Systematic Review and Meta-Analysis

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Inflammatory bowel disease and associated cardiovascular disease outcomes

A systematic review

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Abstract

Background: There is limited and conflicting data available regarding the cardiovascular disease outcomes associated with inflammatory bowel disease (IBD).

Objective: We aim to perform a systematic review to evaluate the cardiovascular outcomes and mortality associated with IBD patients.

Methods: A systematic literature search has been performed on PubMed, Embase, Cochrane, and Scopus from inception till May 2022 without any language restrictions.

Results: A total of 2,029,941 patients were included in the analysis from 16 studies. The mean age of the patients was 45.6 years. More females were found compared with males (57% vs 43%). The most common risk factors for cardiovascular disease (CVD) included smoking (24.19%) and alcohol (4.60%). The most common comorbidities includes hypertension (30%), diabetes mellitus (14.41%), dyslipidemia (18.42%), previous CVD (22%), and renal disease (10%). Among outcomes, all-cause mortality among IBD patients was 1.66%; ulcerative colitis (UC): 15.92%; and Crohn disease (CD): 0.30%. Myocardial Infarction (MI) among IBD patients were 1.47%, UC: 30.96%; and CD: 34.14%. CVD events among IBD patients were 1.95%. Heart failure events among IBD patients were 5.49%, stroke events among IBD patients were 0.95%, UC: 2.63%, and CD: 2.41%, respectively.

Conclusion: IBD patients are at higher risk for adverse cardiovascular outcomes, especially in women. Although there remains a lack of concrete treatment algorithms and assessment parameters that better characterize IBD risk factors, nutritional modifications and physical activity should be at the forefront of CVD prevention in IBD.

Abbreviations: CAD = coronary artery disease, CD = Crohn disease, CVD = cardiovascular disease, HF = heart failure, HTN = hypertension, IBD = inflammatory bowel disease, PCP = primary care physician, UC = ulcerative colitis.

Keywords: atherosclerosis, cardiovascular outcomes, Crohn disease, inflammatory bowel disease

1. Introduction

Inflammatory bowel disease (IBD) is an umbrella term for chronic progressive inflammatory disorders primarily affecting the GI tract with multiple systemic complications. Chronic inflammation has been proven to be one of the risk factors promoting atherosclerosis and vascular thrombosis by inducing endothelial disruption, oxidative injury, lipid accumulation, platelet adhesion,

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What is already known on this topic

- There was conflicting results related to a possible association between IBD-related cardiovascular disease incidence.

What this study adds

- This is the most comprehensive and updated review showing that MI, HF, CVD, and ACM events among IBD (CD and UC patients) are quite high.

How this study might affect research, practice, or policy

- Healthcare practitioners must be aware of CVD risk among IBD patients, and proper screening and safety protocols must be adopted to reduce adverse cardiovascular events.

and plaque rupture.[1,2] Inflammatory rheumatological, dermatological, and infectious diseases such as Lupus, Psoriasis, and AIDS have been proven to increase the risk of ischemic heart disease.[3–5] IBD is a known risk factor for venous thromboembolism and mesenteric ischemia.[6,7] Recently, due to the high burden of ischemic heart disease and cerebrovascular disease, it has also been speculated to contribute to morbidity in cardiovascular diseases.

Inflammatory bowel disease patients have been reported to have higher vascular stiffness and increased thickness of coronary intima, suggesting premature atherosclerosis.[8,9] The macrophages, dendritic cells, and effector T cells produce increased amounts of pro-inflammatory cytokines such as Tumor Necrosis Factor, Interferon Gamma, IL-6, IL -1 beta, and IL-17, which contribute toward endothelial barrier disruption and promotion of atherogenesis.[10] At the same time, some genetic loci mutations commonly associated with IBD, such as the NOD 2 gene, lead to decreased production of anti-inflammatory cytokines like IL-10, thus feeding into the cycle of inflammation and atherogenesis.[11] Infact, these cytokines have also been found to be the culprit in the development of heart failure (HF), arrhythmias, heart blocks, strokes, and coronary artery disease (CAD).[12–14] C Reactive protein is a commonly ordered marker for diagnosing and monitoring IBD. High-sensitivity CRP has also been included in the recent 2018 American College of Cardiology and American Heart Association blood cholesterol guidelines as a risk-enhancing factor for atherosclerotic cardiovascular disease (ASCVD).[15] Chronic inflammation also plays a role in insulin resistance and type 2 diabetes mellitus, for example, a traditional risk factor for ASCVD.[16] Moreover, corticosteroids are commonly used in treating IBD, which have multiple side effects and promote hypertension (HTN), hyperlipidemia, and diabetes, all leading to ASCVD.[17]

