Research Square

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Atherosclerotic Cardiovascular Disease Burden and Mortality in Hospitalized Patients with Inflammatory Bowel Disease: A Dose–Response Analysis from the MIMIC-IV Database

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Abstract

Background

Inflammatory bowel disease (IBD) is characterized by chronic systemic inflammation, which serves as a potent driver for premature atherosclerosis via the "gut-heart axis." The independent prognostic impact of arterial burden on hospitalized IBD patients remains insufficiently characterized. This study investigated the association between atherosclerotic cardiovascular disease (ASCVD) burden and both in-hospital and long-term mortality.

Methods

We analyzed data from 2,790 adult patients hospitalized with IBD from the MIMIC-IV database. The primary exposure was ASCVD burden, defined by the involvement of coronary, cerebrovascular, or peripheral arterial vascular beds. A dose–response analysis was performed to evaluate mortality risk stratified by the number of affected vascular territories.

Results

Patients with concurrent ASCVD (n = 390) demonstrated significantly higher in-hospital mortality (9.5% vs. 1.5%) and overall mortality (37.2% vs. 13.5%) compared to those without ASCVD ($P < 0.001$). After adjusting for potential confounders including demographic factors and major comorbidities, ASCVD remained an independent predictor of in-hospital mortality (aHR 3.69; 95% CI 2.09–6.51) and long-term mortality (aHR 1.26; 95% CI 1.00–1.59). Crucially, a dose–response relationship was observed: each additional involved vascular bed was associated with a 2.4-fold increase in the risk of in-hospital death (aHR 2.40; 95% CI 1.66–3.47).

Conclusion

ASCVD is not merely a comorbidity but a critical "risk enhancer" for both short- and long-term mortality in hospitalized IBD patients. Early identification of the ASCVD burden and multidisciplinary management may be essential to improve outcomes in high-risk adult patients hospitalized with IBD.

Background

Beyond its primary gastrointestinal manifestations, inflammatory bowel disease (IBD) is increasingly recognized as a systemic inflammatory state that significantly impacts extraintestinal organ systems [1–4]. Chronic immune dysregulation in IBD serves as a potent driver for premature vascular aging and atherosclerotic cardiovascular disease (ASCVD), encompassing coronary artery disease (CAD), cerebrovascular disease (stroke), and peripheral arterial disease (PAD). [1, 3–5]. Recent evidence

highlights a "gut-heart axis," where intestinal barrier dysfunction facilitates the translocation of proinflammatory microbial metabolites into the systemic circulation, triggering endothelial dysfunction and accelerating atherosclerosis. Despite this association, conventional cardiovascular risk scores often underestimate the true risk in the IBD population, as they fail to account for the cumulative inflammatory burden [5, 6].

The underlying pathophysiological mechanisms linking IBD and ASCVD are complex and largely driven by chronic systemic inflammation [1, 6, 7]. Patients with IBD present with high circulating levels of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukins (IL)-1β, and IL-6 [1, 6] —mediators that trigger a cascade of events, including increased oxidative stress, altered platelet function, and a hypercoagulable state [5–7]. The resultant pro-inflammatory state promotes endothelial dysfunction and impaired nitric oxide-mediated vasodilation [6, 8]. Although these associations are recognized, ASCVD risk in IBD patients is frequently underestimated [5, 9]. Current cardiovascular risk assessment tools, such as the Framingham Risk Score and the ASCVD Risk Estimator, are based primarily on conventional risk factors such as hypertension, hyperlipidemia, and diabetes mellitus (DM) [10–12], which have not been validated in the IBD population and do not account for the systemic inflammatory burden [9, 13]. Consequently, existing models often perform poorly in predicting events for patients with IBD, resulting in a potential underestimation of the true cardiovascular risk profile.

In patients with IBD, the presence of concurrent ASCVD may signify high multimorbidity risk, profoundly influencing the natural history of the disease, causing higher rates of therapy failure and increased healthcare costs [3, 14, 15]. Furthermore, the interaction between IBD and cardiovascular comorbidities is associated with poorer health outcomes, increased complication rates and higher overall mortality [14, 15]. Hospitalization often represents peak systemic inflammation for patients with IBD, sometimes triggered by acute flares or surgical stress [2, 7, 16, 17]. During these acute episodes, the increased inflammatory state may severely exacerbate endothelial dysfunction and further elevate the risk of ASCVD and venous thromboembolism [2, 16, 17]. The synergistic effect of acute-on-chronic inflammation during a hospital stay may unmask reduced cardiac reserve, potentially leading to fatal cardiovascular events even in patients who were previously stable [6, 17, 18].

