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右心室心肌縱向形變在心室性功能性二尖瓣逆流中的預後價值:多中心研究

Incremental Prognostic Value of Right Ventricular Free Wall Longitudinal Strain in Ventricular Functional Mitral Regurgitation: A multicenter study

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Background

The prognostic significance of right ventricular free wall longitudinal strain(RVfwLS) remains unclear in patients with severe ventricular functional mitral regurgitation(VFMR).

Methods

This retrospective multicenter study included consecutive patients diagnosed with ≧ moderately-severe VFMR by transthoracic echocardiography(TTE) from 3 medical centers. All TTEs were de novo reviewed to assess MR severity, left ventricular(LV) and left atrial(LA) volumes, LV dimensions, mitral inflow, and tissue Doppler velocities. Apical four-chamber longitudinal strain(A4C-LS) and RVfwLS were measured using vendor-independent automated software(TomTec AutoStrain). Baseline characteristics were collected within 30 days of the index TTE, including New York Heart Association functional class, medication use, and Charlson Comorbidity Index. Coronary artery bypass grafting, extracorporeal membrane oxygenation implantation, and mitral valve surgery during the follow-up period were documented and incorporated as time-dependent covariates in the analysis. The primary endpoint was a composite of cardiovascular death, left ventricular assist device implantation, or heart transplantation.

Results

The final cohort comprised 608 patients with \geq moderately-severe VFMR, with a mean age of 67 \pm 14 years. After a median follow-up of 2.2 years, 201 patients(33%) experienced the primary endpoint. The patients who experienced the endpoint were more likely to be male and had a greater burden of coronary artery disease, prior myocardial infarction, and heart failure. In terms of cardiac structure and function, these patients exhibited more advanced remodeling, including larger LV dimensions, mitral annular diameter, and LA volume; lower left ventricular ejection fraction(LVEF), and worse A4C-LS and RVfwLS(all P \leq 0.031). A classification and regression tree model identified A4C-LS \leq 8.7% as the most informative prognostic marker, with RVfwLS \leq 14.1% providing further risk stratification among patients with impaired LV strain. The optimal cutoff value for RVfwLS was determined using maximally selected rank statistics, with 13.8% identified as the threshold yielding the greatest separation in survival curves. Based on these results, a cutoff of 14% was used for subsequent analyses.

In multivariable Cox models adjusted for time-dependent covariates, baseline characteristics, one



of three traditional LV parameters (LVEF, LV end-systolic volume index, or LV end-systolic diameter index), and A4C-LS. RVfwLS—when analyzed as a continuous variable—remained independently associated with the primary endpoint, except in the model adjusting for LVEF(P = 0.055). When dichotomized using established thresholds (A4C-LS < 8.7% and RVfwLS < 14%), RVfwLS < 14% remained significantly associated with the primary endpoint across three models (all P \leq 0.002). Among patients with A4C-LS < 8.7%, Kaplan–Meier analysis showed significantly reduced event-free survival for those with RVfwLS < 14% (P=0.005). Likelihood ratio tests between nested Cox models confirmed that RVfwLS < 14% added significant prognostic information beyond baseline characteristics, conventional LV parameters and A4C-LS in all models (all P \leq 0.002).

Conclusion

In≧moderately-severe VFMR, impaired RVfwLS(<14%) identifies a high-risk subgroup for adverse cardiovascular events, independent of conventional LV parameters and LV strain. RVfwLS enhances risk stratification, and incorporating it into routine assessment may facilitate earlier identification of vulnerable patients, inform clinical decision-making, and prompt timely intervention or closer follow-up.

台灣肺部組織胞漿菌病 27 年興起歷程與流行疆界再定義

A 27-Year Chronicle of Pulmonary Histoplasmosis in Taiwan: Redefining Endemic Boundaries

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Background

Histoplasmosis, caused by *Histoplasma capsulatum*, has traditionally been geographically restricted to endemic regions including the Ohio, Mississippi River valleys and Latin America. Taiwan has historically been classified as non-endemic based on limited documentation. However, sporadic cases over recent decades suggested an evolving epidemiological landscape that challenges conventional geographic boundaries, necessitating comprehensive investigation of histoplasmosis emergence in Taiwan.

Methods

We conducted a retrospective observational study at National Taiwan University Hospital from June 1997 to December 2024. Adult patients (\geq 20 years) with pathologically confirmed histoplasmosis were systematically identified through electronic medical record searches. Diagnosis was confirmed by experienced pathologists based on characteristic intracellular yeast forms of *H. capsulatum* in tissue specimens. Demographics, clinical characteristics, travel history, host immunity, radiological findings, and therapeutic outcomes were systematically analyzed.