Despite having multiple biological evidence connecting the pathophysiology of IBD to ASCVD, the current epidemiological research is mixed and inconclusive. Multiple large-scale studies show an increased incidence of ischemic heart disease in patients with Crohn disease and ulcerative colitis. These results are more skewed towards females and younger patients.[18–20] However, some studies showed no correlation between IBD and ASCVD. Some have proven IBD to be a protective factor, with fewer hospitalizations and mortality in IBD patients compared to controls.[21,22] This systematic review aims to evaluate the cardiovascular outcomes and mortality associated with IBD patients.

2. Method

This systematic review was conducted and reported in conformity with the Cochrane and Preferred Reporting Items for Systematic Review and Meta-analysis 2020 guidelines. It was performed according to established methods, as described previously.[23,24]

2.1. Search strategy

We conducted a systematic literature search in PubMed, Embase, Google Scholar, and Scopus using predefined MESH terms by using "AND" and "OR." The following search terms were used: (((((((inflammatory bowel disease [MeSH Terms]) OR (Crohn's disease [MeSH Terms])) AND (colitis, ulcerative [MeSH Terms])) AND (acute stroke)) AND (Myocardial infarction)) AND (Ischemic Heart disease)) AND (CAD)) AND (autoimmune disease [MeSH Terms])" We queried databases from their inception to June 15, 2022, without restriction on the language of the studies. All the studies were carefully screened and exported to the Endnote 2020 library (X9). A manual check was carried out to remove duplicates. Two reviewers (VJ and SB) reviewed the titles and abstract. The senior author arbitrated discrepancies regarding the inclusion of studies (VJ).

2.2. Eligibility criteria

The following criteria were used for inclusion: studies with an age group >18 years, prospective or retrospective studies with the definitive diagnosis of IBD or Crohn disease (CD), or ulcerative colitis (UC), showing cardiovascular outcomes. Studies that involved animal testing, review articles, studies on patients of <18 years of age, and studies with a mix of autoimmune diseases or studies with adverse cardiovascular outcomes with other etiology were excluded.

2.3. Data extraction and quality assessment and statistical analysis

Data from the eligible selected studies, such as demographic, comorbidities, risk factors, and cardiovascular outcomes among IBD groups, were extracted into a spreadsheet by 2 authors (VJ and SB).

2.4. Data extraction, quality assessment, and statistical analysis

The following data were extracted from the studies: demographic data (study design, country, gender, and age), comorbidity, risk factors, and outcomes. Two authors assembled all available information in a shared spreadsheet (JC and VJ). If any required data needed to be included, written in an incorrect format, or reported in the article, the corresponding authors of the respective articles were contacted via email for clarification. Supplementary material related to the main article was also investigated in such cases. Finally, descriptive statistics were used to summarize the data in this article. The median and interquartile ranges were adopted to describe continuous variables, whereas frequencies and percentages were used for dichotomous data. All statistical analyses were conducted using the software R version 4.1.2 (available at https://cran.r-project.org).

VJ and JEC independently assessed the quality of the included studies using the Newcastle-Ottawa Scale (NOS) for cohort and cross-sectional studies.[25] NOS comprises 8 items within 3 domains and a total maximum score of 9. A study with a score of 7 to 9 was considered high quality; a score of 4 to 6 was considered high risk, whereas a score of 0 to 3 indicated a high risk of bias. In case of disagreement, a group-based discussion was conducted. The details of the quality assessment are presented in Table S1, Supplemental Digital Content, http://links.lww.com/MD/I381.

3. Result

3.1. Study selection

The preliminary database search using the pre-specified keywords yielded 1141 articles, of which 521 studies were excluded after removing duplicates. Five hundred eighty-two studies were excluded from the initial post-title and abstract screening based on the inclusion and exclusion criteria. The full-text review was conducted for the remaining 38 articles identified during the search. Twenty-two studies were excluded as they either had incomplete data, no cardiovascular outcomes, unmatched target populations or were not primary research articles. Hence, a total of 16 studies that met the eligibility criteria were included in our systematic review, in which 15 studies were observational,[5,7,19,21,26–36] and 1 study was cross-sectional[37] (Table 1). The preferred reporting items for systematic reviews and meta-analyses flow diagram is depicted in Figure S1, Supplemental Digital Content, http://links.lww.com/MD/I382.

