorax in our series of 207 PTBD cases was 0.96%. Case 1: An 89-year-old female with a history of hypertension, hyperlipidemia, osteoporosis, and previous cholecystectomy presented with obstructive jaundice due to a common bile duct (CBD) stone. She underwent PTCD, endoscopic sphincterotomy (EST), and CBD stone extraction. Severe abdominal pain and massive right pleural effusion occurred during PTCD pig-tail catheter removal. Bilothorax was diagnosed three days later based on ultrasound, abdominal CT, and pleural fluid analysis. The effusion was exudative, with an LDH level of 2991 IU/L and a fluid-to-serum bilirubin ratio of 11.7 (>1). Management included endoscopic retrograde biliary drainage (ERBD), chest pig-tail drainage for bilothorax, and a chest tube for pig-tail catheter-related pneumothorax. Antibiotics were administered for complicated empyema. Cultures of the pleural effusion grew Candida albicans and Streptococcus agalactiae (Group B). The hospital stay was 34 days. Case 2: An 80-year-old female presented with epigastric pain, a 4-cm mass in the right upper lung, obstructive jaundice due to common bile duct stones (CBDS), common hepatic duct stones (CHDS), intrahepatic duct stones (IHDS), and bacteremia. She underwent PTCD, EST, CBDS removal, and ERBD. A new-onset asymptomatic right pleural effusion developed post-PTCD, possibly due to a sealed-off fistula tract by the PTCD catheter. Twenty days after PTCD, severe epigastric pain and massive right pleural effusion developed following PTCD pig-tail catheter removal. The pleural effusion was exudative, with an LDH level of 973 IU/L and a fluid-to-serum bilirubin ratio of 4.66 (>1). Pleural effusion cultures revealed Klebsiella aerogenes, Escherichia coli, Stenotrophomonas maltophilia, and Enterococcus faecalis. The patient underwent chest pig-tail drainage three times and received antibiotics. The hospital stay lasted 39 days. Both cases had empyema. Common findings included severe abdominal pain and massive right pleural effusion upon PTCD catheter removal.

Conclusions: PTBD related bilothorax is rare. A high index of suspicion for bilothorax should be maintained in patients presenting with severe pain and new-onset pleural effusion after the retrieval of a PTBD pigtail catheter. In cases of asymptomatic new-onset pleural effusion following PTBD observed on CXR, uncoiling the PTCD pigtail catheter with a guidewire prior to removal may theoretically reduce trauma associated with the grapple-hook mechanism.

P.49

腹腔內假性動脈瘤的介入栓塞治療：單一醫學中心的病因、臨床表現與治療結果
RADIOLOGICAL EMBOLIZATION FOR INTRA-ABDOMINAL ARTERY PSEUDOAENEURYSMS: ETIOLOGY, CLINICAL PRESENTATION, AND OUTCOMES IN A SINGLE-CENTER STUDY

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Background: Pseudoaneurysm (PSA) rupture of intra-abdominal arteries is a rare but potentially fatal cause of upper gastrointestinal hemorrhage. Due to its rarity, PSA is often overlooked or misdiagnosed until it presents as life-threatening bleeding. The Society of Vascular Surgery guidelines recommend treating all visceral artery pseudoaneurysms in adults, regardless of symptoms or size, with radiological embolization being one of the preferred treatment modalities. However, there is a paucity of research investigating the outcomes of radiological embolization for intra-abdominal artery PSA. This study aims to analyze the etiology, clinical presentation, and outcomes of radiological intervention for intra-abdominal artery PSA at Changhua Christian Hospital.

Aims: To evaluate the etiology, clinical presentation, and outcomes of radiological embolization in patients with intra-abdominal artery PSA at Changhua Christian Hospital.

Methods: This retrospective study included 10 patients who underwent radiological embolization for intra-abdominal artery PSA between May 2022 and September 2024. Data on patient demographics, etiology, clinical presentation, imaging findings, treatment modalities, and outcomes were analyzed.