Results

Fourteen individuals with pulmonary histoplasmosis were identified over the 27-year period, with mean age 56.6 years and male predominance (57.1%). Remarkably, only three patients (21.4%) had travel history to endemic areas within six months preceding diagnosis, and most were immunocompetent (71.4%). Clinical presentation was heterogeneous, with 64.3% manifesting cardinal symptoms including fever, dyspnea, cough, and weight loss. Nodular lesions predominated (85.7%) as the major radiographic finding. Microbiological confirmation through fungal culture was achieved in only two subjects (14.3%). Most patients (78.6%) received antifungal treatment, with voriconazole being most commonly administrated. Overall prognosis was favorable with only one patient sustained in-hospital mortality due to respiratory failure. Two additional patients with disseminated histoplasmosis without pulmonary involvement were identified.

Conclusion

The 27-year case series provided evidence for the emergence of histoplasmosis in Taiwan, challenging the conventional geographic boundaries of traditional recognized endemic regions. The high proportion of patients without a travel history strongly suggested local acquisition and possible local reservoirs of *H. capsulatum*. The predominance of immunocompetent hosts indicated evolving epidemiological patterns mandating updated clinical recognition strategies. Our study underscored the need for heightened clinical suspicion and advocated adaptive



surveillance strategies of pulmonary histoplasmosis even in previously non-endemic settings and among immunocompetent hosts.

以多腔室應變分析評估系統性紅斑性狼瘡的預後及早期心臟功能不良:前瞻性世代研究

Multichamber Strain Analysis for Early Cardiac Dysfunction and Prognosis in Systemic Lupus Erythematosus: A Prospective Cohort Study

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Background

Systemic lupus erythematosus (SLE) frequently involves the cardiovascular system, yet early cardiac dysfunction often remains subclinical and undetected by conventional echocardiography. Speckle-tracking echocardiography enables sensitive assessment of myocardial deformation across chambers. While prior studies have mainly focused on isolated left ventricular (LV) strain, the prognostic implications of multi-chamber strain dysfunction in SLE remain unclear.

Methods

In this prospective study, 264 consecutive patients with SLE (mean age 45.1±10.7 years, 93.9% female) underwent standardized transthoracic echocardiography with multi-chamber strain analysis at National Taiwan University Hospital between April 2022 and July 2024. LV global longitudinal strain (LVGLS), left atrial strain (LASr), and right ventricular free-wall strain (RVfwLS) were quantified using automated speckle-tracking. Cutoffs of 18% (LVGLS), 39% (LASr), and 24% (RVfwLS) defined abnormal function. The primary composite endpoint included all-cause death, cardiac hospitalization, SLE flare-related hospitalization, flare of lupus nephritis, initiation of new disease-modifying antirheumatic drugs (DMARDs), or new moderate pericardial effusion. Cox regression models, Kaplan–Meier survival analyses, and sensitivity analyses were performed.

Results

At baseline, LV ejection fraction and chamber dimensions were largely normal, yet RVfwLS was lower than expected for age. Patients with impaired LVGLS (<18%) were older, more often male, with longer disease duration, higher blood pressure, and more frequent renal involvement. They also exhibited elevated CRP, reduced complement C3, impaired renal function, and required more DMARDs. Reduced LASr (<39%) was associated with lower eGFR and diastolic dysfunction (higher E/e'), while impaired RVfwLS (<24%) correlated with prior SLE flares, elevated CRP, and concomitant rheumatoid arthritis.

During Median follow-up of 2.1 (IQR, 1.7–2.6) years, 50 patients (19%) experienced a composite event: new DMARD initiation (n=21), SLE flare hospitalization (n=13), lupus nephritis flare (n=10), and less frequent cardiovascular outcomes (n=6). In univariable analysis, higher Charlson Comorbidity Index, greater number of DMARDs, RASi/ARNi use, abnormal LVGLS, and reduced RVfwLS predicted adverse outcomes. LASr was not prognostic.

In multivariable models adjusting for CCI, lupus nephritis, and DMARD burden, RVfwLS emerged as the strongest independent predictor of adverse outcomes (HR per % decrease 0.94, 95% CI 0.90–1.00, p=0.031). This prognostic significance persisted after adjustment for LVGLS. Patients with RVfwLS <24% had significantly worse event-free survival, regardless of LVGLS status. Sensitivity



analyses redefining DMARD exposure to exclude weaker agents showed consistent results, with RVfwLS remaining independently associated with outcomes.

Biventricular strain stratification further revealed stepwise worsening outcomes: patients with combined LVGLS <18% and RVfwLS <24% had the poorest prognosis, with higher CRP, WBC, C3 levels, and echocardiographic evidence of biventricular and atrial dysfunction. Kaplan–Meier curves demonstrated significantly lower survival in patients with dual strain impairment (log-rank p=0.009).

Conclusion

In SLE patients with preserved LVEF, multi-chamber strain abnormalities, particularly RVfwLS impairment, identify subclinical myocardial dysfunction and independently predict adverse outcomes beyond traditional risk factors. RVfwLS provides incremental prognostic value over LVGLS, underscoring its importance in routine echocardiographic evaluation of SLE. Comprehensive strain assessment may facilitate earlier detection of cardiac involvement, guide therapeutic intensity, and improve risk stratification in this high-risk population.