Despite the clear association between IBD and cardiovascular risk, whether ASCVD independently predicts mortality in hospitalized patients with IBD remains insufficiently studied [5, 7, 16]. Although some studies have analyzed the effects of various risk factors on inpatient outcomes, including sepsis, acute kidney injury (AKI), or malnutrition, few have focused specifically on the independent prognostic value of pre-existing or acute ASCVD. Furthermore, while the impact of acute complications on in-hospital death is recognized, studies exploring the influence of ASCVD on long-term mortality after discharge are few [2, 7, 19]. Understanding whether the burden of ASCVD continues to drive survival outcomes months or even years beyond the immediate acute care episode is essential to help refine post-hospitalization follow-up and develop preventive strategies.

We hypothesized that clinical data from a large cohort of patients over several years' time would help to show the relationship between ASCVD and short- and long-term mortality. This study therefore aimed to determine associations between ASCVD and in-hospital and long-term mortality in adults hospitalized with IBD.

Methods

Study design and data source

This retrospective cohort study retrieved data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) version 3.1 database, 2008 to 2022. The database provides de-identified longitudinal records from Beth Israel Deaconess Medical Center, including comprehensive mortality data linked with the Social Security Death Index. [20–22]. The detailed cohort selection process and the validation of IBD diagnoses using ICD-9 and ICD-10 codes have been established in our prior work [2].

Ethics statement

This study adhered to the ethical principles outlined in the Declaration of Helsinki. The research protocol was reviewed and approved by the Institutional Review Board of Mackay Memorial Hospital. Because the analysis was based exclusively on de-identified retrospective data from the MIMIC-IV database, the requirement for informed consent was waived by the IRB.

Study population and definitions

For the current analysis, we focused on 2,790 adult patients (aged 18 and older) hospitalized with a validated diagnosis of CD or UC. Figure 1 depicts the patient selection process. The definition and severity of ASCVD was based on the presence of CAD, PAD and stroke using the relevant ICD-9 and ICD-10 codes. Patients with CAD were identified using the ICD-10 codes I20 ~ I22and I24 ~ I25, and the corresponding ICD-9 codes 410 ~ 414. For those diagnosed with PAD, we applied the ICD-10 codes I740 ~ I745, I748, I7502, I771, E0852, E0952, E105, E115 and E135, along with ICD-9 codes 43300, 43310, 43320, 43330, 43380, 43390, 43400, 43410, 43490, 440, 4439, 44381 and 44389. To identify patients with a history of stroke, we used the ICD-10 codes I63 and G45, and the ICD-9 codes 43311, 43321, 43331, 43381, 43391, 43401, 43411, 43491 and 435. The primary exposure was the presence and burden of ASCVD, defined by the involvement of coronary, cerebrovascular, or peripheral vascular beds. Unlike our previous investigation of venous thromboembolism, the current study stratified patients based on the number of affected arterial vascular beds (none, one, two, or three) to evaluate a potential dose–response relationship regarding mortality risk.

Outcomes

The outcomes include in-hospital and long-term all-cause mortality in patients with IBD. The risk factors of in-hospital and long-term all-cause mortality were assessed in these patients, respectively. Moreover, the long-term mortality was determined through linkage with the Social Security Death Index, which captures over 95% of out-of-hospital deaths in the United States, thereby ensuring robust and reliable follow-up for study participants [20, 21].

Statistical analysis

Data distribution was summarized using means ± standard deviations for continuous parameters, while categorical metrics were reported as frequencies and corresponding percentages. The $\chi 2$ test or Fisher's exact test was used to compare categorical variables between groups, whereas the Students' t-test was used to compare continuous variables. Kaplan–Meier survival curves were used to assess in-hospital and long-term mortality. Associations between ASCVD and mortality outcomes (including in-hospital and long-term mortality) were investigated using univariate and multivariable analyses. ASCVD was evaluated both as a binary status (yes/no) and as a stratified variable based on the number of affected vascular beds (none, one, two, or three). Model 1 was adjusted for age and sex. Model 2 included adjustments for demographic characteristics and laboratory parameters, including liver enzymes alanine transaminase (ALT) and aspartate aminotransferase (AST), hemoglobin, white blood cells (WBC) count, red blood cell (RBC) count, sodium (Na), potassium (K), creatinine, and platelets. Model 3 was further adjusted for comorbidities, specifically *Clostridium difficile* infection, diabetes mellitus (DM), hypertension, dyslipidemia, smoking, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), rheumatic disease, chronic kidney disease (CKD), and malignancy. Computational analysis and statistical modeling were executed utilizing R version 4.2.3 and SPSS version 20.0. A threshold of $p < 0.05$ (two sided) was established as statistical significance.

