(13)

肥胖、代謝性脂肪肝與腸道微菌叢

Obesity, MASLD, and the Microbiota

時　　間：115 年 6 月 27 日(星期六) 13:30~17:30
地　　點：臺北榮民總醫院 致德樓第三會議室

13:30-13:35	***Opening Remarks***	侯明志副院長 Ming-Chih Hou
	座長：李癸泗 教授 (Kuei-Chuan Lee)	
13:35-13:55	肥胖的機制性解析：代謝失調與腸道微生物交互作用 Mechanistic Insights Into Obesity: Metabolic Dysregulation and Microbiota Interactions	張天恩醫師 Tien-En Chang
	座長：陳志彥 教授 (Chih-Yen Chen)	
13:55-14:15	使用降血糖/減重藥物來控制體重：內分泌科醫師的觀點 Use of Glucose-Lowering or Weight-Loss Medications to Control Weight: Endocrinologist's Perspective	胡啟民教授 Chii-Min Hwu
	座長：蘇銘堯 副院長 (Ming-Yao Su)	
14:15-14:35	肥胖的內視鏡治療：當前技術、療效與未來發展方向 Endoscopic Management of Obesity: Current Techniques, Outcomes, and Future Directions	鍾承軒醫師 Chen-Shuan Chung
	座長：羅景全 教授 (Jiing-Chyuan Luo)	
14:35-14:55	減重手術中的代謝-腸道菌交互作用：從機轉到臨床影響 Metabolic-Microbial Interactions in Bariatric Surgery: From Mechanisms to Clinical Impact	方文良教授 Wen-Liang Fang
14:55-15:20	***Coffee Break***	
	座長：蘇建維 教授 (Chien-Wei Su)	
15:20-15:50	新時代背景下的 MASLD：演進中的風險評估與管理策略 MASLD in the New Era: Evolving Risk Assessment and Management Strategies	Daniel Huang 黃庆耀教授 (新加坡)
	座長：陳慧玲 教授 (Huey-Ling Chen)	
15:50-16:10	早期生命期腸道微生物群對肥胖與肝臟脂肪堆積的決定性作用：機制與臨床意涵 Early-Life Gut Microbiota as a Determinant of Obesity and Hepatic Steatosis: Mechanisms and Clinical Implications	林裕誠教授 Yu-Cheng Lin

座長：高嘉宏 副院長 (Jia-Horng Kao)

16:10-16:30	Met-HBV：代謝異常脂肪性肝病對慢性 B 型肝炎自然史及臨床管理的影響 Met-HBV: Impact of MASLD on the Natural History and Management of Chronic Hepatitis B	蘇東弘教授 Tung-Hung Su

座長：黃惠君 教授 (Hui-Chun Huang)

16:30-16:50	C 型肝炎病毒慢性感染至病毒清除後對代謝及腸道微生物群的影響 HCV-Driven Metabolic Reprogramming and Gut Microbiome Remodeling: From Chronic Infection to Post-SVR Outcomes	李騰裕醫師 Teng-Yu Lee

座長：李懿宬 教授 (I-Cheng Lee)

16:50-17:20	代謝功能障礙對肝細胞癌預後的影響 Impact of Metabolic Dysfunction on Prognosis in Hepatocellular Carcinoma	Su Jong Yu (韓國)
17:20-17:30	***Closing Remarks***	羅景全教授 Jiing-Chyuan Luo

Mechanistic insights into obesity: Metabolic dysregulation and microbiota interactions