3.2. Baseline characteristics of included studies

The study characteristics, demographic, and Comorbidities are presented in Tables 1 and 2. A total of 2,029,941 patients were included in the analysis from 16 studies. The mean age of the patients was 45.6 years. Females were more than males (57% vs 43%) (Table 1). The most common risk factors for cardiovascular disease (CVD) were: 24.19% of patients had a history of smoking (435,064/1,797,894), and 4.60% of patients had a history of alcohol use (41,473/901,550). Most common Comorbidity includes: 30% HTN (606,519/2,021,881), 14.41% patients were having diabetes mellitus (292,012/2,021,881), 18.42% patients were having Dyslipidemia (368,466/1,999,994), 22% patients were having a history of previous cardiovascular disease (192,694/892,422), 10% patients were having a renal disease (85,690/871,855).

3.3. Cardiovascular outcomes and mortality

Relevant data on ACM were given in 2 studies[31,36] in which 1.66% of patients with IBD suffered ACM (255/15,292), 15.92% in the UC group (1491/9361), and 0.30% in the CD group (591/201,114) (Table 3).

Twelve studies[7,19,21,27–33,36,37] have given Myocardial Infarction as an outcome among IBD patients. 1.47% of patients among the IBD group reported MI (15,916/1,081,304), 30.96% MI event among UC group (59,015/190,600), 34.14% MI event among CD group (66,986/196,173) respectively (Table 3).

Three studies[29–31] have data on Cardiovascular death among IBD patients. 1.95% of CVD events occurred among IBD-diagnosed Patients (1314/67,262) (Table 3).

Two studies[19,33] have data on HF among IBD patients. 5.49% of HF events occurred among IBD patients (60/1092) (Table 3).

Eight studies[5,7,29,30,34–37] have data on Stroke among IBD patients. 0.95% Stroke events occurred among IBD Patients (2265/237,516), 2.63% Stroke events among UC group (718/27,285), and 2.41% Stroke events among CD group (519/21,497) respectively (Table 3).

3.4. Quality assessment of included studies

Eight of the observational studies were having low risk of bias,[21,26–31,33] while 8 studies[5,7,19,32,34–37] had a high risk of bias, as presented in Table S1, Supplemental Digital Content, http://links.lww.com/MD/I381.

4. Discussion

Globally, IBD saw an astronomical increase in prevalence by 85%, from 3.7 million to over 6.8 million individuals with IBD within the 27-year study period, with an age-standardized increase of 6.1% within the same period, for example, 79·5 (75·9–83·5) per 100,000 population to 84·3 (79·2–89·9) per 100,000 population.[38] In 2021, the CDC published a research study that looked at data from the National Health Interview Survey, which described an estimated 3.1 million (1.2%) Americans receiving a diagnosis of IBD between 2015 and 2016.[39] This revealed a rise from 1.9 (0.9%) Million people in 1999 in the US.[40] Currently, the US has the highest prevalence of age-standardized IBD universally, at 464.5 per 100,000.[41]

4.1. Association of CVD with IBD

The etiology of IBD has only been partially understood. It is considered an inappropriate immune response in susceptible groups due to interactions between the intestinal immune system and environmental and microbial factors.[42] Genetics, environmental, and immune systems all play significant roles in this

Table 1

Study characteristic and demographic details of included studies.