Results

Baseline characteristics and comparisons between ASCVD and non-ASCVD groups

A total of 2,790 adult patients hospitalized with inflammatory bowel disease were included in the final analysis. The mean age of the study cohort was 52.62 ± 19.23 years, and 47.46% of the patients were male. The average length of hospitalization was 7.33 ± 9.93 days.

Baseline characteristics stratified by ASCVD status are summarized in Table 1. Compared with patients without ASCVD, those with ASCVD were substantially older and demonstrated a higher burden of cardiovascular and systemic comorbidities. The mean age was 71.22 years in the ASCVD group and 49.59 years in the non-ASCVD group. Patients with ASCVD also had lower hemoglobin levels, lower red blood cell counts, and lower platelet counts, whereas serum creatinine levels were higher than those observed in patients without ASCVD.

Table 1

Baseline characteristics of patients with IBD (n = 2,790).

Variables	Total (n = 2,790)	Non-ASCVD (n = 2,400)	ASCVD (n = 390)	P-value
Sex (male), n (%)	1324 (47.46)	1093 (45.5)	231 (59.2)	< 0.001*
Age (years), mean (SD)	52.62 (19.23)	49.59 (18.44)	71.22 (12.23)	< 0.001*
Smoking, n (%)	135 (4.84)	112 (4.7)	23 (5.9)	0.308
Clostridium difficile, n (%)	151 (5.41)	125 (5.2)	26 (6.7)	0.229
Comorbidities, n (%)				
DM	360 (12.9)	220 (9.2)	140 (35.9)	< 0.001*
Hypertension	925 (33.15)	631 (26.3)	294 (75.4)	< 0.001*
Dyslipidemia	584 (20.93)	377 (15.7)	207 (53.1)	< 0.001*
CHF	201 (7.2)	86 (3.6)	115 (29.5)	< 0.001*
COPD	438 (15.7)	330 (13.8)	108 (27.7)	< 0.001*
Rheumatic disease	87 (3.12)	64 (2.7)	23 (5.9)	0.002*
CKD	203 (7.28)	109 (4.5)	94 (24.1)	< 0.001*
Malignant cancer	193 (6.92)	158 (6.6)	35 (9)	0.086
Laboratory examination, mean (SD)				
ALT (IU/L)	45.41 (188.62)	46.32 (200.72)	39.85 (81.14)	0.530
AST (IU/L)	106.52 (139.86)	105.89 (136.53)	110.44 (159)	0.551
Hemoglobin (g/dL)	12.15 (2.3)	12.25 (2.28)	11.53 (2.29)	< 0.001*
WBC (K/uL)	10.83 (7.34)	10.81 (7.33)	10.95 (7.39)	0.716
RBC (m/uL)	4.17 (0.74)	4.21 (0.73)	3.9 (0.76)	< 0.001*
Sodium (mEq/L)	137.73 (4.08)	137.73 (4)	137.75 (4.56)	0.934
Potassium (mEq/L)	4.17 (0.76)	4.15 (0.75)	4.32 (0.8)	< 0.001*
Creatinine (mg/dL)	1.06 (1.02)	1 (0.91)	1.41 (1.49)	< 0.001*

IBD, inflammatory bowel disease; ASCVD, atherosclerotic cardiovascular disease; ALT, alanine transaminase; AST, aspartate aminotransferase; WBC, white blood cells; RBC, red blood cells; DM, diabetes mellitus; CHF, Congestive heart failure; COPD, Chronic obstructive pulmonary disease; CKD, chronic kidney disease. *$P < 0.05$.

