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Prevention of Venous Thromboembolism in Patients with Inflammatory Bowel Disease

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Key Takeaways:

- When reviewing inflammatory bowel disease (IBD) patients in the clinical setting, remember to review their medical history and screen for venous thromboembolism (VTE) risk factors. This will help to risk stratify them for future decision-making.
- IBD patients admitted to hospital are at the highest risk of VTE. All IBD patients, regardless of reason for admission and disease activity, should receive VTE prophylaxis.
- In the post-operative and post-discharge setting, all IBD patients should be classified as low, intermediate, or high risk of VTE. After carefully weighing the risks and benefits, high risk patients should be considered for extended VTE prophylaxis beyond hospital discharge.

Introduction

Venous thromboembolism (VTE) is a major cause of morbidity and mortality worldwide and remains a preventable cause of death among hospitalized patients.[1] Given its potential devastating health consequences, VTE is one of the most important intestinal manifestations to monitor and prevent in patients with Inflammatory Bowel Disease (IBD). IBD patients are at an increased risk for VTE due to their underlying inflammatory state, which contributes to aberrant platelet and procoagulant alterations, dysregulated fibrinolysis, and endothelial dysfunction.[2] In addition to this hypercoagulable state, the risk of VTE in IBD patients is often compounded by other co-existing risk factors such as hospitalization or surgery.[3]

At baseline, IBD patients have an up to 3-fold increased risk of VTE compared to those without IBD. This risk climbs even higher during hospitalization, reaching a 6-fold increase.[4,5] The elevated risk of VTE persists after hospitalization, with population-based studies showing VTE rates

as high as 3% within 6 months after discharge.[6,7] Although the incidence is highest during hospitalization, the relative risk of VTE during an ambulatory flare is almost 16-fold greater than that of the general population.[4]

Identifying high-risk patients and providing prophylaxis in the appropriate clinical settings is critical for preventing thrombosis in this susceptible patient group. In this article, I will review the current evidence and recommendations, as well as highlight existing knowledge gaps related to VTE prophylaxis in IBD patients.

What Do the Guidelines and Current Evidence Recommend?

The Toronto and International Consensus guidelines acknowledge the significantly elevated risk of VTE in IBD patients, particularly during periods of active disease and hospitalization.[8,9] Although the highest risk groups are those hospitalized with active disease flares, even patients in clinical remission who are hospitalized for unrelated reasons carry an up to 3-fold risk of VTE compared to non-IBD patients.[5] For this reason, both sets of guidelines have clear recommendations for thromboprophylaxis for hospitalized patients, irrespective of the reason for admission. These recommendations are in line with the most recent guidelines from the American College of Chest Physicians and the American Society of Hematology (ASH) on the prevention and prophylaxis of VTE in medical patients.[10,11]

Previous studies have demonstrated that chemical prophylaxis with anticoagulants is safe for IBD patients without a significant increased risk of bleeding, even among those presenting with rectal bleeding on admission.[12] Apart from clinical situations with severe IBD-related gastrointestinal bleeding, chemical prophylaxis remains the recommended primary treatment. In cases of severe bleeding, mechanical prophylaxis with intermittent pneumatic compression should be used instead until the bleeding is no longer severe.[8]

Although VTE risk is highest during hospital admission, it does not immediately return to baseline upon discharge from hospital. However, considering the diminished risk after hospitalization, there are no guideline recommendations supporting universal extended prophylaxis for all patients. Instead, the International Consensus Guidelines recommend considering extended prophylaxis for those with a "very high risk of VTE".[9] Similarly, the American Society of Colon and Rectal Surgeons recommends considering extended prophylaxis in the postoperative setting for IBD patients deemed to be at high risk.[13] A retrospective study by McCurdy et al. developed a risk prediction model to identify patients with IBD at increased risk for post discharge VTE.[6] This model enabled the authors to better identify patients at high risk of VTE who might benefit from anticoagulation. However, further external validation of this model is required before universal use. Based on available evidence, no guideline recommendations have clearly outlined which specific risk factors should be considered, or how many must be present before initiation of extended prophylaxis is warranted. Physicians caring for IBD patients must use clinical gestalt and shared decision making when considering the need for extended prophylaxis on a case-by-case basis.