Results: The study cohort included 10 patients (7 males; mean age: 62 years) with PSA. The etiology was identified in five cases, with iatrogenic causes (n = 3) and pancreatitis (n = 2) being the primary contributors. Among the iatrogenic cases, two patients had ampullary cancer and underwent Whipple surgery, while one patient with Klatskin tumor underwent endoscopic retrograde cholangiopancreatography (ERCP). All patients presented with symptoms, including bloody drainage postoperatively (n = 3), abdominal pain (n = 4), and hematemesis or melena (n = 3). Computed tomography angiography (CTA) successfully identified PSA in all cases. In two patients presenting with hematemesis, initial attempts at hemostasis using entero-gastroscopy were unsuccessful, and the PSA was incidentally detected during radiological embolization for gastrointestinal bleeding. The anatomical distribution of PSA sites included the gastroduodenal artery (GDA) (n = 5), right hepatic artery (n = 1), inferior mesenteric artery (IMA) (n = 1), and splenic artery (n = 2) in cases associated with pancreatitis. Radiological embolization was performed in all 10 patients, utilizing various techniques: stent placement (n = 2), coil embolization (n = 4), gelfoam embolization (n = 2), and a combination of coil and gelfoam embolization (n = 2). The overall technical success rate of radiological embolization was 80%. Among the two unsuccessful cases, one patient (ampullary cancer) required surgical intervention, while the other (pancreatitis) was managed with regular surveillance. No immediate complications were observed following radiological embolization.

Conclusions: Intra-abdominal artery PSA often presents with gastrointestinal bleeding or abdominal pain. Radiological embolization is a safe and effective treatment option, demonstrating a high success rate in this cohort. Further studies with larger sample sizes are warranted to validate these findings and optimize treatment strategies for PSA of intra-abdominal arteries.

P.50

經導管動脈栓塞術於消化道出血之臨床結果及成效
CLINICAL OUTCOMES AND EFFICACY OF TRANSCATHETER ARTERIAL EMBOLIZATION (TAE) IN GASTROINTESTINAL BLEEDING

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Background: Transcatheter arterial embolization (TAE) is the first-line treatment for refractory hemorrhage from the gastroduodenal region or failure of endoscopic hemostasis. It is preferred over surgery due to lower complication rates and mortality. This retrospective review included 42 patients who underwent TAE for gastrointestinal (GI) bleeding, evaluating the correlation of comorbidities. Clinical outcomes included the rebleeding rate within 30 days.

Aims: To evaluate the efficacy of TAE in managing GI bleeding and the correlation with comorbidities.

Methods: This research accessed the Radiology database at Changhua Christian Hospital (Nov. 2021 to Nov. 2024) for GI bleeding patients undergoing TAE. We retrieved 42 cases, collecting and analyzing epidemiological characteristics, medical history, clinical presentation, and rebleeding within 30 days. In the logistic regression analysis for risk factors, variables that were statistically significant ($p < 0.05$) in the univariate model were further analyzed in the multivariable model. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. All analyses were performed using IBM SPSS Statistics Version 30.

Results: This research summarizes the clinical characteristics and demographics of the 42 cases. Patient ages ranged from 24 to 92 years (mean age 67.4 ± 4.41 years). Comorbidities included diabetes mellitus (n = 19, 45%), hypertension (n = 18, 42%), ischemic heart disease (n = 6, 14%), malignancy (n = 7, 17%), cirrhosis (n = 8, 19%), and renal failure/ESRD (n = 11, 26%). Patients were classified into upper GI bleeding (UGIB) and lower GI bleeding (LGIB) groups. The most common sources of UGIB were the duodenum (n = 18) and stomach (n = 7). For LGIB, the main sources were the rectum (n = 10) and anus (n = 3), with additional cases from the transverse colon (n = 1), hepatic flexure (n = 1), cecum (n = 1), and ileum (n = 1). In total, 13 patients experienced rebleeding after TAE. Among those with TAE failure, 11 underwent repeat endoscopy and 2 required surgery; 5 achieved successful hemostasis, while 8 ultimately expired. Patients with diabetes mellitus, hypertension, and cirrhosis showed a higher risk of rebleeding at 30 days, though the differences were not statistically significant. In 13 patients of post TAE rebleeding, patients with UGIB (n = 11, 44%) had a higher risk of post-TAE rebleeding then patient with LGIB (n = 2, 11%).

