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Review Article

Prevalence, risk factors and implication of venous thromboembolism in inflammatory bowel disease

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ABSTRACT

Inflammatory bowel disease (IBD) is a chronic inflammatory disease that affects the gastrointestinal system and includes Crohn's disease and ulcerative colitis. Globally IBD accounts for approximately 84.3 cases per 100,000 persons. A well-known extraintestinal manifestation of IBD that increases morbidity and mortality in IBD patients is venous thromboembolism additionally its association with IBD is growing in importance as a result of the global incidence and prevalence of IBD being on the rise. Patients with IBD have a higher risk of developing venous thromboembolism. Prothrombotic mechanisms that include triggering activation of coagulation, which is partially mediated by weakening of the intestinal barrier and released bacterial components, predispose people with IBD to arterial and venous thrombosis. Clinical characteristics of venous thromboembolism in IBD include an earlier onset, high rates during active and remission stages, greater recurrence rates, and a poor prognosis. Surgery, old age and the use of drugs like corticosteroids or tofacitinib may raise the risk of venous thromboembolism in IBD patients. Post-thrombotic syndrome and a high recurrence incidence following hospital discharge are two long-term effects of venous thromboembolism. IBD outpatients frequently develop venous thromboembolism, hence it is advised that high-risk patients have prophylactic treatment timely. It is essential to keep emphasising on preventing and treating venous thromboembolism in IBD patients appropriately for which further research can be beneficial. The purpose of this research is to review the available information about prevalence, risk factors and implication of venous thromboembolism in IBD.

Keywords: IBD, Venous, Thromboembolism, Prevalence

INTRODUCTION

Crohn's disease and ulcerative colitis are the two main types of chronic bowel diseases included under idiopathic IBD. IBD has a peak start between the ages of 15 and 30 years and is the second most prevalent inflammatory illness. Although Crohn's disease mostly affects the ileum and colon, it can also frequently affect any other part of the digestive tract. The rectum is affected by ulcerative colitis, which can also continuously affect the entire colon or just a portion of it. In contrast to ulcerative colitis, where the mucosa is often the only area of inflammation, Crohn's disease frequently exhibits transmural inflammation. Although intestinal granulomas, strictures, and fistulas can be found in Crohn's disease, similar conditions are uncommon in ulcerative colitis. However, the exact origin of IBD has not yet been fully determined, it is widely acknowledged that the disease is brought on by a dysregulated mucosal immune response to environmental stimuli in genetically vulnerable hosts.[1] With 84.3 cases per 100,000 persons worldwide, IBD is one of the most common kinds of chronic inflammatory illnesses.[2]

Venous thromboembolism (VTE) is a widespread, fatal condition that affects both hospitalized and outpatient individuals and includes deep vein thrombosis and pulmonary embolism. VTE is common in IBD patients and is a significant source of morbidity and mortality in them.[3] A complex interplay of systems, including the coagulation cascade, natural coagulation inhibitors, fibrinolytic system, endothelium, immune system, and platelets, results in the disease's hypercoagulable character. Pregnancy, active disease, more widespread or complicated disease, hospitalization, the use of certain drugs, and IBD-related procedures are other clinical variables that raise the risk of a VTE incident in IBD patients. Despite the safety of pharmacologic prophylaxis and the elevated risk of VTE in IBD patients, compliance rates among hospitalized IBD patients seem to be low.[4]

Patients with IBD have a 3 to 4-fold higher risk of VTE and are impacted by VTE at a younger age than people without IBD. VTE is more common in IBD patients, and there have been reports of higher fatality rates from pulmonary embolism. The most frequent sites of deep vein thrombosis in individuals with IBD include the lower and upper limbs, as well as pulmonary embolism. However, uncommon sites of thrombosis, such as the cerebral, portal, mesenteric, or retinal veins, have also been reported. The majority of IBD patients have active illness, fistulas, and abscesses at the time of the thromboembolic event. Additionally, IBD patients are more frequently exposed to disease-related risk factors like surgery, immobility, dehydration, and central venous catheters that may cause VTE. The two main side effects of VTE are mortality and recurrence of thromboembolism.[5]

As the prevalence of IBD and life expectancy rise, VTE occurrences in IBD may also rise. Although the incidence of arterial thromboembolism is substantially lower than that of VTE, individuals with IBD need to be closely watched for an elevated risk of cardiovascular illnesses. Patients with IBD have a greater risk of VTE at baseline, and this risk rises further following surgery and corticosteroid treatment. Post-thrombotic syndrome and chronic thromboembolic pulmonary hypertension are examples of long-term effects of VTE. Therefore, continuous efforts should be made to adopt VTE prophylaxis, examine the value of post-discharge prophylaxis, and concentrate on prevention. Incomplete knowledge exists on the complex pathophysiology of thromboembolism in IBD although it is understood that the activation of coagulation plays a crucial role in the development and potential pathophysiology of the inflammatory response in IBD. The gut microbiome may be a novel strategy for reducing the risk of thrombosis in IBD, whereas intestinal bacterial components may cause the coagulation cascade to occur in this condition.[6] The purpose of this research is to review the available information about prevalence, risk factors and implication of VTE in IBD.