Author	Study design	Country	Year	IBD, n	Female	Mean age
Mubasher et al[26]	Observational	USA	2020	847,235	482,125	52.45
Barnes et al[27]	Observational	USA	2016	563,687	326,153	51.6
Panhwar et al[28]	Observational	USA	2019	290,430	174,710	12 mo
Card et al[29]	Observational	UK	2020	31,175	16,292	45.2
Aniwan et al[19]	Observational	USA	2018	736	45	34.1
Kristensen et al[30]	Observational	Denmark	2013	20,795	11,333	43.8
Gill et al[31]	Observational	USA	2020	15,292	8915	50
Ha et al[7]	Observational	USA	2009	17,487	9739	43.25
Bernstein et al[32]	Observational	Canada	2008	8060	4441	39.46
Yarur et al[33]	Observational	USA	2011	356	184	44.62
Osterman et al[21]	Observational	USA	2011	25,327	13,796	47.1
Sridhar et al[37]	Cross-sec	USA	2011	148,228	83,935	NA
Dregan et al[5]	Observational	UK	2014	19,831	10,212	44.5
Keller et al (UC)[34]	Observational	Taiwan	2014	516	244	51.62
Joseph Keller et al (CD)[35]	Observational	Taiwan	2015	3309	1769	51.17
Choi et al[36]	Observational	South Korea	2019	37,477	16,184	40.4

CD = Crohn's disease, IBD = inflammatory bowel disease, NA = not available, UC = ulcerative colitis.

Table 2

Risk factors, and comorbidity among IBD diagnosed patients.

Author	Smoker	Alcohol	HTN	DM	Cardiovascular disease	Renal disease	Dyslipidemia
Mubasher et al[26]	253,100	10,960	265,940	138,090	CAD: 103,900 HF: 66,020 ACS: 21,285	85,400	171,285
Barnes et al[27]	68,985	NA	15,2018	69,802	NA	NA	71,023
Panhwar et al[28]	84,500		133,250	65,270	NA	NA	105,070
Card et al[29]	15,949	19,535	7565	1066	NA	NA	4749
Aniwan et al[19]	95	NA	201	52	Familial CAD: 165	NA	NA
Kristensen et al[30]	NA	NA	635	375	Arrhythmias: 409 HF: 221	102	NA
Gill et al[31]	1575	NA	4627	1762	NA	NA	3925
Ha et al[7]	NA	NA	1577	632	NA	NA	1433
Bernstein et al[32]	NA	NA	NA	NA	NA	NA	NA
Yarur et al[33]	108	NA	73	24	NA	NA	NA
Osterman et al[21]	7233	NA	4292	745	NA	NA	453
Sridhar et al[37]	NA	NA	26837	11758	NA	NA	7142
Dregan et al[5]	3506	10,966	4178	461	CHD: 320	NA	905
Keller et al (UC) [34]	2	NA	116	53	CHD: 54 HF: 09	29	43
Joseph Keller et al (CD)[35]	14	12	636	303	CHD: 261 HF: 50	159	326
Choi et al[36]	NA	NA	4574	1619	NA	NA	2112

CAD = coronary artery disease, CD = Crohn's disease, CHD = congenital heart disease, DM = diabetes mellitus, HF = heart failure, HTN = hypertension, IBD = inflammatory bowel disease, NA = not available, UC = ulcerative colitis.

Table 3

Cardiovascular outcomes, cerebrovascular outcomes, and all-cause mortality among IBD patients.

Author	All-cause mortality	MI	CVD	Heart failure	Stroke	Follow-up duration
Mubasher et al[26]	NA	NA	NA	OR, 3.7 (3.67–3.72)	OR, 1.41 (1.4–1.42)	2 yr
Barnes et al[27]	NA	7328	NA	NA	NA	11 yr
Panhwar et al[28]	NA	UC: 58,060 CD: 66,490	NA	NA	NA	5 yr
Card et al[29]	NA	532	469	NA	555	10 yr
Aniwan et al[19]	NA	75	NA	53	NA	NA
Kristensen et al[30]	NA	365	778	NA	454	6.04 yr
Gill et al[31]	IBD: 255 UC: 137 CD: 136	IBD: 302 UC: 152 CD: 175	IBD: 67 UC: 31 CD: 41	NA	NA	4.4 yr
Ha et al[7]	NA	IBD: 148 UC: 83/9968 CD: 65/7480	NA	NA	IBD: 307 UC: 170 CD: 136	NA
Bernstein et al[32]	NA	NA	NA	NA	NA	NA
Yarur et al[33]	NA	47	NA	7	NA	53.12 mo
Osterman et al[21]	NA	UC: 280 CD: 110	NA	NA	NA	4.5 yr
Sridhar et al[37]	NA	7119	NA	NA	785	NA
Dregan et al[5]	NA	NA	NA	NA	164	NA
Keller et al (UC)[34]	NA	NA	NA	NA	53	NA
Keller et al (CD)[35]	NA	NA	NA	NA	283	NA
Choi et al[36]	CD: 455 UC: 1354	CD: 146 UC: 440	NA	NA	CD: 100 UC: 495	NA

