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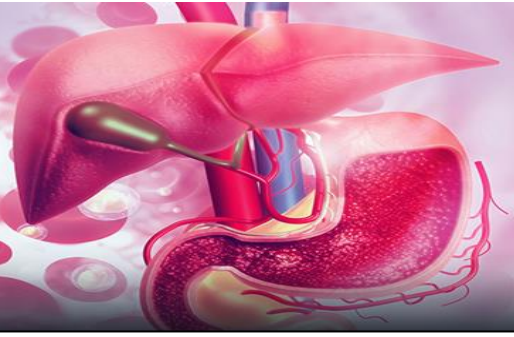

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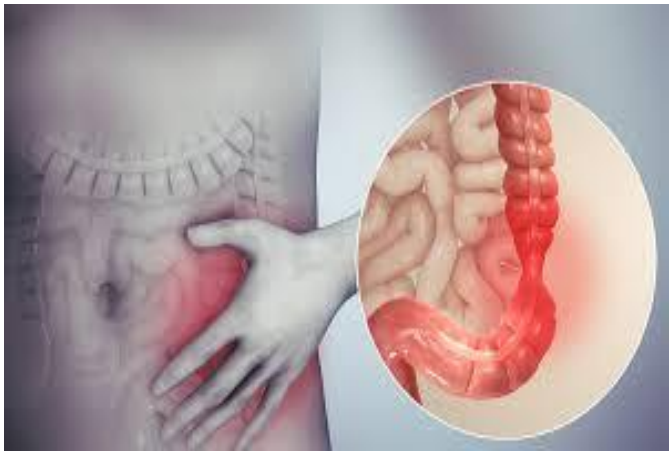
Analysis of the changes in brain function in IBS patients using a Hidden Markov Model



IRRITABLE BOWEL SYNDROME

INTRODUCTION- Irritable bowel syndrome (IBS) is a common disorder of gut-brain interaction, affecting approximately 10% of the global population and characterized by recurrent abdominal pain and altered bowel habits.[1] It is frequently associated with psychiatric comorbidities such as anxiety and depression, underscoring the role of the gut-brain axis in its pathophysiology. Neuroimaging studies using functional MRI (fMRI) have revealed abnormal brain activity in IBS, particularly in regions involved in pain modulation and emotion regulation. While traditional fMRI analyses assume static functional connectivity, emerging evidence suggests that brain networks exhibit dynamic fluctuations over time.[2] So, this study investigated the dynamic changes in brain activity using the Hidden Markov Model (HMM) to provide deeper insights into IBS-related neural alterations.

METHODS- This comparative study recruited 35 IBS patients and 31 age- and sex-matched healthy controls (HCs) to examine brain dynamics using resting-state fMRI (Rs-fMRI) and 3D-T1 imaging. Clinical assessments included the IBS Severity Scoring System (IBS-SSS), Patient Health Questionnaire-9 (PHQ-9), Pain Anxiety Symptom Scale (PASS), and IBS-Specific Quality of Life (IBS-QOL) Scale. Imaging data were acquired on a Siemens Skyra 3.0 T scanner and pre-processed in DPABI (V8.1) with motion correction, spatial normalization, smoothing, and bandpass filtering. A Hidden Markov Model (HMM) with 116 regions of interest (ROIs) identified six optimal states, and temporal metrics (fractional occupancy, lifetime, switching rate, and transition probability) were analysed. Group differences were assessed using a non-parametric permutation test (5,000 permutations, FDR-corrected $p < 0.05$), while Spearman correlation analysed associations between HMM metrics and clinical scores, with significance set at FDR-corrected $p < 0.05$.

RESULTS-

A comparative analysis of 35 IBS patients and 31 healthy controls (HCs) revealed no significant differences in age, sex, or education ($p > 0.05$). HMM analysis of resting-state fMRI data identified six distinct brain states, with IBS patients exhibiting significantly lower fractional occupancy (FO) and lifetime (LT) in state 5 but higher FO and LT in state 6 ($p < 0.05$). While switching rates remained unchanged, IBS patients showed an increased probability of transitioning from state 2 to state 6. Spearman correlation analysis demonstrated a positive association between PHQ-9 and PASS scores, with FO and LT in state 6 correlating with IBS severity (IBS-SSS)

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but not depression or pain anxiety (Figure 1). Functional connectivity analysis highlighted altered network interactions, with state 5 showing reduced DMN-CON connectivity, whereas state 6 exhibited stronger intra-network connectivity within the sensorimotor (SMN) and control (CON) networks. Brain activation mapping indicated that state 5 (HC-dominant) involved increased activation in the anterior cingulate and cerebellum, while state 6 (IBS-dominant) was characterized by enhanced activation in the orbitofrontal middle gyrus and postcentral gyrus, alongside decreased activity in the anterior cingulate and parahippocampal gyrus.