LITERATURE SEARCH

This study is based on a comprehensive literature search conducted on November 9, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about prevalence, risk factors and implication of VTE in IBD. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

IBD is a complicated, systemic, inflammatory disorder that can cause problems within the intestines as well as external problems. The emergence of VTE is one of the most harmful extra-intestinal consequences of IBD. VTE is a well-known IBD complication, especially when there is active inflammation present or in the immediate aftermath of surgery. Current clinical practice guidelines on the use of VTE prophylaxis advise against chemoprophylaxis in children with IBD who are hospitalized and have not experienced a previous VTE incident but advocate treatment for adults with IBD who are hospitalized or have active disease and a previous VTE event. Children with ulcerative colitis who are having surgery or who have acute, severe ulcerative colitis in the presence of other variables known to enhance the risk of VTE are also advised to receive VTE prophylaxis.[7]

Prevalence

IBD increases the likelihood of VTE events. In a population-based study, patients with IBD had rates of deep vein thrombosis and pulmonary embolism of 30 per 10,000 person-years and 10-20 per10,000 person-years respectively. Compared to the general population, people with IBD had a risk of VTE that was more than three times higher. According to several retrospective studies, the death rate for people with IBD after an acute VTE varies from 8% to 25%. Thus, thromboembolism appears to be a disease-specific extraintestinal manifestation of IBD and is a significant source of morbidity and mortality.[8] Results of a population-based study showed that in the IBD group, the incidence of VTE was 7.6%, which was substantially higher than the incidence in the controls (3.3%, p<0.0001). VTE incidence rates overall, age-standardized, were 433 per 100,000 in IBD and 184 per 100,000 in controls. In comparison to ulcerative colitis (6.9%), Crohn's disease (8.4%) had a greater incidence of VTE (p=0.0028). IBD incidence rate ratio was 2.36 (95% confidence interval: 2.16-2.58) compared to controls. When comparing Crohn's disease to ulcerative colitis, the increased risk was comparable for both men and women. Between 1985 and 2018, there was a very modest decline in the incidence rate among IBD patients, with an annual percent change of -0.7% (p=0.0003).[9] McCurdy et al. concluded in their findings that patients with non-surgical IBD and surgical patients with ulcerative colitis are 1.7 times more likely than non-IBD patients to suffer post-discharge VTE.[10]

Hospitalization rates for VTE-related conditions are rising among IBD patients as reported by Faye et al study findings that when stratified by ulcerative colitis, Crohn's disease, deep vein thrombosis, and pulmonary embolism, the risk of VTE among hospitalized IBD patients rose from 192 to 295 occurrences per 10,000 hospitalizations and remained significant.[11] Results of a population-based cohort study showed that compared to controls without IBD, children with IBD have a significantly increased risk of VTE. Compared to 16 289 children without IBD, 3593 children with IBD experienced a 5-year incidence of VTE of 31.2 per 10,000 person-years. Compared to ulcerative colitis, Crohn's disease had a lower incidence of VTE. When comparing children with and without IBD, the results for deep vein thrombosis and pulmonary embolism were comparable.[12] Similarly results of another international cohort study revealed that compared to the overall paediatric population, the group with paediatric-onset IBD has a higher risk of VTE. VTE incidence was 3.72 per 10 000 person-years, which is 14 times greater than the prevalence of VTE in the overall paediatric population. Most cases of cerebral sinus venous thrombosis were reported.[13]

Findings of a meta-analysis concluded that the prevalence and risk of VTE are much higher in children and adolescents with IBD.[14] Heo et al reported in their nationwide cohort study findings that when patients were hospitalized for flare-ups, the incidence rate per 1000 person-years was 15.26, whereas it was 9.83 when patients were hospitalized for non-flare-ups. The incidence rate per 1000 person-years during hospitalizations with flare varied by age category, with young patients including age 20-39 years having a 14.53 incidence rate and older patients having a 34.58 incidence rate including age 60-80 years. The occurrence rate for young patients and older patients during non-flare hospitalization periods was 3.55 and 23.61, respectively.[15] Results of a population-based inception cohort showed that VTE emerged in patients with IBD at a rate of 1.03 per 1000 patient-years. Extensive location was connected to a higher incidence of VTE in ulcerative colitis. Males had a higher frequency of ulcerative colitis, and it was linked to severe disease, fulminant episodes, diseases that required corticosteroids, smoking, but not to age at commencement.[16]