Consensus guidelines do not routinely recommend prophylactic anticoagulation for patients with IBD flares undergoing treatment in the outpatient setting. Although the relative risk of VTE during an outpatient flare can be up to 16-fold higher compared to the general public, the absolute risk remains too low to recommend prophylaxis in the absence of other risk factors.[8,9] In addition, a previous Markov decision analysis found that this intervention is not cost effective.[14] However, certain cases may warrant prophylaxis in the ambulatory setting. Considering that the risk of recurrent VTE in IBD patients is 2.5-fold higher compared with non-IBD patients, the Toronto Consensus recommends thromboprophylaxis to prevent recurrent VTE during moderate-to-severe ambulatory disease flares.[8] Patients omitted from this recommendation include those whose initial episode of VTE was provoked by surgery, as these patients are considered to have a lower risk of recurrence.[15] In contrast, the International Consensus Guidelines recommend considering prophylaxis in ambulatory patients who have known major or multiple risk factors, not just those with a previous VTE history.[9] Given inflammation is a key driver of VTE risk in these cases, prophylaxis, if initiated, should be continued until remission is achieved. As with post discharge management, the decision to initiate VTE prophylaxis in the outpatient setting should be at the discretion of the treating physician on a case-by-case basis after an assessment of the patient's individualized risk.

Where Do Our Guidelines Fall Short?

Evidence and guideline recommendations are clear on the benefits of inpatient VTE prophylaxis and recommend its use for most patient populations. However, the role of extended and ambulatory VTE prophylaxis, is less clearly defined. Although current guidelines recommend consideration of prophylaxis for high-risk patients in these settings, there is a paucity of high-quality evidence to guide clinicians in identifying which patients are most likely to benefit. Key questions remain unanswered, such as which risk factors are most relevant, how many are needed to justify intervention, and what clinical decision tools should be used? Further evidence and guidance is needed to aid in identifying which patients are most likely to benefit from VTE prophylaxis.

How Do We Identify the High-risk Patients?

The challenge in implementing extended prophylaxis is identifying the patient group most likely to benefit. A review of this topic by Murthy et al. proposed an algorithm in which patients are classified into low (<1%), intermediate (1–5%) or high risk (>5%) categories, which recommended extended prophylaxis for the high-risk patient group.[7] This appears to be a reasonable approach, particularly considering a previous study had identified that extended prophylaxis with enoxaparin is cost effective when the risk of VTE exceeds 4.9%.[16] Although several clinical predictive models, such as Padua, IMPROVE, and Caprini are available to help identify high-risk patients, these tools were developed for the general population and are not specific to IBD patients.[17-19] A recent systematic review characterized IBD risk factors across multiple phases of care.[3] While many of the risk factors identified, such as a previous history of VTE and age, are well-established in the general population, the review also identified significant IBD-specific risk factors, such as corticosteroid exposure, *Clostridioides difficile* infection, malnutrition, and inflammatory disease extent. Of note, IBD-related medications were an important group of factors reviewed in the study. Corticosteroids were associated with increased VTE risk, although this is difficult to interpret considering these medications are typically used during active disease flares. Considering that active disease is a known independent risk factor for VTE, this association may simply be a surrogate marker for active disease. Importantly, other IBD therapies, including biologics, Janus kinase (JAK) inhibitors, 5-ASA, and immunomodulators, were not associated with an increased risk of VTE. In fact, anti-tumour necrosis factor (TNF) biologics were found to be protective against VTE with an odds ratio of 0.66 (95% confidence interval 0.46–0.97), which is consistent with previous studies and animal models suggesting that anti-TNF therapy may directly reduce VTE risk.[20,21] Notably, JAK inhibitor therapy was not associated with an increased risk of VTE in this systematic review, despite a potential risk identified in rheumatoid arthritis patients that resulted in an FDA warning.[22] The review examined multiple risk factor categories, including medical comorbidities, IBD characteristics, and surgical characteristics, among others. Many of these risk factors are specific to IBD, and can serve to guide future prospective studies and the development of IBD-specific clinical predictive models. Once developed and validated, these models can better inform clinicians when considering VTE prophylaxis.

How Can We Make VTE Prophylaxis Cost Effective?