Variables	Total (n = 2,790)	Non-ASCVD (n = 2,400)	ASCVD (n = 390)	P-value
Platelet (K/uL)	307.66 (149.57)	316.5 (151.34)	253.26 (125.24)	< 0.001*
Hospital stay (days), mean (SD)	7.33 (9.93)	6.85 (9.33)	10.29 (12.6)	< 0.001*
Follow-up (days), mean (SD)	696.27 (1126.29)	723.39 (1154.87)	529.38 (915.02)	< 0.001*
In-hospital mortality, n (%)	73 (2.62)	36 (1.5)	37 (9.5)	< 0.001*
Long-term mortality, n (%)	468 (16.77)	323 (13.5)	145 (37.2)	< 0.001*

IBD, inflammatory bowel disease; ASCVD, atherosclerotic cardiovascular disease; ALT, alanine transaminase; AST, aspartate aminotransferase; WBC, white blood cells; RBC, red blood cells; DM, diabetes mellitus; CHF, Congestive heart failure; COPD, Chronic obstructive pulmonary disease; CKD, chronic kidney disease. *$P < 0.05$.

Comorbidity profiles differed markedly between the two groups. The ASCVD group had higher proportions of diabetes mellitus, hypertension, dyslipidemia, congestive heart failure, chronic obstructive pulmonary disease, rheumatic disease, and chronic kidney disease. These findings indicate that hospitalized IBD patients with ASCVD represented an older and clinically more complex population.

During a mean follow-up period of 696.27 ± 1126.29 days, patients with ASCVD experienced longer hospitalizations than those without ASCVD (10.29 vs. 6.85 days). Mortality outcomes were also considerably worse in the ASCVD group. In-hospital mortality was 9.5% among patients with ASCVD compared with 1.5% among those without ASCVD. Similarly, long-term mortality was higher in the ASCVD group than in the non-ASCVD group, at 37.2% versus 13.5%, respectively (all $P < 0.001$).

Survival analysis and risk assessment

Kaplan–Meier survival analyses demonstrated poorer survival among IBD patients with ASCVD than among those without ASCVD, both during hospitalization and over long-term follow-up, as shown in Figs. 2 and 3. The separation between survival curves emerged early and persisted throughout the observation period, suggesting that ASCVD was associated with both short-term and sustained mortality risk.

In Cox regression analysis (Table 2), ASCVD was significantly associated with an increased risk of in-hospital mortality, with a hazard ratio of 6.005 ($P < 0.001$). ASCVD was also associated with higher long-term mortality, with a hazard ratio of 3.331 ($P < 0.001$). After adjustment for demographic factors, laboratory parameters, and major comorbidities, ASCVD remained an independent predictor of adverse outcomes. In the fully adjusted model, ASCVD was associated with a more than threefold higher risk of

in-hospital mortality, with an adjusted hazard ratio of 3.692 ($P < 0.001$). The association with long-term mortality also remained statistically significant, with an adjusted hazard ratio of 1.261 ($P < 0.001$).

Table 2

Cox regression analysis of predictors associated with in-hospital and long-term mortality.

	Univariate analysis		Multivariate analysis					
			Model1		Model2		Model3	
Variables	**HR (95% CI)**	***P*-value**	**$_{a}$HR (95% CI)**	***P*-value**	**$_{a}$HR (95% CI)**	***P*-value**	**$_{a}$HR (95% CI)**	***P*-value**
In-hospital mortality								
ASCVD (yes/no)	6.005 (3.795, 9.503)	< 0.001*	3.969 (2.329, 6.764)	< 0.001*	3.651 (2.127, 6.269)	< 0.001*	3.692 (2.094, 6.510)	< 0.001*
ASCVD (0/1/2/3)	3.495 (2.626, 4.653)	< 0.001*	2.676 (1.913, 3.743)	< 0.001*	2.386 (1.699, 3.350)	< 0.001*	2.402 (1.662, 3.472)	< 0.001*
Long-term mortality								
ASCVD (yes/no)	3.331 (2.735, 4.058)	< 0.001*	1.475 (1.188, 1.830)	< 0.001*	1.387 (1.117, 1.723)	0.003*	1.261 (1.003, 1.585)	0.047*
ASCVD (0/1/2/3)	2.592 (2.248, 2.989)	< 0.001*	1.465 (1.242, 1.728)	< 0.001*	1.340 (1.138, 1.578)	< 0.001*	1.242 (1.048, 1.471)	0.012*

Model1: Sex, Age.
Model2: Sex, Age, ALT, AST, Hemoglobin, WBC, RBC, Sodium, Potassium, Creatinine, Platelets.
Model3: Sex, Age, ALT, AST, Hemoglobin, WBC, RBC, Sodium, Potassium, Creatinine, Platelets, *Clostridium difficile*, DM, Hypertension, Dyslipidemia, Smoking, CHF, COPD, Rheumatic disease, CKD, Malignancy.