Risk factors and implications

Ageing, steroid medication, surgery, obesity, and ulcerative colitis are all linked to an increased risk of VTE in people with IBD. One of the frequent co-morbidities of individuals with IBD is a higher propensity to venous thromboembolic events, which is linked to a poor prognosis for short and long-term morbidity and mortality.[2] Ando et al. revealed in their study findings that seven risk variables for VTE with IBD were identified in a univariate analysis. The proportion of elderly patients (p=0.0180), particularly those over 50 (p=0.0012), CV catheters (p<0.0001), prednisolone prescriptions (p<0.0001), and surgery (p<0.0001) was higher in the VTE group with IBD. When the laboratory data from the two groups were compared, the IBD patients with VTE had significantly greater levels of C-reactive protein (p=0.0260), D-dimer (p=0.0022), and serum albumin (p=0.0002) than the other group. Serum albumin 3.0 g/dl (p<0.0001), C-reactive protein >1.0 mg/dl (p=0.015), and D-dimer 1.5 ng/L (p=0.0010) were the cut-off values. Only age >50 years and surgery were identified as independent risk factors in a multivariate analysis with a logistic regression analysis.[17]

IBD itself is believed to be a risk factor for VTE. Two population-based studies have found that people with ulcerative colitis who are hospitalized have a higher relative risk of VTE. People with ulcerative colitis have a greater risk of VTE than those with Crohn's disease. When compared to hospitalized individuals without inflammatory bowel disease, the incidence of VTE in Crohn's disease patients was not significantly different. However, patients with ulcerative colitis had a greater risk of pulmonary embolism. Two further studies demonstrated that the incidence rates of deep venous thrombosis were comparable across the two disorders.[18] Similarly results of a population-based cohort study demonstrated that patients with IBD had a 1.93-fold higher risk (p<0.001) than the general population of having deep vein thrombosis. While the absolute risks

rose with age, hazards ratio were particularly high in the young IBD cohort compared to the non-IBD cohort. Particularly, this increase was more prominent in ulcerative colitis patients compared to Crohn's disease patients. After controlling for common VTE risk factors such as diabetes mellitus, cardiovascular disease, atrial fibrillation, cerebral vascular disease, chronic kidney disease, and malignancy, IBD is a significant independent risk factor for VTE. Patients with IBD had an approximately 90% higher risk of developing VTE than did controls. The adjusted hazards ratio for VTE in IBD patients 60 years of age or older was significantly greater than the adjusted hazards ratio for VTE in patients 19 years of age or younger. Significant risk variables for VTE in individuals with IBD were older age, female sex, higher Charlson comorbidity index scores, cardiovascular illness, chronic kidney disease, use of steroids, and hospitalization.[19]

Magro, Soares and Fernandes described in their study that inflammatory activity, hospitalization, surgery, pregnancy, disease phenotype such as fistulizing disease, colonic involvement, and severe involvement, and pharmacological therapy mainly steroids are some acquired variables that enhance the risk of VTE in IBD. Basic science, clinical, and epidemiological studies have also provided strong evidence that IBD is linked to a number of prothrombotic abnormalities, such as the activation of the coagulation system, downregulation of natural anticoagulant mechanisms, impairment of fibrinolysis, increased platelet count and reactivity, and endothelial dysfunction. IBD patients do not typically exhibit more common classical genetic abnormalities than do non-IBD individuals, indicating that genetics is not the cause of the increased risk of VTE in these patients. Clinical characteristics of IBD with VTE include an earlier first episode of VTE in life, a high likelihood of recurrence, a lower effectiveness of several medicines in preventing further episodes, and a poor prognosis. Clinicians need to be aware of these risks and take the proper preventative measures for patients who are hospitalized, undergoing surgery, or receiving treatment.[20]

Nguyen et al stated that patients with IBD have a risk of VTE that is almost three times higher than that of people without the condition, and disease flares make the risk much higher. For IBD patients who are hospitalized for IBD flares without active bleeding and when bleeding is mild to moderate, anticoagulant thromboprophylaxis is advised. In outpatients with a history of VTE triggered by an IBD flare or an unprovoked VTE, anticoagulant thromboprophylaxis is advised only during moderate-to-severe IBD flares. Based on the presence of inciting factors, the length of anticoagulation after a first VTE is advised. For the prevention and treatment of VTE in young patients with IBD who are pregnant, specific recommendations are offered.[21] Literature elaborately explains the association of VTE and IBD hence further research can be beneficial in developing evidence based preventive therapeutic strategies to reduce the risk of VTE events in IBD patients.