To expand the use of VTE prophylaxis among IBD patient groups, it needs to demonstrate effectiveness in preventing VTE, maintain a favourable safety profile, and be cost effective. A 2019 Canadian study showed that a 28-day course of extended prophylaxis with enoxaparin, while associated with higher costs, improved quality-adjusted life-years along with incremental cost-effectiveness ratios in IBD patients undergoing colorectal surgery.[23] However, two additional cost-benefit decision analyses in IBD patients undergoing surgery found that extended prophylaxis was not a cost-effective intervention.[24,25] As discussed earlier, a previous decision analysis assessing the cost-effectiveness of VTE prophylaxis in ambulatory patients also concluded that it was not a cost-effective strategy.[14]

Several therapeutic options for anticoagulation prophylaxis exist, each with widely variable costs. Historically, studies on the cost-effectiveness of VTE prophylaxis in IBD

patients have largely investigated low molecular weight heparin (LMWH). However, alternative agents such as direct oral anticoagulants (DOACs) offer effective VTE prevention and treatment at significantly lower costs compared to LMWH. In the orthopedic literature, DOACs have been shown to be effective in preventing VTE after surgery,[26] and have been incorporated into Thrombosis Canada guidelines for extended prophylaxis.[27] Regarding non-orthopedic surgery, a 2022 study showed that oral rivaroxaban was more effective than placebo for extended VTE prophylaxis after laparoscopic surgery for colorectal cancer without an increase in major bleeding.[28] Finally, the ASH guidelines on VTE prevention in hospitalized surgical patients suggests using extended prophylaxis over short-term prophylaxis, citing a likely modest benefit in reducing VTE with comparable bleeding rates.[29] Importantly, the guidelines recognized that the evidence was limited to orthopedic and major oncologic surgeries.

In medical patients, there is currently no confirmed benefit to using DOACs for extended VTE prophylaxis after hospital discharge.[30,31] It is important to note that IBD patients are underrepresented in these studies, despite their inflammatory burden that places them at a greater risk for VTE compared to the general medical population. As such, more evidence is needed before these therapies can be recommended for routine use in IBD patients. However, if DOACS are shown to be effective for VTE prevention in carefully selected high-risk patient groups, they could offer a more cost-effective intervention compared to LMWH.

Conclusion

While the evidence and guidelines on inpatient VTE prophylaxis is clear, this does not always translate into clinical practice. Despite clear recommendations, adherence rates for VTE prophylaxis is suboptimal, with some studies reporting prophylaxis rates as low as 39.7% among hospitalized patients.[32] Physicians who care for patients with IBD should be aware of the benefits and safety of VTE prophylaxis for hospitalized patients.

To expand the use of extended VTE prophylaxis in IBD populations, it is essential to identify those who may benefit from targeted prophylaxis. This requires further research to stratify patients by risk and guide targeted prophylaxis. As our knowledge of IBD risk factors continues to grow, prospective studies will be needed for creating and validating clinical predictive models that can accurately and reliably identify these high-risk patients. To optimize the cost-benefit of extended and ambulatory prophylaxis interventions, future studies could investigate the use of low dose DOACs, particularly in the post surgical setting where evidence already exists for some patient populations. For now, clinicians will need to consider the known risk factors identified in the literature and assess patients on a case-by-case basis.