肥胖的機制性解析：代謝失調與腸道微生物交互作用

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Obesity is a complex metabolic disorder and a major global health challenge associated with an increased risk of type 2 diabetes, cardiovascular disease, fatty liver disease, and certain cancers. This speech will focus on the mechanistic basis of obesity, with particular emphasis on metabolic dysregulation and the interactions between host physiology and the gut microbiota. Beyond excessive calorie intake and physical inactivity, alterations in gut microbial composition and diversity have emerged as important contributors to obesity-related metabolic disturbances. Gut microbiota can influence energy harvest, fat storage, systemic inflammation, and insulin resistance, thereby playing a critical role in the development and progression of obesity. The session will also discuss how lifestyle factors, including diet, physical activity, sleep, and stress, affect both metabolic homeostasis and microbial balance. In particular, dietary strategies such as increasing fiber intake and incorporating fermented foods may beneficially modulate the gut microbiota and improve metabolic health. By integrating current understanding of host–microbiota interactions, this lecture aims to provide a mechanistic framework for obesity management and to highlight practical approaches that support long-term metabolic well-being.

Use of glucose-lowering or weight-loss medications to control weight: Endocrinologist's perspective

使用降血糖 / 減重藥物來控制體重：內分泌科醫師的觀點

Chii-Min Hwu

胡啟民

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Endocrinologists emphasize that the use of antidiabetic or weight-loss medications for weight management should be approached comprehensively, rather than relying on pharmacotherapy alone. While these medications can help regulate blood glucose levels and reduce appetite, optimal and sustainable weight control is best achieved by integrating pharmacological treatment with lifestyle modifications, including dietary changes and regular physical activity.

This discussion highlights key perspectives from endocrinology experts: medications should be considered adjunctive tools rather than stand-alone solutions. Healthy dietary practices are fundamental, including caloric control, limiting high-fat and high-sugar foods, and increasing the intake of vegetables and lean proteins. Regular physical activity further enhances energy expenditure and improves insulin sensitivity, contributing to better glycemic control and weight management. In addition, weight reduction is associated with a lower risk of cardiovascular disease, hypertension, and other chronic conditions.

Professional guidance from endocrinologists is essential for individualized assessment and tailored treatment strategies. Long-term success depends on sustained behavioral changes to prevent weight regain. Certain agents, such as GLP-1 receptor agonists, have demonstrated significant efficacy in appetite suppression and glucose regulation, thereby supporting weight loss.

In conclusion, effective and sustainable weight management requires a multidisciplinary approach that combines pharmacological therapy, lifestyle intervention, and expert medical supervision.

Endoscopic management of obesity: Current techniques, outcomes, and future directions

肥胖的內視鏡治療：當前技術、療效與未來發展方向

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Obesity has emerged as a global health crisis, contributing significantly to the burden of metabolic disorders, cardiovascular diseases, and reduced quality of life. While lifestyle modification and pharmacotherapy remain first-line treatments, their long-term efficacy is often limited. Bariatric surgery, although effective, is invasive and not suitable or acceptable for all patients. In this context, endoscopic management of obesity has gained increasing attention as a minimally invasive, safe, and effective alternative.

This presentation reviews the current techniques in endoscopic bariatric and metabolic therapies (EBMTs), including gastric and intestinal approaches, such as intragastric balloons, endoscopic sleeve gastroplasty (ESG), aspiration therapy and duodenal mucosal resurfacing (EMR). These modalities aim to induce weight loss through gastric volume reduction, delayed gastric emptying, metabolic control and behavioral modification. Clinical evidence has demonstrated that EBMTs can achieve significant total body weight loss, with favorable safety profiles compared to surgical approaches.

Outcomes from recent studies suggest that EBMTs are preferred than lifestyle modification alone. Additionally, combination therapy with obesity management medications are also promising. Despite these advances, challenges remain, including variability in patient response, durability of outcomes, and the need for standardized protocols.

Looking forward, future directions in endoscopic obesity management include the development of novel devices, combination therapies integrating pharmacological agents such as GLP-1 receptor agonists, and personalized treatment strategies based on patient characteristics. Advances in endoscopic techniques and improved understanding of metabolic mechanisms are expected to further enhance efficacy and expand indications.

In conclusion, endoscopic management represents a rapidly evolving field that bridges the gap between medical and surgical therapies for obesity. With ongoing innovation and growing clinical evidence, EBTs are poised to play an increasingly important role in the multidisciplinary management of obesity.