CONCLUSION

VTE is a prevalent complication of IBD and contributes to significant morbidity and mortality in IBD patients. Prophylactic treatment among high-risk IBD patients can reduce the risk of VTE however further clinical research is required to develop more effective treatment guidelines for the prevention of VTE in IBD patients hence reducing the burden of the disease.

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REFERENCES

1. Corridoni D, Arseneau KO, Cominelli F. Inflammatory bowel disease. Immunol Letters. 2014;161(2):231-5.
2. Zhang H, Wang X. Risk Factors of Venous Thromboembolism in Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. Frontiers Med. 2021;8:693927.
3. Bruni-Fitzgerald KR. Venous thromboembolism: An overview. J Vascular Nursing. 2015;33(3):95-9.
4. Cheng K, Faye AS. Venous thromboembolism in inflammatory bowel disease. World J Gastroenterol. 2020;26(12):1231-41.
5. Novacek G, Weltermann A, Sobala A. Inflammatory Bowel Disease Is a Risk Factor for Recurrent Venous Thromboembolism. Gastroenterology. 2010;139(3):779-87.
6. Stadnicki A, Stadnicka I. Venous and arterial thromboembolism in patients with inflammatory bowel diseases. World J Gastroenterol. 2021;27(40):6757-74.
7. Scoville EA, Konijeti GG, Nguyen DD, Sauk J, Yajnik V, Ananthakrishnan AN. Venous thromboembolism in patients with inflammatory bowel diseases: a case-control study of risk factors. Inflammatory Bowel Dis. 2014;20(4):631-6.
8. Nguyen GC, Sam J. Rising prevalence of venous thromboembolism and its impact on mortality among hospitalized inflammatory bowel disease patients. Am J Gastroenterol. 2008;103(9):2272-80.
9. Bernstein CN, Nugent Z, Singh H. Persistently High Rate of Venous Thromboembolic Disease in Inflammatory Bowel Disease: A Population-Based Study. Am J Gastroenterol. 2021;116(7):1476-84.
10. McCurdy JD, Kuenzig ME, Smith G. Risk of Venous Thromboembolism After Hospital Discharge in Patients With Inflammatory Bowel Disease: A Population-based Study. Inflammatory Bowel Dis. 2020;26(11):1761-8.
11. Faye AS, Lee KE, Dodson J. Increasing rates of venous thromboembolism among hospitalised patients with inflammatory bowel disease: a

nationwide analysis. Aliment Pharmacol Ther. 2022;56(7):1157-67.
12. Kuenzig ME, Bitton A, Carroll MW. Inflammatory Bowel Disease Increases the Risk of Venous Thromboembolism in Children: A Population-Based Matched Cohort Study. J Crohn's Colitis. 2021;15(12):2031-40.
13. Aardoom MA, Klomberg RCW, Kemos P. The Incidence and Characteristics of Venous Thromboembolisms in Paediatric-Onset Inflammatory Bowel Disease: A Prospective International Cohort Study Based on the PIBD-SETQuality Safety Registry. J Crohn's Colitis. 2022;16(5):695-707.
14. Zhang XY, Dong HC, Wang WF, Zhang Y. Risk of venous thromboembolism in children and adolescents with inflammatory bowel disease: A systematic review and meta-analysis. World J Gastroenterol. 2022;28(16):1705-17.
15. Heo CM, Kim TJ, Kim ER. Risk of venous thromboembolism in Asian patients with inflammatory bowel disease: a nationwide cohort study. Sci Rep. 2021;11(1):2025.
16. Vegh Z, Golovics PA, Lovasz BD. Low incidence of venous thromboembolism in inflammatory bowel diseases: prevalence and predictors from a population-based inception cohort. Scandinavian J Gastroenterol. 2015;50(3):306-11.
17. Ando K, Fujiya M, Nomura Y, et al. The incidence and risk factors of venous thromboembolism in Japanese inpatients with inflammatory bowel disease: a retrospective cohort study. Intestinal Res. 2018;16(3):416-25.
18. Saleh T, Matta F, Yaekoub AY, Danescu S, Stein PD. Risk of venous thromboembolism with inflammatory bowel disease. Clin Appl Thrombosis/hemostasis. 2011;17(3):254-8.
19. Kim SY, Cho YS, Kim HS. Venous Thromboembolism Risk in Asian Patients with Inflammatory Bowel Disease: A Population-Based Nationwide Inception Cohort Study. Gut Liver. 2022;16(4):555-66.
20. Magro F, Soares JB, Fernandes D. Venous thrombosis and prothrombotic factors in inflammatory bowel disease. World J Gastroenterol. 2014;20(17):4857-72.
21. Nguyen GC, Bernstein CN, Bitton A. Consensus statements on the risk, prevention, and treatment of venous thromboembolism in inflammatory bowel disease: Canadian Association of Gastroenterology. Gastroenterology. 2014;146(3):835-8.

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