Conclusions: TAE is an effective first-line treatment for GI bleeding due to refractory hemorrhage or failure of endoscopic hemostasis. The most common bleeding sources were the duodenum, stomach, and rectum. Patients with UGIB are at a higher risk of rebleeding within 30 days post-TAE.

P.51

胃腸神經內分泌瘤：一個醫學中心的臨床經驗
A CLINICAL EXPERIENCE IN ONE MEDICAL CENTER – GASTRIC NEUROENDOCRINE NEOPLASMS

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Background: Neuroendocrine neoplasms (NEN) are rare epithelial neoplasms, with neuroendocrine differentiation, which can arise from any organ. Most common site is the gastrointestinal (GI) tract, frequently in the midgut, followed by the foregut, then the hindgut. The presence of these neoplasms in extra-thoracic and extra-digestive systems are rare.
Aims: Incidental findings of grade 1 gastric NET may require close observation or endoscopy removal. However, patient presenting with symptoms such as GI tract bleeding requires emergent intervention. Understanding common symptoms arising from gastric NET, early diagnosing and provide treatment to prevent further complications.
Methods: This is a retrospective study, the data were collected from medical records, from January 2014 to May 2024. A total of 25 patients were collected initially, and 6 of them were excluded as the tumors arise from the pancreas. The remaining 19 of them arise from gastric, and were included in this study.
Results: Among all these patients, the median age of diagnosis is 56 years old. Most common site of NEN is found to be the antrum. The most ubiquitous chief complaint upon presenting is epigastric discomfort, followed by anemia or tarry stool. Over half of these patients were found to have grade 3 NEN with size ranging from 3cm or maybe up to 5cm. In the midst of these patients, 8 patients were found to have grade 3 poorly differentiated NEN metastasis at the time of diagnosis, with the most common metastasis site being the liver. Patients with metastatic disease are treated with capecitabine or platinum-based chemotherapy, followed by radical subtotal gastrectomy. Among these 19 patients, 8 of them die from multiorgan failure or severe sepsis and 4 of them loss to follow-up. One of the cases, a 78 year-old male patient, presented with GI bleeding, was diagnosed with a stage III disease. However, his family refuses to receive any medical treatment and chooses to discharge against medical advice.
Conclusions: Patients presenting with non-specific complaints, requiring intervention and further assessment, allowing us to find out the reason behind. Early diagnosing NEN often has a good survival rate with regular follow up.

P.52

使用 YOLACT 對 CT 圖像中的 L3 腹部肌肉進行自動分割與優化以用於肌少症評估
AUTOMATIC SEGMENTATION AND OPTIMIZATION OF L3 ABDOMINAL MUSCLES ON CT IMAGES FOR SARCOPENIA EVALUATION USING YOLACT

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Background: Sarcopenia is characterized by a substantial loss of muscle mass and function, and it has been acknowledged as an independent risk factor for various adverse health outcomes. Computed Tomography (CT) can provide detailed information about muscle quality and specific attenuation based on fat density. The CT images of the L3 (third lumbar vertebra) are considered the gold standard for assessing both quantitative and qualitative alterations in muscle and fat. The investigation of sarcopenia using CT necessitates the manual identification of the L3 vertebra. However, computer-aided automatic detection of the L3 vertebra can significantly enhance the efficiency and accuracy of sarcopenia diagnosis.
Aims: The objective is to develop standardized, reliable, and accurate evaluation techniques for using CT to recognize the L3 vertebra and muscle metrics, develop analysis methods, and establish diagnostic criteria for sarcopenia. Computer-aided analysis, which automates the measurement of surrounding muscle and fat, is a novel approach to achieve these goals. This study aims to use computer-aided automation to detect the muscle area.
Methods: This study used a dataset of CT image slices provided by Dalin Tzu Chi Hospital in Chiayi (IRB number: B11102012). The dataset includes a total of 84 patients, each with 4 to 6 CT images of the T12 and the L1 to L4 vertebrae, totaling 2512 CT images. The process begins with the selection of L3 images from the patient's CT scans, followed by manual or semi-automatic annotation of the skeletal muscle region by professionals to establish a reference for further processing. The annotated images are then filtered based on specific HU (Hounsfield Unit) ranges to create masks highlighting different tissue characteristics: Mask0 retains the original image without