ASCVD, atherosclerotic cardiovascular disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cells; RBC, red blood cells; DM, diabetes mellitus; CHF, Congestive heart failure; COPD, Chronic obstructive pulmonary disease; CKD, chronic kidney disease; HR, hazard ratio; aHR, adjusted HR; 95% CI, 95% confidence interval. *$P < 0.05$.

The burden of ASCVD was further evaluated according to the number of affected arterial vascular beds. When ASCVD burden was analyzed as a continuous variable, each additional involved vascular territory

was associated with a progressively higher mortality risk. In the fully adjusted model, the adjusted hazard ratio for in-hospital mortality was 2.402 for each increase in the number of affected vascular beds ($P < 0.001$). A similar pattern was observed for long-term mortality, with an adjusted hazard ratio of 1.242 ($P < 0.001$). These results support a dose–response relationship between cumulative ASCVD burden and mortality among hospitalized patients with IBD.

Discussion

The present study identified ASCVD as a strong independent predictor of both in-hospital and long-term mortality in adults hospitalized with IBD. Adults with IBD and comorbid ASCVD exhibited significantly higher in-hospital death rates (9.5% vs. 1.5%) and a strikingly elevated overall mortality rate compared to those without ASCVD (37.2% vs. 13.5%). Even after rigorous multivariate adjustments for demographic factors and major comorbidities—including CHF, CKD, and DM, multivariate analysis revealed that the association between ASCVD and in-hospital mortality remained statistically significant (aHR of 3.692), strongly echoing findings in critically ill sepsis populations within the MIMIC-IV database, in whom pre-existing arterial damage from ASCVD was shown to compromise vascular integrity and exacerbate systemic inflammatory response [18]. A defining feature of the present study is the observation of a clear "dose-response" relationship regarding polyvascular disease, suggesting that the mortality risk escalates linearly with the number of involved vascular beds, as also suggested in previous studies [18, 23]. For hospitalized adults with IBD, each additional vascular bed—encompassing coronary, cerebrovascular, and peripheral areas—increased the risk of in-hospital mortality, with the aHR for the number of affected vascular beds reaching 2.402 in our fully adjusted model, aligning with results of a previous study suggesting that the cumulative vascular burden serves as an independent high-risk marker beyond individual comorbidities [18].

Furthermore, the present study also provides critical evidence on long-term mortality, a domain largely overlooked in previous IBD literature [24]. Results of the present study demonstrated that the lethal impact of ASCVD is not confined to acute admissions but continues to drive survival outcomes for years post-discharge, with an aHR of 1.261 for overall mortality. It is well-established that IBD patients face an increased risk of developing cardiovascular events [5, 25, 26]. Previous studies have mainly examined ASCVD incidence in the general IBD population rather than in hospitalized patients [1, 4, 25]. Our study helps fill this gap by showing that ASCVD is associated with worse prognosis in hospitalized patients with IBD. This is consistent with recent U.S. trend data showing that IBD- and CVD-related mortality rose sharply from 2018 to 2021 after years of relative stability.Currently, CVD is the second leading cause of mortality in the IBD population, after gastrointestinal causes [3, 27].

Mechanically, the intricate connection between IBD and arterial pathology can be fundamentally understood through the "gut-heart axis" paradigm [1, 6, 25]. Chronic intestinal inflammation leads to intestinal barrier dysfunction (leaky gut), facilitating the translocation of luminal pathogens and proinflammatory microbial metabolites, such as lipopolysaccharides (LPS) and phenylacetylglutamine (PAGln), into the systemic circulation, as previously described[1, 25]. Once in the bloodstream, these

endotoxins trigger a cascade of events, including the upregulation of cell adhesion molecules (e.g., VCAM-1 and ICAM-1) and the release of pro-inflammatory cytokines like TNF-α, IL-6, and IL-1β [1, 6, 28]. This specific pro-inflammatory milieu serves as a primary driver of endothelial dysfunction, thereby accelerating the progression of atherosclerosis even in the absence of traditional lipid-related risk factors [1, 28, 29].