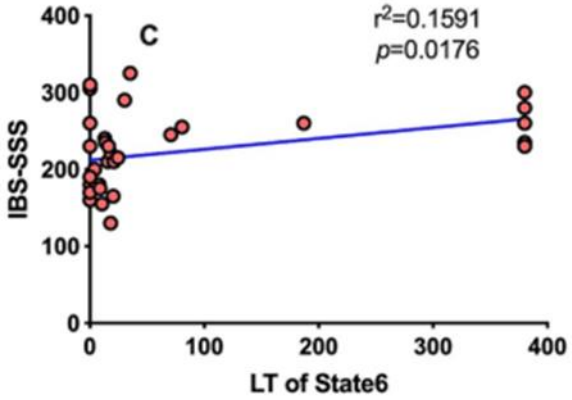

Figure 1. A Positive correlation between the lifetime (LT) of HMM state 6 and the IBS-SSS score ($r^2 = 0.1591$, $p = 0.0264$).

DISCUSSION- This study identified six distinct HMM states and analyzed their temporal properties, revealing significant reconfiguration of brain network dynamics in IBS. The reduced FO and LT in state 5 indicate instability in brain activity, a pattern consistent with findings in MDD, where similar temporal disruptions are associated with impaired emotional regulation.[3] Additionally, the increased FO and LT in state 6 suggest a more stable yet maladaptive brain state, potentially linked to symptom severity. This aligns with prior research on gut-brain axis dysfunction, where altered serotonergic and noradrenergic signaling contributes to abnormal pain processing.[4] These findings provide new insights into the temporal dynamics of brain activity in IBS, particularly in relation to depressive symptoms.

CONCLUSION- This study applied HMM to analyze brain dynamics in IBS and HCs, identifying six states with significant temporal differences in states 5 and 6. IBS patients exhibited altered functional connectivity and activation patterns, suggesting disruptions in emotion regulation and symptom processing.

HMM analysis of brain dynamics in IBS identified six states, with significant temporal differences in states 5 and 6. Altered functional connectivity and activation patterns suggest disruptions in emotion regulation and symptom processing.

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Association Between Gastroesophageal Reflux Disease and Chronic Obstructive Respiratory Disease

INTRODUCTION- Chronic obstructive pulmonary disease (COPD) is a complex respiratory condition characterized by persistent airflow limitation and significant global health burden. While smoking remains the primary risk factor, a substantial proportion of COPD cases occur in non-smokers due to environmental exposures, genetic predisposition, and other factors.[1] Gastroesophageal reflux disease (GERD) is a prevalent comorbidity in COPD and asthma, contributing to exacerbations and worsening clinical outcomes through aspiration and airway inflammation. Despite strong epidemiological associations, the causal mechanisms linking GERD to COPD and asthma remain unclear.[2] This study employed Mendelian randomization (MR) using genome-wide association study (GWAS) data to investigate potential causal relationships, aiming to improve disease understanding and inform targeted screening and preventive strategies.

METHODS- A two-sample bidirectional Mendelian Randomization (MR) study was conducted to assess the causal relationship between GERD and chronic obstructive respiratory diseases (COPD and asthma). The GWAS data for GERD (N=602,604) were sourced from the GWAS catalog, and COPD (N=20,066 cases, 338,303 controls) and asthma (N=56,167 cases, 352,255 controls) data from FinnGen and the IEU Open Database, respectively. Instrumental SNPs were selected based on genome-wide significance ($P < 5\times10^{-8}$), linkage disequilibrium ($r^2 < 0.001$), and F-statistics (>10), with exclusion of pleiotropic and palindromic SNPs. Causal effects were estimated using inverse variance-weighted (IVW) as the primary method, complemented by weighted median, MR-Egger, and mode-based approaches. Sensitivity analyses included Cochran's Q test, MR-Egger regression, leave-one-out analysis, MR-Rucker test, and the Steiger directionality test. Confounder-associated SNPs were excluded via PhenoScanner. Analyses were conducted using Two Sample MR and RadialMR in R, with statistical power (>80%) assessed via the mRnd tool. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs), and $P < 0.05$ was considered as statistically significant.