HU filtering, Mask1 isolates tissues with HU values between 0 and 100 (focusing on fat and muscle), and Mask2 captures a broader range of muscle and fat tissues with HU values from -29 to 150. The YOLACT model is directly trained using the annotated skeletal muscle data, excluding the HU-filtered masks from the training input. These masks serve as auxiliary tools for understanding tissue characteristics but are not utilized for model training. The trained model is subsequently tested to generate automated segmentation results for further analysis.

Results: From the analysis of the images, it is evident that the detection performance for the peripheral rectus abdominis (RA) and lumbar muscle (LS) is relatively suboptimal compared to other regions. This suggests that the current model may face challenges in accurately segmenting and detecting these specific muscle groups, possibly due to their complex structures, subtle boundaries, or limited representation in the training dataset. The training results currently demonstrate a mean average precision (mAP) of 88.9 for box predictions and 75.44 for mask predictions. While these metrics indicate a high level of accuracy overall, there is still room for improvement, especially in refining the segmentation of challenging areas like the RA and LS. The collection of additional high-quality annotated data, combined with the adoption of advanced image preprocessing techniques, is anticipated to significantly enhance the model's performance. These improvements could lead to higher mAP values and more robust detection results, ensuring better segmentation accuracy across all muscle regions.

Conclusions: The ultimate goal is to develop an automated segmentation method for abdominal CT images based on deep learning algorithms. By incorporating HU value filtering techniques, the aim is to enhance the clarity and distinguishability of various regions within the images, thereby further improving segmentation accuracy and stability. This automated segmentation approach will effectively quantify and segment abdominal muscle areas, assisting doctors in making more accurate diagnoses and treatment decisions for sarcopenia patients, ultimately reducing the chances of misdiagnosis and missed diagnoses. To achieve this goal, future research will focus on further improving the accuracy and efficiency of image segmentation, particularly under the constraints of limited data.

P.53

探討功能性消化不良患者在合併腸躁症與否情況下的症狀、內臟敏感性、心理困擾及自律神經功能之差異

INVESTIGATING SYMPTOMS, VISCERAL SENSITIVITY, PSYCHOLOGICAL DISTRESS, AND AUTONOMIC FUNCTION IN FUNCTIONAL DYSPEPSIA WITH OR WITHOUT IRRITABLE BOWEL SYNDROME OVERLAP: IS THERE A DIFFERENCE?

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Background: Disorders of gut-brain interactions (DGBIs), also known as functional gastrointestinal disorders, are defined by chronic or recurrent gastrointestinal symptoms without identifiable structural or biochemical abnormalities. Among the DGBIs defined by the Rome Foundation, functional dyspepsia (FD) and irritable bowel syndrome (IBS) are the most common and widely recognized conditions. DGBIs frequently overlap, leading to increased symptom severity. FD has also been linked toreduced vagal activity compared to healthy controls.

Aims: This study aimed to investigate whether the overlap of FD and IBS negatively impacts gastrointestinal symptoms, psychological conditions, and heart rate variability (HRV) parameters.

Methods: Our study included healthy controls, patients with FD, and patients with FD and IBS overlap. Diagnoses of FD and IBS were according to Rome IV criteria. Patient-reported outcomes, such as gastrointestinal symptom intensity, visceral sensitivity, stress, sleep disturbances, depression, and anxiety, were assessed using validated questionnaires. HRV was measured during a stress autonomic nervous system (ANS) protocol, including rest (5 minutes), a pressured mental arithmetic test (3 minutes), and a recovery period (5 minutes). When comparing the three groups, continuous variables were analyzed using a one-way analysis of variance (ANOVA), and categorical variables were analyzed with the chi-square test.