The observation in the present study of the dose-response relationship in polyvascular disease also suggests that adults with IBD and multiple affected vascular sites have a profoundly reduced cardiovascular reserve [18, 25]. Hospitalization often represents the peak of systemic inflammation and acute physiological stress for these patients, typically triggered by acute flares or surgical stress [3, 25, 28]. In this setting, the heightened inflammatory state severely exacerbates existing endothelial injury and induces a prothrombotic state characterized by altered platelet function and hypercoagulability [1, 5, 6, 28, 29]. Patients with pre-existing ASCVD are particularly vulnerable; their compromised vascular systems are less able to manage the acute hemodynamic challenges—such as vasodilation, capillary leak, and fluid shifts—inherent to systemic inflammation [18, 25, 27]. This leads to a higher propensity for multi-organ failure and death during the acute stress of hospitalization [16–18, 26]. The persistent nature of this vascular damage also explains why the risk remains elevated in the long term; once the vascular bed is compromised, the patient remains in a heightened state of vulnerability to future inflammatory insults [5, 25].

The findings of this study have profound implications for both inpatient and outpatient management of IBD. Inpatient IBD patients with concurrent ASCVD must be recognized as a very high-risk group [16, 25, 30]. We recommend that clinicians implement stricter hemodynamic monitoring for these individuals, as they are at an elevated risk for sudden cardiovascular collapse or acute thrombotic events during flares. Furthermore, ASCVD should be viewed not merely as a comorbidity but as a "risk enhancer" for IBD mortality. Given that the increased risk of death persists even after discharge, post-hospitalization follow-up should involve multidisciplinary coordination between gastroenterologists and cardiologists to ensure optimized secondary prevention and long-term surveillance [3, 14, 16, 31].

The data of discharged patients in the present study suggests the need to initiate cardiovascular risk assessment much earlier in the disease course. Because IBD patients may have "normal" conventional metrics (e.g., lipids and BMI) that mask underlying vascular damage [4, 13, 32], clinicians should proactively monitor blood pressure, blood glucose, and lifestyle factors from the time of IBD diagnosis [25, 31]. Cost-benefit analyses suggest that early intervention—such as aggressive control of blood pressure, patient education on lifestyle adjustments (e.g., Mediterranean diet), and early statin initiation—may significantly improve long-term survival and reduce the overall global burden of IBD complications. Looking forward, the development of an IBD-specific cardiovascular risk model that incorporates markers of systemic inflammation is essential to accurately identify and protect adults with IBD and comorbid CVD. By shifting from a reactive to a proactive paradigm, the rising trend of cardiovascular mortality in patients living with IBD may be mitigated to some extent.

Limitations

Several constraints inherent to this study's design and data source must be acknowledged. First, the reliance on the MIMIC-IV database restricts the study population to a single tertiary academic medical center in the United States. While this ensures high-quality data collection, the findings may reflect specific institutional practices and may not be fully generalizable to diverse geographical regions or community-based healthcare settings. Second, the retrospective nature of this analysis introduces potential selection bias and limits our ability to control for all confounding variables. A significant challenge was the absence of standardized longitudinal severity metrics, such as Crohn’s Disease Activity Index or Mayo scores, which are not systematically captured within the administrative structure of the MIMIC-IV database. The absence of specific markers for active intestinal inflammation and hypercoagulability prevents a more nuanced exploration of how acute flare severity interacts with arterial pathology. Third, our analysis was constrained by inconsistent documentation regarding the dosage and timing of IBD-specific pharmacotherapies. Since medications like corticosteroids and biologics can independently influence cardiovascular risk, this remains an unmeasured confounding factor. Furthermore, as is common with administrative datasets, the reliance on ICD-9 and ICD-10 codes without confirmatory imaging or physiological testing (such as pulse wave velocity) may lead to the misclassification of ASCVD burden. Finally, the MIMIC-IV database does not provide a clear temporal distinction between pre-existing ASCVD and acute arterial events occurring during the index hospitalization. Consequently, we could not determine whether the observed mortality risk was primarily driven by the chronic burden of atherosclerosis or by acute cardiovascular complications triggered by the hospital stay.