臨床顯著門脈高壓和肝纖維化對膽管癌患者存活之綜合影響:台灣的一項隊列研究

Combined Impact of Clinically Significant Portal Hypertension and Liver Fibrosis on Survival in Patients with Cholangiocarcinoma: A Cohort Study from Taiwan

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Background

Cholangiocarcinoma (CCA) is an aggressive malignancy with persistently poor survival, largely due to late presentation, limited opportunity for curative resection, and modest responsiveness to systemic therapies. The prognostic impact of clinically significant portal hypertension (CSPH) in CCA has not been clearly defined. In parallel, liver fibrosis—assessed by the FIB-4 index—provides additional information on hepatic reserve. This study aimed to evaluate whether CSPH and liver fibrosis are independent prognostic factors in patients with CCA.

Methods

We performed a retrospective cohort study including 841 patients with histologically confirmed CCA diagnosed at Taipei Veterans General Hospital between January 2013 and December 2023. Data were de-identified prior to analysis, and no exclusion criteria were applied. CSPH was defined as the presence of ascites, esophageal varices, or splenomegaly with thrombocytopenia. Advanced fibrosis was defined as FIB-4 >3.26. Patients were categorized into three groups based on hepatic reserve at diagnosis: Group 1(no CSPH and FIB-4 \leq 3.26), Group 2(either CSPH or FIB-4 >3.26, but not both), and Group 3(CSPH with FIB-4 >3.26). The primary outcome was overall survival (OS).

Results

Of the 841 patients, 147 (17.5%) were classified into Group 3 (CSPH with advanced fibrosis). Compared with Groups 1 and 2, Group 3 patients were more often hepatitis B carriers (24.4% vs. 27.6% vs. 37.3%, p=0.018) and demonstrated significantly worse liver function, including lower platelet counts (257.4 vs. 236.5 vs. 145.9 \times 10³/ μ L, p<0.001), higher INR (1.1 vs. 1.2 vs. 1.2, p<0.001), lower albumin (3.9 vs. 3.7 vs. 3.4 g/dL, p<0.001), and higher bilirubin (2.6 vs. 2.7 vs. 3.4 mg/dL, p<0.001). Surgical resection was performed less frequently in Group 3 (46.7% vs. 32.1% vs. 20.4%, p<0.001). After a median follow-up of 374 days, 399 patients had died. Median OS was significantly different across the groups: 24.1 months in Group 1, 9.8 months in Group 2, and 5.4 months in Group 3 (p<0.001).

Conclusion

CSPH with advanced liver fibrosis is an independent predictor of poor survival in patients with CCA. Combining CSPH with FIB-4 provides a clinically meaningful stratification of hepatic reserve and identifies patient subgroups with markedly different outcomes. Incorporating these factors into routine prognostic assessment may improve risk stratification and treatment planning.

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.

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

A total of 129 cirrhotic patients (mean age 59.3 \pm 10.3 years, 77.5% male) were enrolled, most commonly due to HBV (41.9%) and HCV (10.1%). Most of the patients were classified in Child-Pugh A (47.3%), with a mean MELD of 12.3 \pm 4.7, FIB-4 of 6.8 \pm 4.7, APRI of 1.5 \pm 1.2, and ALBI of -2.02 \pm 0.70. During 814 \pm 303 days of follow-up, 8.5% died; the most frequent events were acute kidney injury (24%) and sponteanous bacterial peritonitis (23.3%). Compared with healthy controls, cirrhosis patients had higher GLP-1 (18,523 vs 743 pg/mL, p<0.001), CCK (0.79 vs 0.53 pg/mL, p<0.001), and ghrelin (4.18 vs 0.28 ng/mL, p=0.009), but lower serotonin (60.7 vs 182.5 ng/mL, p<0.001); PYY and GIP did not differ. Ghrelin and serotonin level seems to have statistically difference between different Child-Pugh class. GLP-1 was markedly higher in those with jaundice or pre-existing hepatic encephalopathy (HE) before entering trial. Patients who expired or underwent transplant had lower GLP-1level. Patients who developed or worsened HE or SBP during the 1-year follow-up had higher baseline GLP-1. Overall infections events were strongly associated with GLP-1 elevation. SBP and AKI were additionally linked to lower serotonin. A GLP-1 cutoff of 3,875 pg/mL predicted 1-year HE development (HR 3.50, 95% CI 1.01–12.20, p=0.049). No significant differences were observed in lipopolysaccharide, fecal albumin, or bacterial DNA between high and low GLP-1 groups.

Conclusion



Gut hormones differ significantly in cirrhotic patients compared to healthy individuals with specific hormone levels linked to cirrhosis-related complications. Furthermore, GLP-1 level seems to be connected to 1-year HE development. These findings highlight potential roles of gut hormones in disease progression and complications, warranting further research for validation.