Results: The study included 30 healthy controls, 39 patients with FD, and 18 patients with FD and IBS overlap (mean age: 46.2 years; 56.3% female). Patients with FD

and IBS overlap exhibited the most severe gastrointestinal symptoms and visceral sensitivity, followed by patients with FD alone, and were mildest in healthy controls ($P < 0.001$). Sleep disturbances and depression were more severe in patients with FD and IBS overlap compared to healthy controls ($P < 0.05$). During recovery, patients with FD and IBS overlap exhibited lower parasympathetic activity than healthy controls (4.15 ln ms2 vs. 4.9 ln ms2, $P = 0.041$), and other HRV metrics showed no significant differences among groups ($P > 0.05$).

Conclusions: This study highlighted that the FD and IBS overlap appears to have worse gastrointestinal symptoms, psychological distress, and autonomic dysfunction, including reduced parasympathetic activity during recovery. Further investigation is warranted to determine whether autonomic dysfunction is associated with disease severity and treatment outcome in patients with FD and IBS overlap.

P.54

轉移性小腸腫瘤的臨床病理學研究：中台灣一醫學中心之經驗
CLINICOPATHOLOGICAL STUDY OF METASTATIC SMALL BOWEL TUMOR: A SINGLE INSTITUTE EXPERIENCE IN TAIWAN

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Background: Small bowel occupies 75% of the length of the digestive tract and 90% of mucosal surface. However, the small bowel tumor remain rare and only represent around 3% of digestive cancers. In past time, because of endoscopic inaccessibility, the small intestine tumor was difficulty approach compare to stomach and colon. In addition, metastatic small bowel tumor is less than primary small bowel cancer.

Aims: The aim of the study was to investigate the epidemiological data and clinical presentation of metastatic small bowel intestine tumor was diagnosed by double balloon enteroscopy in a single institute experience in Taiwan.

Methods: From October 2009 to December 2024, we retrospectively reviewed the medical charts at China Medical University Hospital. Patients who were found metastatic small intestine via double balloon enteroscopy (DBE) were included into this study. Clinical data were obtained from the medical records and from the physicians responsible for patient care. Epidemiological data included histologic type, age, gender, symptoms, tumor location and outcomes.

Results: A total of 10 patients with metastatic small intestine were enrolled into this study. There were 5 males and 5 females. The mean age was 68.3 years (range, 52–86 years). The origin of metastatic small bowel tumor, including 2 case (2/10, 20%) from gastric adenocarcinoma, 2 case (2/10, 20%) from pancreatic adenocarcinoma, 1 case from colorectal cancer, 1 case from hepatocellular carcinoma, 1 case from methothelioma, 1 case from breast carcinoma, 1 case from urothelial cell carcinoma and 1 case undeterminated origin. In our present study, as regards clinical symptoms, 10 patients were symptomatic. In 10 symptomatic patients, they most commonly presented with ileus (4 patients, 40%). Followed by abdominal pain in three, bleeding in two, and weight loss in one patient.

Metastatic small bowel tumor involved the duodenum in 6 (60%) of 10 patient, the jejunum in 4 (40%) of 10 patients, and no ileal tumor was found in this study. The prognosis of metastatic small bowel tumor was poor, all 10 patients expired even underwent surgical intervention, chemotherapy, target therapy.

Conclusions: Review of reported related literature, the most common origin of metastatic tumor of the small bowel tumor is lung cancer, followed by breast cancer and gastric cancer. In contrast, the result of our study did not have case origin from lung cancer. The cause of difference of primary origin still need to be determined. But the similar condition, the patient suffered from metastatic small bowel tumor usually old age and poor prognosis.