CD = Crohn disease, CVD = cardiovascular disease, IBD = inflammatory bowel disease, NA = not available, UC = ulcerative colitis.

disease process resulting in systemic inflammation and inflammatory reactions within the intestinal lumen.[42,43] The systemic inflammatory state in IBD sets in motion events that favor cardiovascular disease, the elevation of Tumor Necrosis Factor Alpha (TNF-α), interleukin (IL) 1, 6, 8, and 12, C-reactive protein (CRP), and calprotectin trigger the increase in reactive oxygen species (ROS), decreased proliferation, increased apoptosis leading to endothelial dysfunction, atherosclerosis, and hypercoagulability.[44] Patients with IBD have abnormal increases in carotid intimal thickening and stiffness; these findings are strong indicators of atherosclerosis; the use of steroids in the treatment of IBD is another huge factor for the initiation and acceleration of cardiovascular disease (Fig. 1).[45]

Recent studies have shown that a novel group of stromal cells underneath the epithelium in the lamina propria have key roles in worsening UC through over-expression of immune-cell-attractant chemokines (CCL) 19 & 21, and IL-33.[46]

In 2018, a retrospective study at Mayo Clinic revealed that IBD patients had twice as much risk for HF than their non-IBD counterparts after adjusting for traditional cardiovascular risk factors (HR, 2.03; 95% CI, 1.36–3.03), with the highest incidence in females with UC.[19] This was similar to a Danish