RESULTS- A total of 52 SNPs for COPD and 68 for asthma were selected, demonstrating strong instrumental validity (F-statistics: 207.50–669.24). IVW analysis revealed a significant causal association between GERD and increased risks of COPD (OR = 1.520, 95% CI: 1.376–1.680, $P = 2.17 \times 10^{-16}$) and asthma (OR = 1.420, 95% CI: 1.340–1.504, $P = 1.27 \times 10^{-32}$), supported by additional MR methods (Figure 1). Sensitivity analyses confirmed the robustness of these findings, with Cochran's Q test indicating no significant heterogeneity (P >

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0.05), symmetrical SNP distribution in funnel plots, and leave-one-out analysis ruling out disproportionate SNP influence. MR-Egger regression and MR-PRESSO confirmed no pleiotropy, while the Steiger test validated the causal direction ($P < 10^{-92}$), confirming GERD as the causal factor. Reverse MR analysis found no evidence of COPD or asthma causing GERD ($P > 0.05$), with sensitivity tests further confirming the absence of heterogeneity and pleiotropy, reinforcing the unidirectional causal link from GERD to respiratory diseases.

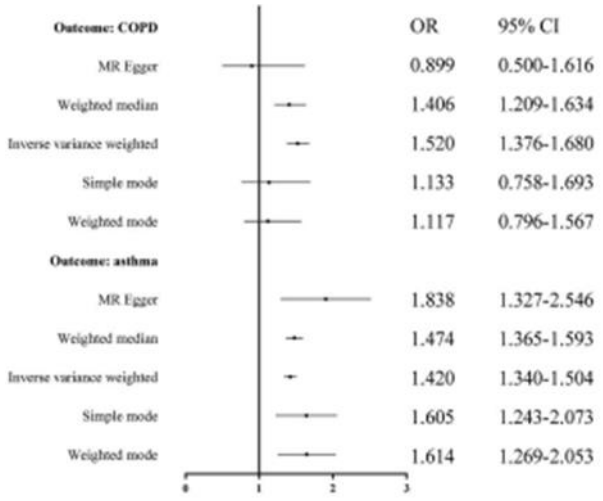

Figure 1. Forest plot depicting the causal effect of GERD on COPD and asthma risk based on MR estimates

DISCUSSION- The current study established a strong causal link between GERD and an increased risk of COPD and asthma, with no reverse causality observed, indicating GERD-driven respiratory impairment through microaspiration, vagally mediated bronchoconstriction, and systemic inflammation. While these findings align with prior epidemiological evidence, they challenge studies suggesting a bidirectional relationship.[3,4] Additionally, the study underscores the importance of GERD management in preventing COPD and asthma progression; however, the role of PPIs remains controversial. Some studies support their use in reducing exacerbations and improving outcomes, whereas others highlight potential risks, including lung function decline and pneumonia.[5]

CONCLUSION- This study established a strong causal association between GERD and an elevated risk of COPD and asthma, providing a basis for integrating GERD management into preventive and therapeutic approaches for these chronic respiratory diseases.

GERD increases the risk of COPD and asthma, emphasizing its role in respiratory disease management.

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Incidence of pancreatic diseases in patients with Metabolic Dysfunction-Associated Steatotic Liver Disease

INTRODUCTION- The increasing prevalence of metabolic dysfunction–associated steatotic liver disease (MASLD) parallels the global rise in obesity and metabolic syndrome.[1] MASLD is a multisystem disorder associated with cardiovascular disease, chronic kidney disease, increased infection risk, and overall mortality. Emerging evidence suggests a potential link between MASLD and pancreatic diseases; however, population-based studies incorporating liver histology remain limited**.** Given the shared metabolic risk factors between MASLD and fatty pancreas, MASLD may contribute to pancreatic disorders such as pancreatic cancer and acute pancreatitis.[2] To address this gap, this longitudinal cohort study investigates the incidence of acute and chronic pancreatic diseases, pancreatic cancer, and pancreas-related mortality in individuals with biopsy-proven MASLD, compared to matched population controls and full siblings, accounting for intrafamilial confounding.