P.55

隱藏式鼻胃管與傳統鼻胃管對吞嚥困難患者之臉部美觀、自尊心與臨床灌食之影響
IMPACTS OF CONCEALABLE NASOGASTRIC TUBE AND TRADITIONAL TUBE ON FACIAL AESTHETICS, SELF-ESTEEM, AND FEEDING PRACTICABILITY IN DYSPHAGIA PATIENTS

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Background: Clinically, many patients with stroke and gastrointestinal motility disorders experience swallowing difficulties and require the placement of a nasogastric tube for feeding and nutrition. However, patients often experience reduced self-esteem and willingness to interact with friends and the public due to the impact of the nasogastric tube on facial aesthetics. Our innovation team has developed a “concealable nasogastric tube” that allows users to maintain good feeding function and improve facial outlook.

Aims: To compare whether there is a difference in self-esteem and the practicality of feeding between the “concealable nasogastric tube” and the “traditional nasogastric tube.”

Methods: Adult patients with dysphagia requiring a nasogastric tube feeding due to swallowing problems were enrolled. Participants first used the “traditional nasogastric tube” for a week, and then completed a satisfaction survey regarding the aesthetics of the patient’s face and self-esteem. At the same time, caregivers who assisted with feeding completed a survey on the smoothness of the feeding tube, ease of use, and the number of times the patient removed the feeding tube within a week. Afterwards, the “traditional nasogastric tube” was removed and replaced with a “concealable nasogastric tube,” and feeding was continued for another week. The patient then completed a satisfaction survey on the use of the “concealable nasogastric tube.” The experiences with both types of tubes were then compared in terms of facial aesthetics, self-esteem, social impact, caregiver ease of use, and the rate at which patients removed their feeding tubes.

Results: Twelve patients were recruited for the study. In terms of aesthetics, the scores were higher when using the concealable nasogastric tube compared to the traditional

one (7.9 ± 0.8 vs 1.4 ± 0.6; P < 0.001). In terms of self-esteem, using the concealable tube also resulted in higher self-esteem 7.6 ± 0.5 vs 1.5 ± 0.5; P < 0.001). However, in terms of ease of use for caregivers, the concealable tube was less convenient than the traditional tube (7.3 ± 0.9 vs 9.4 ± 0.5; P < 0.001); there was no difference in the frequency of patients removing their feeding tubes between the two types.

Conclusions: The use of the "concealable nasogastric tube" offers better aesthetics and can improve patient self-esteem, making it more likely for them to engage in social interactions.

P.56

結合現代內視鏡與病理學，探討幽門螺旋桿菌的最佳切片部位

COMBINING MODERN ENDOSCOPIC AND PATHOLOGICAL INSIGHTS INTO THE HABITAT OF *H. PYLORI*: GIVING AN OLD CLASSIC A NEW TWIST

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Background: *Helicobacter pylori* (*H. pylori*) infection, as described in the Correa sequence, causes atrophic gastritis (AG), intestinal metaplasia (IM), and gastric cancer. Histopathology is essential for simultaneously evaluating premalignant lesions and detecting *H. pylori*, but detection accuracy varies by biopsy site and the extent of AG and IM. Previous studies in gastric cancer patients suggest severe AG or IM lowers detection in antral biopsies, favoring biopsies at the gastric body. However, the optimal biopsy site for detecting *H. pylori* in non-cancer patients with various degrees of AG or IM remains unclear. While the Kimura-Takemoto classification and Endoscopic Grading of Gastric Intestinal Metaplasia (EGGIM) correlate with histology, we aim to study the use of these endoscopic features to guide biopsy site selection for *H. pylori* detection.

Aims: This study aims to determine the optimal biopsy strategies for *H. pylori* detection by applying the updated Sydney gastric mapping protocol along with endoscopic assessment using the Kimura-Takemoto classification and the EGGIM scores.

Methods: This retrospective cohort included patients undergoing routine gastroscopy at National Taiwan University Cancer Center. High-resolution white-light endoscopy and narrow-band imaging were used for Kimura-Takemoto classification and EGGIM scoring, with scores of 1-4 classified as focal IM and 5-10 as extensive IM. Antral and body biopsies were obtained according to updated Sydney protocol and analyzed for histopathological severity.