Conclusion

Concurrent ASCVD is an independent predictor of both in-hospital and long-term mortality in hospitalized patients with IBD. Results of this study identified a distinct dose-response relationship, in which the cumulative vascular burden linearly escalated mortality risk, strongly suggesting that ASCVD should be recognized as a critical "risk enhancer" rather than simply a comorbidity. Early identification of the CVD burden and multidisciplinary management may be essential to improve outcomes in high-risk adult patients hospitalized with IBD, reducing the global burden of mortality in patients living with IBD and concurrent cardiovascular disease.

Abbreviations

aHR
adjusted hazard ratio
AKI
acute kidney injury
ALP
alkaline phosphatase

ALT
alanine transaminase
ASCVD
atherosclerotic cardiovascular disease
AST
aspartate aminotransferase
BUN
blood urea nitrogen
CAD
coronary artery disease
CD
Crohn’s disease
CHF
congestive heart failure
CI
confidence interval
CKD
chronic kidney disease
COPD
chronic obstructive pulmonary disease
DM
diabetes mellitus
IBD
Inflammatory bowel disease
ICD
International Classification of Diseases
IL
interleukins
IRB
Institutional Review Board
LPS
lipopolysaccharides
MIMIC-IV
Medical Information Mart for Intensive Care IV
PAD
peripheral arterial disease
PAGln
phenylacetylglutamine
RBC
red blood cells

SD
standard deviation
TNF-α
tumor necrosis factor-alpha
UC
ulcerative colitis
WBC
white blood cells

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki, and the study protocol was approved by the Institutional Review Board (IRB) of Mackay Memorial Hospital (Number 24MMHIS460e). The IRB waived informed consent of the included patients because the research involved analysis of anonymized, retrospective data.

Clinical trial number

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

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Author Contribution

Conceptualization, Kuang-Te Wang and Chun-Han Cheng; Methodology, Chuan-Lei Chao and Chun-Han Cheng; Data curation, Min-I Su and Wei-Ru Chiou; Formal analysis, Meng-Ying Lu and Yi-Fan Huang; writing—original draft preparation, Kuang-Te Wang, Min-I Su and Meng-Ying Lu; writing—review and

editing, Chuan-Lei Chao, Wei-Ru Chiou, Yi-Fan Huang, and Chun-Han Cheng; All authors have read and agreed to the published version of the manuscript.

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Data Availability

The data used to support the findings of this study are included within the article and its supplementary information files.

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Figures

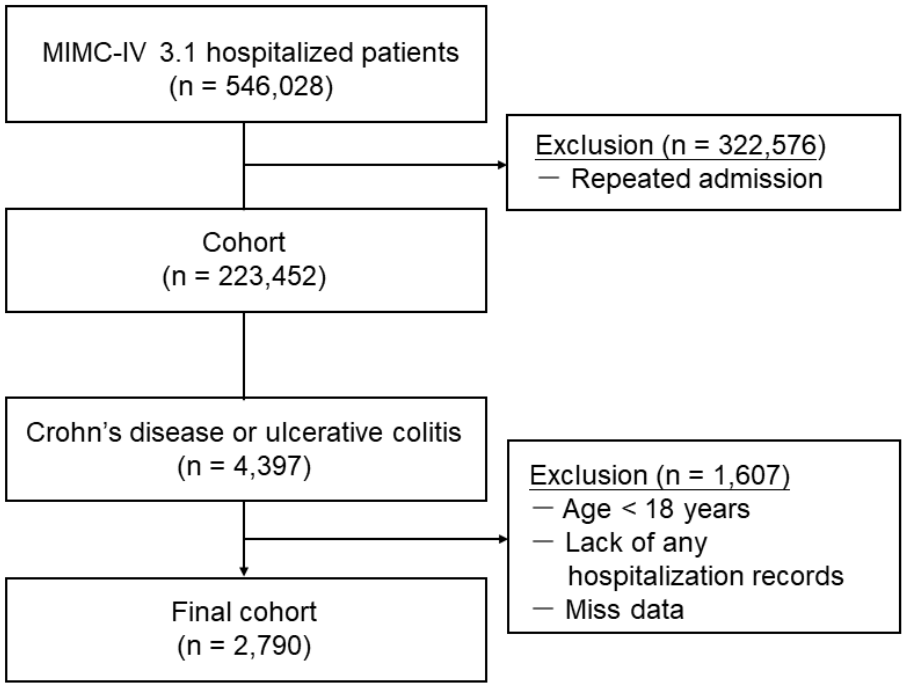


Figure 1

Flowchart of patient selection.