METHODS-

This population-based cohort study investigated the association between MASLD and pancreatic disease using a nation-wide histopathology database. Adult patients (≥30 years) with histopathologically confirmed MASLD were included, excluding those with competing liver diseases, alcohol misuse, prior liver transplantation, or pancreatic disorders. Each MASLD patient was matched to up to five reference individuals based on age, sex, calendar year, and residence. Outcomes, including acute non-biliary pancreatitis, chronic pancreatitis, pancreatic cancer, and pancreas-related mortality, were identified through validated national health registers. Incidence rates were calculated per 1000 person-years, and Cox proportional hazard models estimated adjusted hazard ratios, accounting for demographics and metabolic comorbidities. Stratified and sensitivity analyses were performed to assess confounders, genetic influences, and potential biases. Statistical analyses were conducted using appropriate software, with significance set at $p < 0.05$.

RESULTS- A total of 8,563 biopsy-confirmed MASLD patients and 38,858 matched reference individuals were included. MASLD patients had a mean age of 54.5 years, with 56.9% being male. Disease severity was classified as simple steatosis (67.8%), non-fibrotic MASH (11.2%), and MASLD with fibrosis/cirrhosis (21.0%). The median follow-up was 15.1 years for MASLD patients and 19.4 years for controls.

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MASLD was associated with a higher incidence of pancreatic disease (2.74 vs. 1.19 per 1000 person-years [PY]), yielding an adjusted hazard ratio (aHR) of 2.19 (Figure 1). The risk was highest in the first two years but remained elevated over long-term follow-up. Risk increased with histological severity, with the highest rates in fibrosis/cirrhosis (3.56 per 1000 PY, aHR 2.53). Acute non-biliary pancreatitis was the most frequent pancreatic disease (1.44 vs. 0.44 per 1000 PY, aHR 2.24), with the highest risk in fibrosis/cirrhosis (aHR 3.09). Chronic pancreatitis incidence was significantly higher in MASLD patients (0.54 vs. 0.12 per 1000 PY, aHR 3.78), particularly in those with fibrosis/cirrhosis (aHR 7.57). Further, pancreatic cancer incidence was increased in MASLD (0.88 vs. 0.47 per 1000 PY), with an aHR of 2.12. Risk was highest in non-fibrotic MASH (1.75 per 1000 PY, aHR 4.70). Pancreas-related mortality was also higher (0.97 vs. 0.46 per 1000 PY, aHR 2.41), with the highest risk in MASH (1.68 per 1000 PY, aHR 4.72). Sensitivity analyses confirmed the robustness of findings, including sibling-matched comparisons and adjustments for early detection bias. The risk of pancreatic disease progressively increased with worsening MASLD severity, reinforcing the association between MASLD and pancreatic complications.

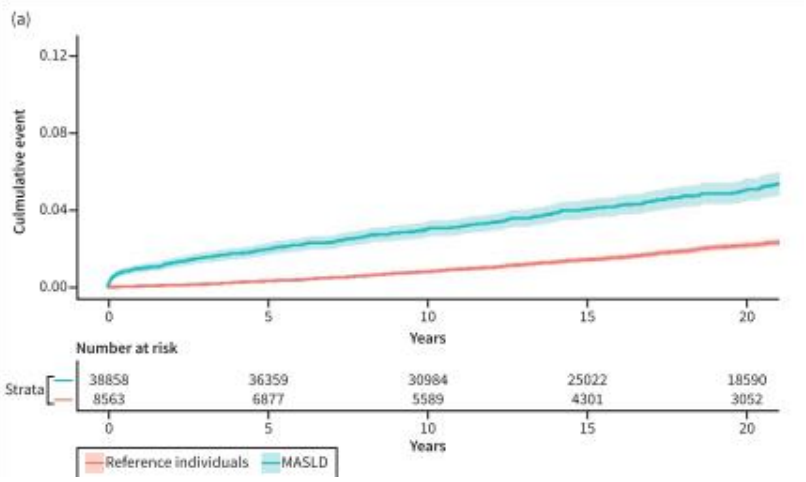

Figure 1. Cumulative incidence curves depicting the time to occurrence of any pancreatic disease in patients with biopsy-confirmed MASLD.

DISCUSSION- This study established a strong link between MASLD and increased risks of acute and chronic pancreatitis as well as pancreatic cancer, independent of alcohol or biliary causes. This aligns with prior research indicating a sixfold higher prevalence of fatty pancreas in pancreatic cancer patients, suggesting ectopic fat deposition as a potential contributing factor.[3] The present findings indicate that even non-fibrotic MASLD significantly increases the risk of pancreatic disease, emphasizing the importance of early metabolic interventions beyond advanced fibrosis stages. In contrast, previous meta-analyses reported odds ratios of 6.18 before and 9.56 after MASLD diagnosis, suggesting a progressive risk increase with disease severity.[4]

CONCLUSION- MASLD significantly increases the risk of pancreatitis, pancreatic cancer, and pancreas-related mortality, with severity-dependent escalation.