Metabolic-microbial interactions in bariatric surgery: From mechanisms to clinical impact

減重手術中的代謝 - 腸道菌交互作用：從機轉到臨床影響

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Bariatric and metabolic surgery is currently the most effective treatment for severe obesity and obesity-related metabolic diseases, producing substantial and durable weight loss as well as high remission rates of type 2 diabetes. While anatomical restriction and nutrient malabsorption were historically considered the primary mechanisms, accumulating evidence suggests that metabolic improvements following bariatric surgery are strongly influenced by complex interactions between the gut microbiota and host metabolic pathways.

Recent studies have demonstrated profound and rapid alterations in gut microbial composition following procedures such as sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB). These changes are accompanied by functional shifts in microbial metabolism, including altered bile acid transformation, short-chain fatty acid production, and microbial signaling pathways that interact with host metabolic regulators. Experimental studies using germ-free animal models have further shown that transplantation of post-bariatric surgery microbiota can partially reproduce weight reduction and metabolic improvements, supporting a causal role for the gut microbiome in mediating surgical outcomes.

Mechanistically, several key pathways have been proposed to explain these metabolic-microbial interactions. These include enhanced bile acid signaling through FXR and TGR5 receptors, increased secretion of incretin hormones such as GLP-1 and PYY, modulation of intestinal nutrient sensing, and reduced systemic inflammation. Together, these pathways contribute to improved insulin sensitivity, energy expenditure, and glucose homeostasis following metabolic surgery.

Clinically, the recognition of microbiome-mediated mechanisms has important implications. Microbial signatures may serve as predictive biomarkers for surgical outcomes, while microbiome-targeted interventions—including probiotics, prebiotics, dietary modulation, or fecal microbiota transplantation—are being explored as adjunctive strategies to enhance metabolic benefits. Moreover, understanding these interactions may help explain heterogeneity in weight loss response and diabetes remission after bariatric procedures.

In conclusion, metabolic surgery represents a unique human model to study host–microbiome interactions in metabolic regulation. Integrating microbiome research with surgical and metabolic medicine may not only improve patient selection and postoperative management but also provide insights for the development of novel microbiome-based therapies for obesity and metabolic disease.

MASLD in the new era: Evolving risk assessment and management strategies

新時代背景下的 MASLD：演進中的風險評估與管理策略

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Metabolic Associated Steatotic Liver Disease (MASLD) has become the dominant driver of chronic liver disease worldwide, with a growing proportion of patients presenting with advanced fibrosis and hepatocellular carcinoma. The clinical challenge is no longer simply identifying steatosis but determining who will progress and who requires intervention.

Risk stratification in MASLD is now anchored on scalable, non-invasive pathways. Simple tools such as FIB-4 remain useful at the front line, but their value lies in integration with second-line tests including elastography and imaging-based assessment. Increasingly, risk is understood as multidimensional—fibrosis stage, metabolic burden, and genetic susceptibility all contribute. In particular, the interaction between type 2 diabetes and genetic variants such as *PNPLA3* appears to identify a subgroup at disproportionate risk of hepatocellular carcinoma, even outside traditional cirrhosis-based frameworks.

Assessment of treatment response is also moving away from biopsy toward quantitative, repeatable measures. Imaging-based techniques such as proton density fat fraction provide sensitive readouts of hepatic fat, and when interpreted alongside biochemical and clinical changes, allow a more nuanced assessment of disease trajectory. Composite endpoints, including those capturing meaningful metabolic and hepatic improvement, are beginning to emerge as practical alternatives in both trials and early clinical adoption.

Therapeutically, lifestyle modification remains central but is often insufficient in higher-risk disease. Pharmacologic options are expanding, with agents targeting weight, insulin resistance, and inflammatory pathways showing consistent benefit. GLP-1 receptor agonists in particular have demonstrated clinically meaningful reductions in steatosis and weight, while antifibrotic strategies are advancing in parallel.