NALIRIFOX 或 nal-IRI/FL 做為胰腺癌二線治療-一個真實世界研究

NALIRIFOX versus Liposomal irinotecan plus fluorouracil/leucovorin as the second-line chemotherapy in gemcitabine refractory pancreatic adenocarcinoma: A real-world study

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Background

Pancreatic adenocarcinoma carries a high mortality rate. Nanoliposomal irinotecan plus 5-fluorouracil and leucovorin (nal-IRI/FL) is the standard second-line chemotherapy. Nanoliposomal irinotecan plus oxaliplatin, fluorouracil and leucovorin (NALIRIFOX) has shown superior efficacy as first-line therapy, but its second-line role remains undefined. We conducted a real-world study to compare the efficacy and safety of NALIRIFOX with nal-IRI/FL.

Methods

This retrospective study enrolled patients with locally advanced or metastatic pancreatic adenocarcinoma who received NALIRIFOX or nal-IRI/FL following progression on first-line gemcitabine-based therapy from September, 2020, through October, 2024.

Results

A total of 62 patients in the NALIRIFOX group and 131 in the nal-IRI/FL group were analyzed. Cumulative dose intensity ≥80% over four cycles was achieved in 81.4% and 73.1%, respectively (P = 0.32). Median progression-free survival was 4.0 months (95% CI 3.6–4.5) for NALIRIFOX versus 2.5 months (95% CI 2.1–3.0) for nal-IRI/FL (hazard ratio 0.686; 95% CI 0.497–0.947; P = 0.021). Median overall survival was 7.0 months (95% CI 5.0–9.1) for NALIRIFOX versus 6.3 months (95% CI 4.4–8.1) for nal-IRI/FL (P = 0.827). 69.1% of patients with disease progression after nal-IRI/FL received oxaliplatin-containing chemotherapy. Grade 3–4 adverse events were more frequent with NALIRIFOX, including febrile neutropenia, neutropenia, thrombocytopenia, and peripheral neuropathy. Most were transient and manageable.

Conclusion

NALIRIFOX provides superior progression-free survival compared to nal-IRI/FL as second-line therapy for advanced or metastatic pancreatic cancer after gemcitabine failure. Although associated with higher rates of hematologic and neurologic toxicities, these were manageable with careful monitoring.

代謝脂肪肝病對於年輕肝細胞癌患者之預後影響

Impact of metabolic dysfunction–associated steatotic liver disease on young hepatocellular carcinoma patients following curative resection

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Background

The prognostic impact of metabolic dysfunction—associated steatotic liver disease (MASLD) in hepatocellular carcinoma (HCC) remains controversial, particularly among younger patients. We investigated the clinicopathological features and survival outcomes of young HCC patients with and without MASLD after curative resection.

Methods

We retrospectively analyzed 289 treatment-naïve HCC patients aged ≦60 years who underwent curative resection between 2016 and 2022. Patients were categorized as non-MASLD (n=154) or MASLD (n=135) based on non-tumor liver histology. Overall survival (OS) was the primary endpoint; recurrence-free survival (RFS) was secondary. Survival analyses were performed using Kaplan–Meier and Cox proportional hazards models.

Results

Compared with the non-MASLD group, patients with MASLD had higher body mass index, more cardiometabolic risk factors, lower aspartate aminotransferase (AST) and alpha-fetoprotein levels, earlier tumor stage, and smaller tumor size. After a median follow-up of 59.2 months, 56 deaths were recorded, with a 5-year OS of 76.9% overall. MASLD patients had significantly better 5-year OS (84.2% vs. 70.1%, p=0.018) and RFS (51.3% vs. 37.0%, p=0.010). However, in multivariate Cox analysis, MASLD was not an independent predictor of OS or RFS. Larger tumor size (> 5cm) independently predicted poorer OS (hazard ratio 2.10, 95% confidence interval 1.14–3.86, p=0.017), while elevated AST, larger tumor size, and microvascular invasion were independent predictors of poorer RFS.

Conclusion

Young HCC patients with MASLD presented with more favorable tumor characteristics and showed superior unadjusted OS and RFS after curative resection. However, MASLD itself was not an independent prognostic factor after adjustment, with tumor burden remaining the key determinant of outcomes.



代謝功能障礙相關脂肪性肝病與小氣道功能障礙對阻塞性氣道疾病急性惡化風險之影響從代謝功能 障礙相關脂肪性肝到小氣道——揭開阻塞性氣道疾病急性惡化的隱形推手

From MASLD to Small Airways: Unmasking the Hidden Drivers of Acute Exacerbation

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Background

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a metabolic condition that leads to systemic inflammation. Obstructive airway diseases (OAD) are characterized by chronic airway inflammation, with small airway dysfunction (SAD) regarded as an early indicator. However, it is unknown whether MASLD contributes to SAD or the risk of acute exacerbation (AE) in OAD.