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References

1. Wendelboe A, Weitz JI. Global health burden of venous thromboembolism. Arterioscler Thromb Vasc Biol. 2024;44(5):1007-1011. doi:10.1161/ATVBAHA.124.320151
2. Danese S, Papa A, Saibeni S, Repici A, Malesci A, Vecchi M. Inflammation and coagulation in inflammatory bowel disease: the clot thickens. Am J Gastroenterol. 2007;102(1):174-186. doi:10.1111/j.1572-0241.2006.00943.x
3. Gozdzik M, Unninayar D, Siegal DM, Sarker AK, Kim E, Murthy S, et al. Risk factors for venous thromboembolism in inflammatory bowel disease: a systematic review and meta-analysis by phase of care. Inflamm Bowel Dis. Published online May 9, 2025. doi:10.1093/ibd/izaf078
4. Bernstein CN, Blanchard JF, Houston DS, Wajda A. The incidence of deep venous thrombosis and pulmonary embolism among patients with inflammatory bowel disease: a population-based cohort study. Thromb Haemost. 2001;85(3):430-434.
5. Grainge MJ, West J, Card TR. Venous thromboembolism during active disease and remission in inflammatory bowel disease: a cohort study. Lancet. 2010;375(9715):657-663. doi:10.1016/S0140-6736(09)61963-2
6. McCurdy JD, Israel A, Hasan M, Weng R, Mallick R, Ramsay T, et al. A clinical predictive model for post-hospitalisation venous thromboembolism in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2019;49(12):1493-1501. doi:10.1111/apt.15286
7. Murthy SK, McCurdy AB, Carrier M, McCurdy JD. Venous thromboembolic events in inflammatory bowel diseases: a review of current evidence and guidance on risk in the post-hospitalization setting. Thromb Res. 2020;194:26-32. doi:10.1016/j.thromres.2020.06.005
8. Nguyen GC, Bernstein CN, Bitton A, Chan AK, Griffiths AM, Leontiadis GI, et al. Consensus statements on the risk, prevention, and treatment of venous thromboembolism in inflammatory bowel disease: Canadian Association of Gastroenterology. Gastroenterology. 2014;146(3):835-848.e6. doi:10.1053/j.gastro.2014.01.042
9. Olivera PA, Zuily S, Kotze PG, Regnault V, Al Awadhi S, Bossuyt P, et al. International consensus on the prevention of venous and arterial thrombotic events in patients with inflammatory bowel disease. Nat Rev Gastroenterol Hepatol. 2021;18(12):857-873. doi:10.1038/s41575-021-00492-8
10. Kahn SR, Lim W, Dunn AS, Cushman M, Dentali F, Akl EA, et al. Prevention of VTE in nonsurgical patients: antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e195S-e226S. doi:10.1378/chest.11-2296
11. Schünemann HJ, Cushman M, Burnett AE, Kahn SR, Beyer-Westendorf J, Spencer FA, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. [published correction appears in Blood Adv. 2023 May 09;7(9):1671. doi: 10.1182/bloodadvances.2022008147.]. Blood Adv. 2018;2(22):3198-3225. doi:10.1182/bloodadvances.2018022954
12. Ra G, Thanabalan R, Ratneswaran S, Nguyen GC. Predictors and safety of venous thromboembolism prophylaxis among hospitalized inflammatory bowel disease patients. J Crohns Colitis. 2013;7(10):e479-e485. doi:10.1016/j.crohns.2013.03.002
13. Patel SV, Liberman SA, Burgess PL, Goldberg JE, Poylin VY, Messick CA, et al. The American Society of Colon and Rectal Surgeons clinical practice guidelines for the reduction of venous thromboembolic disease in colorectal surgery. Dis Colon Rectum. 2023;66(9):1162-1173. doi:10.1097/DCR.0000000000002975
14. Nguyen GC, Sharma S. Feasibility of venous thromboembolism prophylaxis during inflammatory bowel disease flares in the outpatient setting: a decision analysis. Inflamm Bowel Dis. 2013;19(10):2182-2189. doi:10.1097/MIB.0b013e31829c01ef
15. Iorio A, Kearon C, Filippucci E, Marcucci M, Macura A, Pengo V, et al. Risk of recurrence after a first episode of symptomatic venous thromboembolism provoked by a transient risk factor: a systematic review. Arch Intern Med. 2010;170(19):1710-1716. doi:10.1001/archinternmed.2010.367
16. Leeds IL, DiBrito SR, Canner JK, Haut ER, Safar B. Cost-benefit limitations of extended, outpatient venous thromboembolism prophylaxis following surgery for Crohn's disease. Dis Colon Rectum. 2019;62(11):1371-1380. doi:10.1097/DCR.0000000000001461
17. Vardi M, Ghanem-Zoubi NO, Zidan R, Yurin V, Bitterman H. Venous thromboembolism and the utility of the Padua Prediction Score in patients with sepsis admitted to internal medicine departments. J Thromb Haemost. 2013;11(3):467-473. doi:10.1111/jth.12108
18. Rosenberg D, Eichorn A, Alarcon M, McCullagh L, McGinn T, Spyropoulos AC. External validation of the risk assessment model of the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) for medical patients in a tertiary health system. J Am Heart Assoc. 2014;3(6):e001152. doi:10.1161/JAHA.114.001152
19. Chen X, Pan L, Deng H, Zhang J, Tong X, Huang H, et al. Risk assessment in Chinese hospitalized patients comparing the Padua and Caprini scoring algorithms. Clin Appl Thromb Hemost. 2018 Dec;24(9_suppl):127S-135S. doi:10.1177/1076029618797465
20. Sarlos P, Szemes K, Hegyi P, Garami A, Szabo I, Illes A, et al. Steroid but not biological therapy elevates the risk of venous thromboembolic events in inflammatory bowel disease: a meta-analysis. J Crohn's Colitis. 2018;12(4):489-498. doi:10.1093/ecco-jcc/jjx162