Taken together, MASLD management is evolving toward an integrated model: risk stratified, biomarker-driven, and increasingly personalized, where the goal is not simply disease detection, but altering its natural history.

Early-life gut microbiota as a determinant of obesity and hepatic steatosis: Mechanisms and clinical implications

早期生命期腸道微生物群對肥胖與肝臟脂肪堆積的決定性作用：機制與臨床意涵

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The first 1,000 days of life represent a critical developmental window during which the gut microbiota, host metabolism, and nutritional exposures co-evolve to shape long-term metabolic health. Increasing evidence indicates that early-life microbial colonization patterns may influence susceptibility to childhood obesity and metabolic dysfunction-associated steatotic liver disease (MASLD). Perturbations in early microbial development—driven by factors such as delivery mode, feeding practices, antibiotic exposure, and diet—can alter microbial diversity and metabolic signaling pathways.

In this presentation, I will review emerging mechanistic insights linking early-life microbiota to metabolic regulation, including microbial modulation of energy harvest, bile acid metabolism, intestinal barrier function, and hepatic lipid metabolism. Longitudinal studies further suggest that altered microbial trajectories during infancy may predispose individuals to excessive weight gain and hepatic steatosis later in childhood.

I will also present findings from our pediatric cohort demonstrating that children with obesity and MASLD exhibit a reduced abundance of Bacteroides ovatus, which is associated with increased liver steatosis and elevated alanine aminotransferase levels. In high-fat diet mouse models, oral supplementation with B. ovatus attenuated hepatic lipid accumulation and improved metabolic parameters, supporting a microbiota-mediated protective effect against hepatic steatosis.

Together, these findings support the concept that pediatric metabolic health represents an ecological phenotype shaped by early-life gut microbial development. Recognizing the gut microbiome as a modifiable organ highlights opportunities for early-life preventive strategies—including breastfeeding promotion, appropriate complementary feeding, prudent antibiotic use, and targeted microbiome-based interventions—to reduce the risk of obesity and MASLD.

Met-HBV: Impact of MASLD on the natural history and management of chronic hepatitis B

Met-HBV：代謝異常脂肪性肝病對慢性 B 型肝炎自然史及臨床管理的影響

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Steatotic liver disease is an emerging problem, and it usually coexists with metabolic dysfunction. These factors may lead to adverse liver and cardiometabolic outcomes. After the introduction of metabolic dysfunction-associated steatotic liver disease (MASLD), HBV infection does not need to be excluded from the entity of MASLD. As HBV carriers age, they develop more comorbidities. HBV patients with concurrent MASLD, or Met-HBV, are becoming a new issue, which is around 30% of HBV carriers.

Having two diseases, “MASLD” and “HBV”, together is expected to have a synergistic worse outcome. However, after dissecting its components, “metabolic dysfunction” and “steatotic liver disease” have different impacts on the HBV activity. While metabolic dysfunction increases the risk of cirrhosis, HCC, and all-cause mortality in HBV patients, steatosis seems to be protective, reducing these risks and associated with a higher chance of HBsAg seroclearance. Among these metabolic dysfunctions, type 2 diabetes has a major impact on the natural course of chronic hepatitis B.

For the management of Met-HBV, we need to manage metabolic dysfunction and HBV concurrently. Lifestyle modification, exercise, and weight reduction remain the cornerstone of management, helping to control both conditions. The severity of liver fibrosis and steatosis should be assessed before initiating medical management. Specific medication for metabolic dysfunction should be utilized with caution in patients with cirrhosis or decompensation. GLP-1 agonist-based therapy is emerging, and its impact on HBV patients should be monitored.

On the other hand, different antiviral therapies in Met-HBV seem to achieve similar viral suppression. The underlying metabolic inflammation often persists, potentially masking residual risk for disease progression. We should be aware of the lipid profiles and renal dysfunction during antiviral therapy.