Methods

In this retrospective cohort study, 2,572 patients who underwent spirometry, impulse oscillometry (IOS), and abdominal CT scans were enrolled. Patients were divided according to MASLD status to compare their pulmonary function and clinical outcomes, including OAD AE over a follow-up period of up to six years.

Results

349 patients exhibited MASLD (13.6%). The peripheral airway resistance measured by IOS are significantly higher in MASLD patients (X5 values: -0.14 vs. -0.16 kPa/(L/s), p = 0.002; AX : 0.76 vs. 0.89, p = 0.044). After six-year of follow up, patients with both MASLD and SAD exhibited the highest rate of OAD AE (34.8%, p = 0.016) than other groups, the coexistence of MASLD and SAD remained an independent predictor of exacerbations after adjustment by logistic regression. Hepatic steatosis was also identified as a potential contributing factor of OAD AE.

Conclusion

MASLD is associated with a higher risk of SAD, and together they markedly increase OAD AE risk. Hepatic steatosis appears to be a major driver of this risk. These findings highlight the need for integrated management of MASLD patients, addressing both liver and respiratory health to improve outcomes.

Anifrolumab 治療紅斑性狼瘡對臨床指標與干擾素標誌之變化:單一中心世代研究初探

The responsiveness of Anifrolumab treatment in lupus patients through clinical indexes and interferon signature: a single-center preliminary cohort study

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Background

Systemic lupus erythematosus (SLE) is a complex disease that involves major organs with great treatment challenges. Anifrolumab, a type I interferon receptor antagonist, has shown to be effective lupus treatment, yet real-world experience on Taiwanese patients and the consequence of molecular changes after treatment remained unclear.

Methods

We conducted a single-center, retrospective case series of seven Taiwanese SLE patients treated with Anifrolumab. Disease activity was assessed using SLEDAI-2K and BILAG-2004 indices. Laboratory parameters including hemoglobin, platelet count, complement, and anti-dsDNA levels were tracked longitudinally. In a subset of patients, expressions of two interferon signature genes, *ISG15* and *NLRP12*, were measured to through neutrophils isolated from lupus patients to quantify the interferon activity. Regression analyses were performed to evaluate relationships in between interferon signatures and clinical indices before and after treatment.

Results

All patients demonstrated marked reduction in SLEDAI-2K scores and domain-specific improvements, notably in mucocutaneous, musculoskeletal, hematologic, and gastrointestinal domains. Anemia and thrombocytopenia showed sustained resolution. Improvement of interferon signatures, including decreasing of *ISG15* expression and increasing *NLRP12* expression, could be measured after Anifrolumab treatment. Positive correlations with titer of *ISG15* and anti-dsDNA antibody could be detected. Also, after treatment of Anifrolumab, the regression slopes between the expression of *ISG15* and anti-dsDNA becoming flattened, and the expression of *NLRP12* with hemoglobin and platelets becoming steepened. These findings suggested the ameliorating of interferon activity on clinical presentations following Anifrolumab treatment.

Conclusion

Anifrolumab improved global and organ-specific lupus activity while dampening interferon-driven hematologic abnormalities as well as clinical indexes, supported by ISG15 and NLRP12 expression.

肝癌接受根治性切除後之復發模式與復發後存活分析

Patterns and Outcomes of Recurrence Following Curative Resection of Hepatocellular Carcinoma

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Background

Recurrence after curative resection of hepatocellular carcinoma (HCC) remains common, yet the patterns of recurrence and their impact on outcomes are not well understood. We aimed to characterize recurrence patterns and evaluate their influence on long-term outcomes after resection.

Methods

Between 2007 and 2024, 1,816 patients who underwent curative resection for HCC were retrospectively analyzed. Recurrence patterns, post-recurrence treatments, and predictors of post-recurrence survival (PRS) were assessed.

Results

During a median follow-up of 48.3 months, 901 patients experienced recurrence, including 612 (67.9%) with early recurrence and 358 (39.7%) beyond the Milan criteria. Recurrence stages were BCLC 0 (31.7%), A (29.6%), B (16.8%), and C (21.2%). Post-recurrence treatments included repeat surgery (21.2%), thermal ablation (31.7%), transarterial chemoembolization (30.4%), and systemic therapy (11.2%). Median PRS was 87.2 months for recurrence within Milan criteria and 18.9 months for recurrence beyond Milan (p<0.001). In patients with recurrence within Milan criteria, independent predictors of PRS included early recurrence (hazard ratio (HR)=2.334, p<0.001), diabetes mellitus (HR=1.458, p=0.036), multiple tumors (HR=1.554, p=0.032), BCLC stage A vs. 0 (HR=1.688, p=0.009), AFP >20 ng/mL (HR=1.805, p<0.001), and ALBI grade 2–3 (HR=1.698, p=0.001). Among patients with recurrence beyond Milan criteria, independent predictors of PRS included poorly differentiated HCC (HR=1.448, p=0.014), diabetes mellitus (HR=1.745, p=0.001), tumor size >5 cm (HR=1.760, p=0.011), multiple tumors (HR=2.550, p<0.001), macrovascular invasion (HR=1.617, p=0.027), extrahepatic metastasis (HR=1.699, p=0.002), AFP >400 ng/mL (HR=1.771, p=0.001), and ALBI grade 2–3 (HR=1.964, p<0.001).