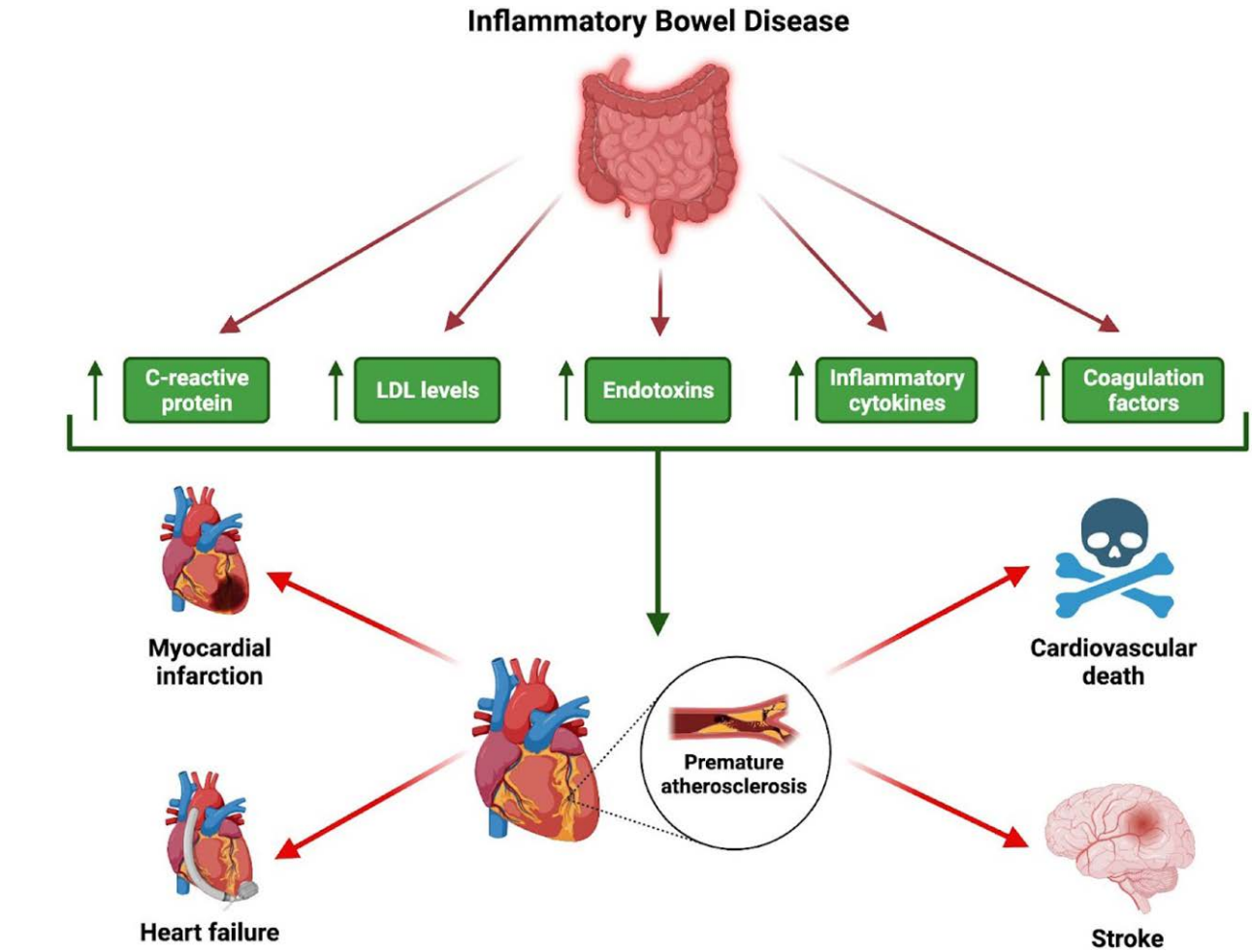

Figure 1. Central illustrations showing possible association between IBD patients and cardiovascular outcomes. IBD = inflammatory bowel disease.

cohort study where IBD patients had a 37% increase in risk for hospitalization for HF compared to the control group.[30] In a meta-analysis by Siddharth et al[1–4], individuals with IBD showed a 20% increased risk of CVD.[47] Lee et al found a significant association between patients with IBD having a higher likelihood of premature (i.e., age less than 55 years), and extremely premature (less than 40 years) risk for ASCVD. Interestingly, this association was stronger among the younger group (i.e., those less than 40 years old).[48] This study is in concordance with the National Health Interview Survey study by Khurram et al, where there was an independent association between IBD and ASCVD with a predominantly stronger association among the younger individuals between 18 and to 44 years of age.[41]

The stronger association in the younger population is probably a result of higher flares and active disease in the select population; this was noted in a study conducted by Panhwar et al,[28] they noted that individuals diagnosed with IBD had the highest risk of ASCVD during the first year of diagnosis than later in life. The Danish study, which included 20,795 patients, also showed that the risk of myocardial infarction, stroke, and cardiovascular death was significantly increased during IBD flares.[30] The US has one of the greatest burdens of IBD. With the potential risk to the young population, more research is warranted to understand the phenomenon and ways to reduce morbidity and health care burden.

4.2. CVD prevention in IBD

One of the greatest challenges clinicians face in this area is the lack of concrete recommendations available to guide clinical decisions; This is made more complex because the commonly used risk assessment parameters do not capture the risk in those with IBD. More studies and collaborative efforts between preventive cardiologists and gastroenterologists are essential in this area.[49] The primary prevention for ASCVD by the American heart association, American College of Cardiology, and European Society of Cardiology (AHA/ACC/ESC) have acknowledged that certain conditions with inflammatory states, such as IBD, have increased risk for ASCVD. According to ACC/AHA recommendations for chronic inflammatory conditions such as psoriasis, rheumatoid arthritis, lupus, and HIV/AIDS in individuals with intermediate risk (>7.5% to <20%), coronary artery calcium measurement can be a useful tool for opting nonintervention therapies, for example, statins,[50] however, there are no clear-cut recommendations for patients with IBD. Recently ESC recommendations for cardiovascular prevention highlighted IBD conditions as one of the risk factors for CVD. These patients must be treated with a similar approach as in high-risk populations with the evidence of beneficial traditional methods to reduce risk and prevent ASCVD.[51] Like most preventive approaches in medicine, the primary care physician (PCP) plays an important role in CVD prevention in IBD patients. Some studies have shown that individuals with IBD are less likely to be given preventive care when compared to individuals without IBD; The suggested reason for the disparity includes; greater focus on the disease itself, lack of consensus between the gastroenterologist and the PCP in regards to which provider is responsible with providing preventive healthcare services in these subgroups, a collaboration between the PCP,

preventive cardiologist, and gastroenterologist is crucial for holistic care.[52]