Results: Among 127 patients (63% female; median age 63 years) with histologically confirmed *H. pylori* infection, detection accuracy was significantly higher with two antral biopsies compared to body biopsies (89.8% vs. 59.1%, p < 0.001) and was highest among all site combinations in antrum and body. Antral detection remained higher

in patients without AG and those with atrophic gastritis classified as C-type or O-type by Kimura-Takemoto classification. With increasing severity of IM, antral detection decreased while body detection increased, though antral detection remained higher (Focal IM: 92.7% vs. 54.5%, p < 0.001; Extensive IM: 84.4% vs. 68.8%, p = 0.302). Pathologically, the antrum consistently showed higher detection in all OLGA stages. As OLGIM stages increased, antral detection decreased and body detection increased, with similar accuracy in OLGIM stage III/IV. Antral detection was significantly lower in patients aged ≥65 compared to those <65 years (80.4% vs. 96.1%, p = 0.011), while body detection was not associated with age.

Conclusions: This study presents the most recent comprehensive analysis of *H. pylori* detection accuracy across different biopsy sites, guided by modern endoscopic evaluations using the Kimura-Takemoto classification and EGGIM scores. Biopsies from both the lesser and greater curvature of the antrum yielded the highest detection accuracy. However, in older patients or with endoscopically severe IM, regardless of Kimura-Takemoto classification of atrophy, additional biopsies from the body should be considered for optimizing *H. pylori* detection.

P.57

十天鉍劑四合一療法作為老年患者第一線幽門螺旋桿菌除菌治療之療效：台灣多中心研究報告

EFFICACY AND SAFETY OF TEN-DAY BISMUTH QUADRUPLE THERAPY FOR FIRST-LINE ANTI-*HELICOBACTER PYLORI* INFECTION IN THE ELDERLY: A MULTICENTER REALWORLD REPORT

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Background: Aging may influence the effectiveness of *Helicobacter pylori* (*H. pylori*) eradication.

Aims: The purpose of this study was to evaluate the efficacy and safety of 10-day bismuth quadruple therapy as a first-line treatment for *H. pylori* infection in elderly individuals.

Methods: We conducted a retrospective analysis of prospectively collected data from September 2018 to December 2021 at multiple hospitals in southern Taiwan. The study included 231 treatment-naive patients aged 20 years or older who received 10-day bismuth quadruple therapy as a first-line regimen for *H. pylori* eradication. Patients were categorized into two groups: an elderly group (aged ≥ 65) and a control group (aged < 65).

Results: The eradication rates in the elderly and control groups were 80.3% (95% confidence interval [CI]: 68.1% to 89.4%) and 85.3% (95% CI: 79.1% to 90.3%) (P = 0.364), respectively, in the intention-to-treat analysis. In the per-protocol analysis, eradication rates were 89.1% (95% CI: 77.8% to 95.9%) for the elderly group and 94.8% (95% CI: 90.0% to 97.7%) for the control group (P = 0.149). Adverse event rates were 34.5% in the elderly group and 27.5% in the control group (P = 0.322). Compliance was slightly lower in the elderly group compared to the control group (89.1% vs. 95.4%, P = 0.096). There were no significant differences in antibiotic resistance between the two groups.

Conclusions: The efficacy of 10-day bismuth quadruple therapy as a first-line treatment for *H. pylori* was comparable between elderly and non-elderly cohorts, with similar levels of adverse effects.

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單一抗生素療法在幽門螺旋桿菌第一線除菌治療之療效
THE EFFICACY OF MONO-ANTIBIOTIC THERAPIES IN THE FIRST-LINE TREATMENT OF *H. PYLORI* INFECTION

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Background: Due to the increasing prevalence of antimicrobial resistance, the efficacy of standard triple therapy for *Helicobacter pylori* (*H. pylori*) infection has declined, with eradication rates now falling below 80% in most countries. Although bismuth quadruple therapy and concomitant therapy are advised in regions with high clarithromycin resistance, these treatments commonly cause frequent adverse events and require the use of two or three antibiotics.

Aims: To evaluates the effectiveness of 14-day mono-antibiotic therapies for the first-line treatment of *H. pylori* infection.