Conclusion



Post-recurrence survival after curative resection of HCC is determined by recurrence patterns, tumor burden, AFP levels, and liver function at recurrence. These findings may inform individualized treatment strategies and the design of future clinical trials.

艱難梭菌與無害梭菌之共感染加重發炎性腸道疾病之預後:一項回溯性世代研究

Co-infection with *Clostridioides difficile* and *Clostridium innocuum* Aggravates Outcomes in Inflammatory Bowel Disease: A Retrospective Cohort Study

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Background

Clostridioides difficile infection (CDI) is common in inflammatory bowel disease (IBD) and is associated with increased hospitalization, treatment failure, colectomy, and mortality. Clostridium innocuum (CI), intrinsically resistant to vancomycin, is an emerging but underrecognized co-pathogen in IBD flares, which has been implicated in antibiotic-associated diarrhea, colitis, and refractory disease. However, the clinical significance of CI co-infection in IBD patients with CDI remains unclear. This study aimed to evaluate outcomes and risk factors associated with CDI and CI co-infection in IBD.

Methods

We conducted a retrospective cohort study at Linkou Chang Gung Memorial Hospital (Jan 2000–May 2021). Of 142 acute flare-up hospitalized IBD patients, 79 had CDI confirmed by stool toxin A/B tests. Among them, 29 (36.7%) had concurrent CI infection (co-infection group), and 50 (63.3%) had CDI alone (CDI-only group). Baseline characteristics and clinical outcomes were compared. Cox regression analysis was used to evaluate factors associated with time to clinical and steroid-free remission, while multivariable logistic regression identified independent risk factors for CI co-infection. The primary endpoints were clinical remission and steroid-free remission. Patients were followed from enrollment until death or last outpatient clinic visit.

Results

Patients with CDI/CI co-infection had a significantly longer median time to clinical remission (6.5 vs. 2 months, p=0.002) and steroid-free remission (11 vs. 6 months, p=0.016) compared with those with CDI alone. Kaplan–Meier analysis further confirmed a significantly delayed cumulative incidence of both clinical and steroid-free remission in the co-infection group (p=0.001 and p=0.014, respectively) over a median follow-up of 53 months. In Cox regression analysis, both biologic therapy failure (HR 0.553, 95% CI 0.316–0.969, p=0.038) and CDI/CI co-infection (HR 0.445, 95% CI 0.256–0.772, p=0.004) were independently associated with delayed clinical remission. Similarly, biologic therapy failure (HR 0.546, 95% CI 0.299–1.000, p=0.05) and CDI/CI co-infection (HR 0.361, 95% CI 0.198–0.660, p=0.001) predicted delayed steroid-free remission. Multivariable logistic regression identified biologic therapy as an independent predictor of CI co-infection (OR 5.375, 95% CI 1.822–15.857, p=0.002).

Conclusion

Concurrent *Clostridium innocuum* infection adversely affects clinical outcomes in IBD patients with CDI, as evidenced by prolonged time to clinical and steroid-free remission. These findings



underscore the importance of early identification and targeted management of CI, particularly among patients receiving biologic therapy, to optimize clinical management and outcomes.

肝細胞癌中 ATG4B 失調與腫瘤侵襲性、復發及患者生存的相關性

Dysregulation of ATG4B in Hepatocellular Carcinoma Correlates with Tumor Aggressiveness, Recurrence, and Patient Survival

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Background

Autophagy is a critical cellular physiopathological process and acts in dual roles in either tumor suppression or tumor promotion during cancer development. Until now, the roles of autophagy in tumorigenesis remain controversial. The elongation of the phagophore is one of the important steps of autophagy progression, which consists of the ATG12-conjugation system and the LC3-conjugation system. ATG4B, LC3B, and SQSTM1/P62 are categorized in the LC3-conjugation system and play pivotal roles in disease development, including cancers. Dysregulation of those proteins has been mentioned in many cancerous types, such as colorectal cancer, gastric cancer, and breast cancer. However, the roles of ATG4B, LC3B, and SQSTM1/P62 in hepatocellular carcinoma (HCC) remain unclear.

Methods

In this study, we collected 90 pairs of human hepatocellular carcinoma (HCC) tissues and corresponding adjacent hepatic tissues to examine the expression of ATG4B, SQSTM1/p62, and LC3B using an immunoblotting assay. We next explored the correlation among these proteins, clinical parameters, and overall survival (OS) and recurrence.