MASLD was associated with significantly higher rates of acute non-biliary pancreatitis, chronic pancreatitis, and pancreatic cancer compared with matched reference individuals.

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Case report on Respiratory Failure Due to Perforated Peptic Ulcer and Severe Scoliosis

INTRODUCTION- Laparoscopic surgery has evolved from a diagnostic tool in the 1960s to a widely used surgical technique, becoming the gold standard for various procedures, particularly in gynecology and digestive surgery. Advances in training, instrumentation, and imaging have enhanced its safety and feasibility.[1] While laparoscopic surgery offers benefits such as reduced mortality, complications, and postoperative pain, its application in patients with severe scoliosis remains challenging due to anatomical constraints and respiratory risks.[2] This report presents a case of severe scoliosis with respiratory failure due to a perforated peptic ulcer, successfully managed with emergency laparoscopic surgery, in accordance with the SCARE criteria.

CASE PRESENTATION-

A 51-year-old male presented to the emergency department with acute-onset epigastric pain lasting three hours, along with a three-day history of anorexia. His medical history included depression and a previous appendectomy. Computed tomography (CT) revealed congenital left kidney deficiency. A Helicobacter pylori test was negative. Although prescribed four major tranquilizers for depression, he had no history of NSAID use. He was a former smoker but did not consume alcohol.

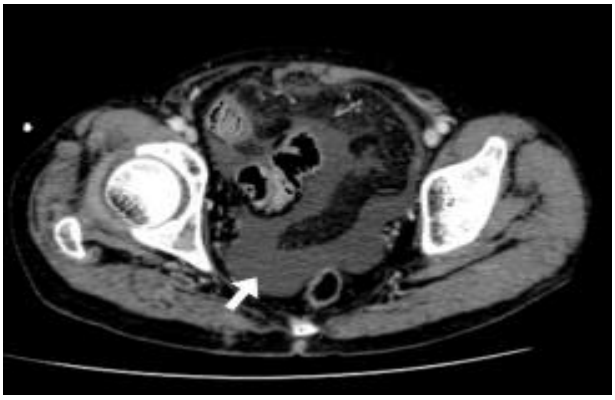

Figure 1. CT scan showing moderate ascites (white arrow) in the Douglas fossa.

On examination, his temperature was 37.0°C, blood pressure 107/86 mmHg, and heart rate 120 bpm. Localized tenderness was noted in the right upper abdomen. Hypoxemia persisted despite oxygen administration (PaO_2 66.7 mmHg), raising concerns for respiratory failure. The patient had severe scoliosis with a Cobb angle of 87°.

Contrast-enhanced abdominal CT showed duodenal wall discontinuity, free intraperitoneal air, and moderate ascites (Figure 1), consistent with duodenal bulb perforation. Emergency laparoscopic surgery confirmed a 10-mm anterior duodenal wall perforation with biliary ascites. Three additional ports were placed, and laparoscopic

primary suturing with an omental patch, peritoneal lavage with 10 L saline, and multichannel drainage were performed.

Postoperatively, respiratory support was required for atelectasis, with extubation on postoperative day 4. Drains were removed on days three and five, without intra-abdominal infectious complications. Oral intake resumed on day 7, and the patient was discharged on postoperative day 22.

DISCUSSION- This case highlights the impact of scoliosis on respiratory function and perioperative management in emergency laparoscopic surgery for perforated peptic ulcer. While previous studies recommend lower pneumoperitoneum pressure (6 mmHg) to mitigate respiratory dysfunction, this case demonstrated the feasibility of higher pressure (10 mmHg) with careful monitoring, contrasting with existing recommendations and suggesting an individualized approach.[3] Additionally, trocar placement was adapted to optimize the surgical field in a distorted anatomy, aligning with reports advocating alternative port sites, such as intercostal approaches for severe deformities, yet contrasting with those supporting standard intraperitoneal placement, emphasizing the need for case-specific strategies.[2]

CONCLUSION- Emergency laparoscopic surgery can be a safe and effective approach for patients with severe scoliosis and perforated peptic ulcers, requiring timely decision-making, coordinated perioperative management, and optimized port placement to ensure surgical feasibility and minimize complications.

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Emergency laparoscopic surgery is a viable option for severe scoliosis with perforated peptic ulcers, requiring careful planning to ensure safety and efficacy.