Methods: Randomized controlled trials published in English that reported the efficacy of 14-day high-dose amoxicillin/proton pump inhibitor dual, 14-day high-dose amoxicillin/vonoprazan dual, 14-day amoxicillin/vonoprazan/bismuth triple, and 14-day tetracycline/vonoprazan dual therapies for the first-line treatment of *H. pylori* infection in adults were included in our literature search. Medical literature searches were conducted using PubMed from October 1, 2014, to October 1, 2024.

Results: The pooled eradication rates for 14-day high-dose amoxicillin/proton-pump inhibitor dual therapies were 86.1% (3335/3875) by intention-to-treat (ITT) analysis and 87.3% (3232/3702) by per-protocol (PP) analysis. For 14-day high-dose amoxicillin/vonoprazan dual therapies, the rates were 87.4% (1085/1241) by ITT and 93.0% (1044/1124) by PP. Fourteen-day amoxicillin/vonoprazan/bismuth triple therapy achieved eradication rates of 83.7% (251/300) by ITT and 90.9% (251/276) by PP. In the penicillin-allergic population, 14-day tetracycline/vonoprazan dual therapy showed eradication rates of 92.0% (138/150) by ITT and 95.1% (135/142) by PP.

Conclusions: 14-day tetracycline/vonoprazan dual therapy presents an effective option for eradicating *H. pylori* in patients allergic to penicillin. For those without a penicillin allergy, first-line treatments can include 14-day mono-antibiotic regimens such as high-dose amoxicillin/proton pump inhibitor dual, high-dose amoxicillin/vonoprazan dual, amoxicillin/vonoprazan/bismuth triple, and tetracycline/vonoprazan dual therapies.

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ERCP 中導線斷裂之處置與預後：單中心經驗及文獻回顧分析
MANAGEMENT AND OUTCOMES OF GUIDEWIRE FRACTURE DURING ENDOSCOPIC RETROGRADE CHOLANGIO PANCREATOGRAPHY (ERCP): A SINGLE-CENTER EXPERIENCE AND LITERATURE REVIEW

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Background: Guidewire fracture is a rare but potentially serious complication during ERCP procedures. Understanding its characteristics, management strategies, and prevention methods is crucial for optimal patient care.
Aims: To analyze the incidence, risk factors, management approaches, and outcomes of guidewire fracture during ERCP procedures at our institution and compare these with published literature.
Methods: A retrospective analysis was conducted using our prospectively maintained ERCP database from July 2020 to July 2024. Additionally, we performed a comprehensive literature review to identify published cases of guidewire fracture during ERCP from 1992 to July 2024. Patient demographics, procedural details, fracture characteristics, management strategies, and outcomes were analyzed.
Results: Three cases of guidewire fracture were identified at our institution (2 females, 1 male; age range 49–66 years). The fractures occurred during stone removal by basket, endoscopic sphincterotomy, and removal of previous main pancreatic duct (MPD) stents. Fracture locations included right intrahepatic duct, common bile duct, and main pancreatic duct. Literature review identified 17 published cases. The pancreatic duct was the most frequent location for guidewire fracture, followed by intrahepatic bile duct and common bile duct. Management strategies included retrieval using rat tooth forceps, balloon extraction, basket retrieval, biliary stent delivery systems, PTBD, and ESWL. The technical success rate for guidewire retrieval was 82.4% (14/17 cases), with fractured guidewires left in place in 3 cases. Complications were reported in 23.5% (4/17) of cases, including pain, edema and inflammation, hemorrhage, and intravascular wire migration. In our institutional cases, successful endoscopic retrieval was achieved using forceps (n = 2) or retrieval balloon (n = 1), with no immediate post-procedure complications. The technical success rate for fragment retrieval was 100%.
Conclusions: Guidewire fracture during ERCP, while rare, requires careful attention to both prevention and management. Key risk factors include mechanical stress, thermal damage, anatomical challenges, and compromised wire integrity. Prevention focuses on proper wire selection, gentle manipulation techniques, and thorough equipment inspection. When fracture occurs, endoscopic retrieval remains the first-line treatment with high success rates.

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