Results

Our results showed that ATG4B, not SQSTM1/p62 and LC3BII, was significantly downregulated in the HCC tissues compared to the adjacent hepatic tissues. Further analysis also validated that lower ATG4B expression is highly associated with increasing tumor grades, advanced tumor stages, increased tumor size, higher serum alpha-fetoprotein (AFP) levels, and positive vascular invasion. Moreover, patients with higher ATG4B expression are likely to exhibit a longer survival rate and lower tumor recurrence compared to those with lower ATG4B expression. Univariate and multivariate Cox proportional hazards models for overall survival and recurrence demonstrated that low ATG4B expression and TNM stage III and IV were significantly associated with mortality. In addition, low ATG4B expression, TNM stage III and IV, higher AFP level (> 200 ng/mL), poor histology grade (II and III), AST (> 40 U/L), positive liver cirrhosis, fibrosis (III and IV), and positive vascular invasion were markedly correlated with HCC recurrence.

Conclusion

These results suggest that lower ATG4B expression is highly associated with tumor progression, shortening survival rate, and promoting tumor recurrence. Accordingly, our findings will provide a novel insight that ATG4B may serve as a potent biomarker and prognostic factor in the tumor



progression of human hepatocellular carcinoma.



Oral presentation 114_013

心房顫動導管燒灼術中不同抗凝策略之比較: warfarin 與 NOACs 之安全性與併發症分析

Comparative Safety of Warfarin and NOACs in Patients Undergoing Catheter Ablation for Atrial Fibrillation: A Retrospective Analysis of Periprocedural Complications

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Background

Catheter ablation has become a cornerstone in the management of atrial fibrillation (AF), particularly for rhythm control in symptomatic or drug-refractory patients. Periprocedural anticoagulation is essential to mitigate thromboembolic risk; however, the optimal anticoagulant strategy remains a subject of ongoing debate. Both vitamin K antagonists (VKAs), such as warfarin, and non-vitamin K antagonist oral anticoagulants (NOACs) are widely employed in clinical practice, yet comparative data regarding their safety profiles in the ablation setting are limited. This study aimed to evaluate baseline characteristics and procedural complication rates between patients receiving warfarin and those on NOACs, with additional subgroup analyses among individual NOAC agents.

Methods

We retrospectively reviewed 410 consecutive patients who underwent catheter ablation for AF and received periprocedural anticoagulation at our institution. Patients were stratified into warfarin (n = 97) and NOAC (n = 313) groups. Baseline demographics, comorbidities, CHA₂DS₂-VASc scores, and procedural complication rates were compared. Subgroup analyses were conducted among NOAC agents: dabigatran, rivaroxaban, apixaban, and edoxaban. Primary outcomes included pericardial effusion, ischemic stroke, pseudoaneurysm formation, other procedural complications, and composite bleeding risk.

Results

Patients receiving NOACs were significantly older than those on warfarin (mean age 61.9 \pm 10.6 vs. 58.1 ± 10.3 years, P = 0.002). No significant differences were observed in baseline comorbidities or CHA₂DS₂-VASc scores between the two groups. Warfarin use was associated with a higher incidence of pericardial effusion (6.2% vs. 1.6%, P = 0.015) and composite bleeding complications (11.3% vs. 4.5%, P = 0.014).

Subgroup analysis among NOACs revealed significant heterogeneity in baseline stroke risk: dabigatran users had a markedly higher prevalence of prior stroke (30.8%) compared to rivaroxaban (6.9%), apixaban (13.3%), and edoxaban (3.7%) (P < 0.001). Correspondingly, CHA₂DS₂-VASc scores were highest in the dabigatran group (2.64 \pm 1.20, P = 0.024). Despite these differences, periprocedural complication rates — including pericardial effusion, stroke, pseudoaneurysm, and bleeding risk—did not differ significantly among NOAC subgroups.

Conclusion

In patients undergoing catheter ablation for AF, NOACs demonstrated a favorable safety profile



compared to warfarin, with significantly lower rates of pericardial effusion and bleeding complications. Among NOAC agents, dabigatran users exhibited higher baseline stroke risk, as reflected by prior cerebrovascular events and elevated CHA_2DS_2 -VASc scores; however, procedural safety outcomes remained comparable across NOAC subgroups. These findings support the preferential use of NOACs in the periprocedural setting and underscore the importance of individualized anticoagulant selection based on thromboembolic risk stratification.