Exercise and weight loss can often aid in the prevention of CVD outcomes in IBD, as they are important contributors to years lived with disability. A study involving 240,984 military adolescent male recruits revealed that exercise and physical fitness might reduce systemic inflammation, which is likely beneficial for patients with symptomatic disease.[53] Although malnutrition can complicate and worsen the outcomes of IBD, obesity may be associated with higher disease activity.[54,55] Physical activities to improve muscle mass and prevent osteoporosis help improve the quality of life and overall prognosis.[55] Smoking cessation can affect the overall prognosis for IBD patients, which depends on the subtypes: CD or UC. Smoking is protective in patients with UC. However, it has a devastating effect on patients with CD.[56] Therefore, the gastroenterologist and PCP should perform a smoking screening during clinical encounters. Achieving cessation requires a multifaceted approach; nicotine replacement therapy alone or in combination with bupropion or varenicline has been shown to have superior results than placebo by 20%.[57] In addition to this, the prevention of venous thromboembolism is crucial in IBD patients. Due to the pro-atherogenic factors driving pro-inflammatory states in IBD patients, these patient groups are at a 3.5 times higher rate of developing venous thromboembolism (VTE) compared to control groups. Although the relative risk of VTE in this group is inversely correlated with age, the incidence does increase with age.[58] Prophylaxis for VTE during hospitalization and an extended duration after hospital discharge has been shown to reduce VTE incidence in this population.[59]

4.3. Treatment of IBD and prospective outcomes for cardiovascular disease

The mainstay treatment options for IBD include steroids, anti-inflammatory salicylates, and immunotherapies such as anti-TNF-α agents. While the efficacy of these therapies are well studied in achieving symptomatic relief amongst patients with UC and CD, there are emerging concerns regarding ASCVD risk. For example, oral corticosteroid usage has been shown to potentially increase the risk of HF and adverse cardiovascular events such as thromboembolism.[44] It is thought that long-term usage of steroids can cause insulin resistance, thus attenuating traditional risk factors for ASCVD, such as hyperlipidemia and hyperglycemia. Moreover, increased sodium water retention can often increase blood pressure, exacerbating HTN. As a result, the risk of cardiovascular events could be driven by short-term steroid usage for acute inflammatory flares among IBD patients.

On the other hand, the outcomes of salicylate usage, the first-line drug for UC, is not entirely clear. 5-aminosalicylic acid exerts anti-inflammatory and anti-platelet effects, which could reduce the risk of CAD and thromboembolism in IBD patients.[44] However, a recent multicentre study suggested that IBD patients on high doses of salicylates experienced aortic stiffness, which conferred with an earlier study suggesting a higher risk of CVD amongst a cohort in the UK.[60]

Treatment with anti-TNF-α agents is often recommended to reduce overall inflammation in IBD patients. The literature suggests that the risk of CVD is also significantly lower in IBD patients taking anti-TNF-α therapy by reducing aortic stiffness and imbalances in pro-coagulants (i.e., C-reactive protein and fibrinogen).[61] Certain cardiovascular medications, though they can prevent the risk of CVD, could attenuate the progression and risk of IBD. Statins, first-line lipid-lowering agents, can reduce inflammatory states in IBD patients and can also reduce the usage of oral steroids.[44] As a result, therapies that can reduce gut inflammation while also preventing the risk of adverse cardiovascular events should be considered when choosing the drug of choice for IBD.[62]

JAK inhibitors are small molecules, orally available, which is more acceptable than intravenous or subcutaneous administration, rapidly enter the systemic circulations and induce fast symptomatic relief in IBD patients.[63] In recent studies, JAKinibs have been shown to increase lipid levels, which can be a potential risk factor for cardiovascular diseases.[64,65] Similarly, a study conducted by Ytterberg et al[66] showed an increased risk of major adverse cardiovascular events in those patients receiving Tofacitinib compared to those receiving TNF inhibitors.

4.4. Strength and limitations

To our knowledge, this review comprises a comprehensive number of patients with IBD to highlight the cardiovascular risk among IBD patients (CD and UC). The major limitation of our study was the lack of randomized controlled trials among IBD patients with adverse cardiovascular events. We have excluded studies such as case reports and case series, including small sample size.

5. Conclusion

IBD patients are at higher risk for adverse cardiovascular outcomes, especially in women.

Although there remains a lack of concrete treatment algorithms and assessment parameters that better characterize IBD risk factors, nutritional modifications, and physical activity should be at the forefront of CVD prevention in IBD. Future large randomized controlled trials are warranted for proper management and cardiovascular prevention.

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