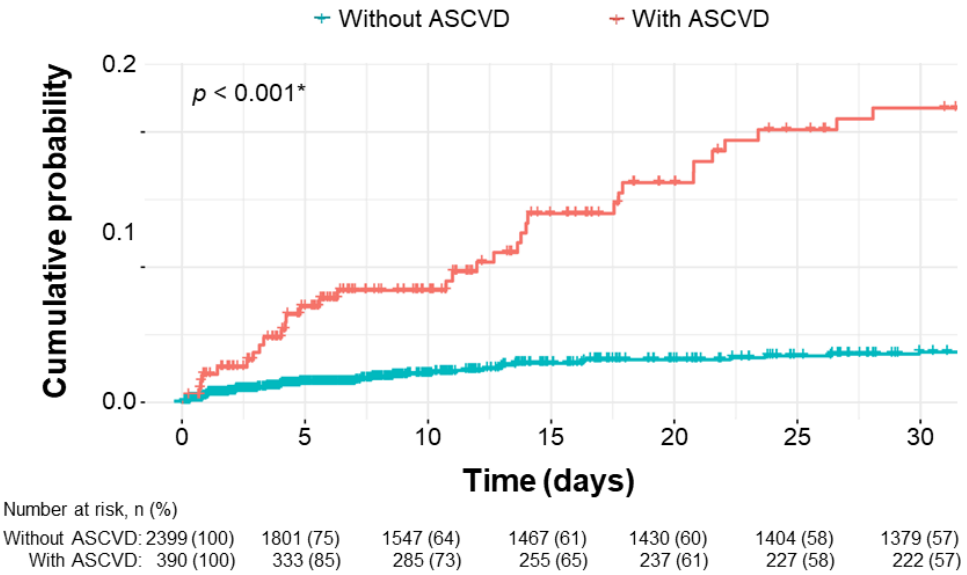


Figure 2

Kaplan-Meier survival curves of in-hospital mortality, showing that IBD patients with ASCVD have higher in-hospital mortality risk compared to those without ASCVD. IBD, inflammatory bowel disease; ASCVD, atherosclerotic cardiovascular disease. *$P < 0.05$.

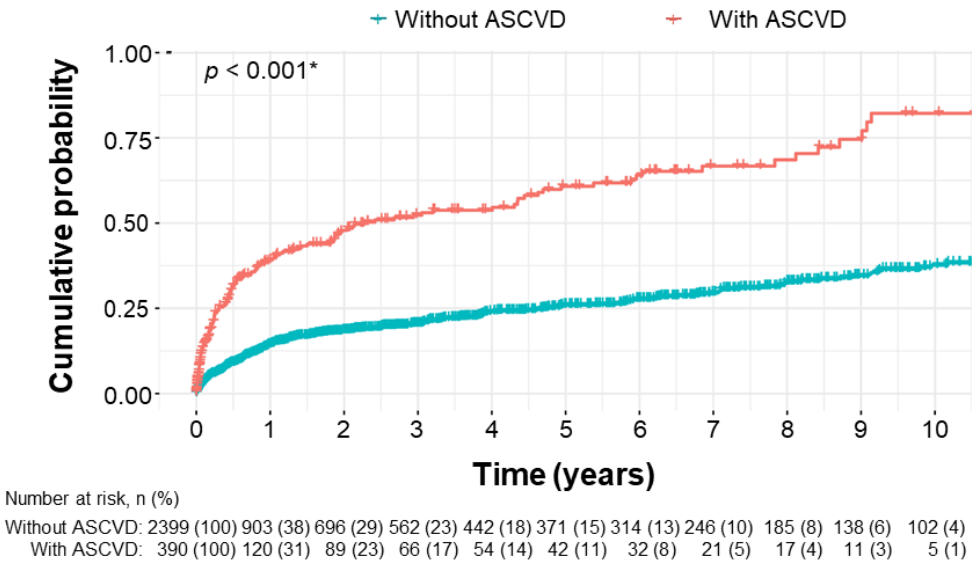


Figure 3

Kaplan-Meier curves of long-term mortality, showing an increased long-term (10-year) mortality risk in IBD patients with ASCVD and a significant difference between the two groups. IBD, inflammatory bowel disease; ASCVD, atherosclerotic cardiovascular disease. *$P < 0.05$.