Oral presentation 114_014

「Bismuth/amoxicillin/vonoprazan 三合療法」之幽門螺旋桿菌除菌除菌率優於「Amoxicillin/vonoprazan 二合療法」與「clarithromycin/amoxicillin/rabeprazole 三合療法」-一多中心隨機試驗

Bismuth/amoxicillin/vonoprazan triple therapy is More Effective than Amoxicillin/vonoprazan Dual and Clarithromycin/amoxicillin/rabeprazole standard triple therapies for first-line treatment of *H. pylori* Infection: A multicenter randomized trial

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Background

High-dose amoxicillin/vonoprazan (AV) dual therapy is a single-antibiotic regimen for *Helicobacter pylori* infection that offers several advantages: it reduces unnecessary antibiotic exposure, minimizes gut microbiota disruption, lowers adverse event rates, and supports environmental sustainability. However, its efficacy varies by region. We recently developed a novel triple regimen — bismuth, high-dose amoxicillin, and a potassium-competitive acid blocker (BAP therapy)—which demonstrated an eradication rate of $\geq 95\%$ in Taiwan.

To evaluate whether 14-day BAP triple therapy is superior to AV dual therapy and to clarithromycin-based standard triple therapy in the first-line treatment of *H. pylori* infection.

Methods

In this multicenter, randomized, open-label trial, adult patients with *H. pylori* infection were enrolled from seven study centers across Taiwan. Participants were randomly assigned (1:1:1) to receive one of the following 14-day regimens: BAP triple therapy, AV dual therapy, or clarithromycin/amoxicillin/rabeprazole (CAR) standard triple therapy. The primary outcome was *H. pylori* eradication, assessed in the intention-to-treat (ITT) population.

Results

The trial was terminated early following interim analysis. From November 2023 to April 2025, 390 patients were enrolled. Antibiotic resistance rates were 10.8% for amoxicillin and 26.2% for clarithromycin. In the ITT population, eradication rates were significantly higher with BAP therapy than with AV or CAR therapy (93.8% vs. 83.8% and 83.1%, respectively; 95% CI: 2.4%–17.6% and 3.0%–18.4%; both p < 0.001). Modified ITT analysis yielded consistent results (97.6% vs. 88.0% and 87.7%; 95% CI: 3.3%–15.9% and 3.5%–16.3%; both p < 0.001). Adverse event rates (10.8%, 8.5%, 13.8%) and drug adherence (96.9%, 95.4%, 94.6%) were comparable across groups.

Conclusion

With intragastric pH elevation and the synergistic effect of bismuth, high-dose amoxicillin achieved nearly 98% eradication in modified ITT analysis. This novel mono-antibiotic regimen—14-day BAP triple therapy—proved superior to both AV dual therapy and clarithromycin-based standard triple therapy as first-line treatment for *H. pylori* infection in Taiwan. It is a promising option in regions



with high clarithromycin resistance and eliminates the need for pretreatment clarithromycin susceptibility testing.

亞洲中重度克隆氏症患者使用 Risankizumab 的真實世界治療經驗

Real-World Treatment Experience with Risankizumab for Moderate-to-Severe Crohn's Disease in Asia

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Background

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic intestinal inflammation with increasing incidence worldwide, particularly in Asia. Early diagnosis, risk stratification, and treat-to-target strategies with advanced therapies are crucial to prevent long-term complications. Interleukin-23 (IL-23) has emerged as a key driver of immune-mediated inflammation. Risankizumab (RZB), a monoclonal antibody targeting the p19 subunit of IL-23, has demonstrated efficacy in clinical trials for moderate-to-severe CD. However, real-world evidence in Asian populations remains limited. This study aimed to evaluate the efficacy and safety of risankizumab in Taiwanese patients with moderate-to-severe Crohn's disease in a real-world setting.

Methods

This multicenter retrospective cohort study (Sept 2024–Mar 2025) enrolled adults with moderate-to-severe Crohn's disease (CDAI 220–450) treated with risankizumab at seven tertiary centers in Taiwan. Clinical, laboratory, and endoscopic data were collected. Endpoints included clinical response (CDAI decrease ≥100), remission (CDAI <150 or HBI <5), PRO2 remission, endoscopic outcomes (SES-CD, ulcer-free), transmural healing, and corticosteroid-free remission. Adverse events, hospitalizations, and surgeries were recorded. Week 12 binary outcomes were analyzed with non-responder imputation; categorical variables were compared using chi-squared tests, with p<0.05 considered significant.

Results

A total of 49 patients with moderate-to-severe Crohn's disease were enrolled (mean age 41.5 years, 69% male). At week 12, clinical response and remission rates reached 91.8% and 42.9%, with PRO2 remission in 53.5% and CFCR in 30.6%. Endoscopic response, remission, and transmural healing were achieved in 16.3%, 28.6%, and 18.4%, respectively. Biologic-naïve patients tended to have higher remission rates, though differences were not significant. No severe adverse events occurred; only mild headache and liver enzyme elevation (2.0% each) were observed.

Conclusion

In conclusion, this multicenter real-world study shows risankizumab is effective and well tolerated for moderate-to-severe Crohn's disease in Asian patients, with outcomes consistent with clinical trials. It offers value in biologics-experienced and ileal disease cases, though long-term data remain warranted