HCV-Driven metabolic reprogramming and gut microbiome remodeling: From chronic infection to post-SVR outcomes

C 型肝炎病毒慢性感染至病毒清除後對代謝及腸道微生物群的影響

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Chronic hepatitis C virus (HCV) infection induces profound alterations in host metabolism and the gut-liver axis, contributing to liver disease progression and systemic complications. This speech will highlight how HCV reshapes host metabolic pathways and gut microbial composition during chronic infection and after viral eradication through sustained virologic response (SVR). Viral replication and host-virus interactions drive metabolic reprogramming in hepatocytes, affecting lipid metabolism, glucose regulation, and mitochondrial function. These changes promote steatosis, insulin resistance, and persistent inflammatory signaling, thereby facilitating fibrosis progression and increasing the risk of hepatocellular carcinoma (HCC).

A key component of this pathophysiology involves the gut-liver axis, where HCV-associated liver injury alters intestinal permeability and disrupts the gut microbial ecosystem. Chronic infection is commonly associated with gut dysbiosis, characterized by reduced microbial diversity, depletion of beneficial short-chain fatty acid-producing bacteria, and expansion of potentially pathogenic taxa. These microbial shifts can enhance microbial translocation and endotoxin exposure through the portal circulation, amplifying hepatic inflammation and metabolic disturbances.

The advent of direct-acting antivirals (DAAs) has dramatically improved treatment outcomes, enabling most patients to achieve SVR. Viral clearance partially restores metabolic homeostasis and can improve the gut microbial profile; however, emerging evidence suggests that some metabolic abnormalities and microbiome alterations may persist even after successful therapy. Consequently, patients who achieve SVR may still exhibit residual risks for metabolic dysfunction, fibrosis progression, or HCC.

Overall, HCV infection should be viewed as a systemic metabolic disease involving complex interactions among viral factors, host metabolism, and the gut microbiome. Understanding these interconnected mechanisms may help identify biomarkers for disease progression and guide new therapeutic strategies targeting metabolic pathways and microbiome modulation to improve long-term outcomes after SVR.

Impact of metabolic dysfunction on prognosis in hepatocellular carcinoma

代謝功能障礙對肝細胞癌預後的影響

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Metabolic dysfunction is a major determinant of outcome in hepatocellular carcinoma (HCC). In the era of metabolic dysfunction-associated steatotic liver disease (MASLD), prognosis depends not only on tumor burden and liver reserve but also on obesity, diabetes, sarcopenia, cardiovascular disease, and chronic inflammation. MASLD-related HCC can arise outside the classic cirrhosis-dominant pathway, yet surveillance remains centered largely on cirrhosis. As a result, some at-risk patients may fall outside routine surveillance and present with more advanced tumours rather than early-stage disease, potentially worsening prognosis from the outset.

Recent evidence suggests that metabolic dysfunction influences prognosis at several levels. Patients with obesity, diabetes, or steatohepatitis may enter treatment with a remnant liver already primed for further carcinogenesis. After curative-intent resection, obesity and diabetes have been linked to increased late recurrence, consistent with persistent lipotoxicity, insulin resistance, and fibrogenic signalling. MASLD has also been associated with shorter overall survival after resection even when time to recurrence is similar, suggesting that frailty, competing cardiometabolic mortality, and reduced treatment tolerance contribute to outcome. Obesity may further reduce the performance of ultrasound-based surveillance and make percutaneous ablation technically more difficult in selected patients.

The systemic therapy setting remains more complex. Experimental studies indicate that steatohepatitis can impair antitumour immune surveillance and may alter responsiveness to immune checkpoint blockade. However, contemporary clinical data have not shown a uniformly inferior outcome for broadly defined non-viral HCC, implying that this category is too heterogeneous and may conceal biologically distinct subgroups within metabolically driven disease.

Taken together, metabolic dysfunction should be regarded as a prognostic axis rather than a background comorbidity in HCC. Future management will require better identification of at-risk non-cirrhotic MASLD populations, longer postoperative surveillance, more precise etiologic stratification, and integrated assessment of tumor factors, liver reserve, body composition, and cardiometabolic risk.