21. Yoshida H, Yilmaz CE, Granger ND. Role of tumor necrosis factor-α in the extraintestinal thrombosis associated with colonic inflammation. Inflamm Bowel Dis. 2011;17(11):2217-2223. doi:10.1002/ibd.21593
22. Food and Drug Administration Drug Safety Communication. FDA approves Boxed Warning about increased risk of blood clots and death with higher dose of arthritis and ulcerative colitis medicine tofacitinib (Xeljanz, Xeljanz XR). 2021: [Updated 4 February 2021, cited 26 June 2025]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-boxed-warning-about-increased-risk-blood-clots-and-death-higher-dose-arthritis-and
23. Trepanier M, Alhassan N, Sabapathy CA, Liberman AS, Charlebois P, Stein BL, et al. Cost-effectiveness of extended thromboprophylaxis in patients undergoing colorectal surgery from a Canadian health care system perspective. Dis Colon Rectum. 2019;62(11):1381-1389. doi:10.1097/DCR.0000000000001438
24. Leeds IL, DiBrito SR, Canner JK, Haut ER, Safar B. Cost-benefit limitations of extended, outpatient venous thromboembolism prophylaxis following surgery for Crohn's disease. Dis Colon Rectum. 2019;62(11):1371-1380. doi:10.1097/DCR.0000000000001461
25. Leeds IL, Sklow B, Gorgun E, Liska D, Lightner AL, Hull TL, et al. Cost-effectiveness of aspirin for extended venous thromboembolism prophylaxis after major surgery for inflammatory bowel disease. J Gastrointest Surg. 2022;26(6):1275-1285. doi:10.1007/s11605-022-05287-z
26. Samama CM, Laporte S, Rosencher N, Girard P, Llau J, Mouret P, et al. Rivaroxaban or enoxaparin in nonmajor orthopedic surgery. N Engl J Med. 2020;382(20):1916-1925. doi:10.1056/NEJMoa1913808
27. Thrombosis Canada. Thromboprophylaxis: orthopedic surgery [Internet]. Toronto: Thrombosis Canada; 2020 May 11 [updated 13 March 2025, cited 2025 May 23]. Available from: https://thrombosiscanada.ca/hcp/practice/clinical_guides?language=en-ca&guideID=THROMBOPROPHYLAXISAFTERORTHOPE
28. Becattini C, Pace U, Pirozzi F, Donini A, Avruscio G, Rondelli F, et al. Rivaroxaban vs placebo for extended antithrombotic prophylaxis after laparoscopic surgery for colorectal cancer. Blood. 2022;140(8):900-908. doi:10.1182/blood.2022015796
29. Anderson DR, Morgano GP, Bennett C, Dentali F, Francis CW, Garcia DA, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. Blood Adv. 2019;3(23):3898-3944. doi:10.1182/bloodadvances.2019000975
30. Cohen AT, Harrington RA, Goldhaber SZ, Hull RD, Wiens BL, Gold A, et al. Extended thromboprophylaxis with betrixaban in acutely ill medical patients. N Engl J Med. 2016;375(6):534-544. doi:10.1056/NEJMoa1601747
31. Spyropoulos AC, Ageno W, Albers GW, Elliott CG, Halperin JL, Hiatt WR, et al. Rivaroxaban for thromboprophylaxis after hospitalization for medical illness. N Engl J Med. 2018;379(12):1118-1127. doi:10.1056/NEJMoa1805090
32. Kaddourah O, Numan L, Jeepalyam S, Abughanimeh O, Ghanimeh MA, Abuamr K. Venous thromboembolism prophylaxis in inflammatory bowel disease flare-ups. Ann Gastroenterol. 2019;32(6):578-583. doi:10.20524/aog.2019.0412

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