Should Surgical Inflammatory Bowel Disease Patients Be Given Extended Venous Thromboembolic Prophylaxis Postoperatively?

Amy L. Lightner, MD

Venous thromboembolism (VTE) is a significant health problem in the United States, with nearly 1 million cases each year,[1, 2] resulting in significantly increased cost[3] and mortality.[4] It has been well described that patients with inflammatory bowel disease (IBD) are hypercoagulable and at increased risk of venous thromboembolism.[5] The added insult of surgical intervention puts IBD patients at even higher risk for a venous thromboembolic event in the perioperative period. This is due to intraoperative patient positioning, stretch on the mesentery, and pelvic dissection. Thus, there has been an increasing body of evidence looking at the risk of deep VTE and pulmonary embolism (PE) in patients with IBD undergoing abdominopelvic surgery.[6–9] Unlike the well-established increased risk of VTE in colorectal cancer patients[10] and subsequent national recommendations by the National Comprehensive Cancer Network (NCCN) and the CHEST guidelines[4, 11] for extended postoperative VTE prophylaxis, there are few published data for patients with IBD and, thus, no strong recommendations regarding prolonged postoperative VTE prophylaxis. Rather, more subjective statements based on low-quality evidence such as those made by the American Society of Colon and Rectal Surgeons (ASCRS), which state that "patients with IBD are at high risk for DVT [deep vein thrombosis] and select patients may benefit from extended prophylaxis," guide surgeons regarding the management of extended postoperative VTE prophylaxis in IBD patients.[12] However, as the IBD patient population is becoming a cohort subject to increasing scrutiny due to studies reporting higher rates of postoperative VTE in ulcerative colitis (UC) patients than colorectal cancer patients,[13] national guidelines are inevitable.[8, 14]

Although VTE most commonly refers to lower extremity DVT and PE, portomesenteric venous thrombosis (PMVT) can also present as a significant complication of abdominopelvic surgery in patients with IBD. Reported incidence rates of 3–10%[15, 16] are probably lower than true incidence because most patients are diagnosed by abdominal imaging, and not all patients have computed tomography (CT) scans in the postoperative period. There are likely many asymptomatic patients who never get abdominal imaging who may have a PMVT that goes undiagnosed and untreated with unknown consequences. Kayal et al. have sought to better understand the risk factors for PMVT in patients undergoing surgery for medically refractory UC by doing a retrospective review of 6 years of surgical data at a tertiary IBD referral center. The purpose was to answer an important question: Which patients are at greatest benefit to receive extended postoperative VTE prophylaxis? This is important because PMVT has the potential to result in life-threatening bowel ischemia; administration of systemic anticoagulation fortunately results in the resolution of a PMVT and decreased mortality from PMVT.[17]

Kayal et al. included a total of 434 patients in their analysis, of whom nearly two-thirds had elective surgery and half had a 3-stage approach to restorative proctocolectomy with an ileal pouch anal anastomosis (IPAA). Although no patients were discharged on extended VTE postoperative prophylaxis, nearly all (98.5%) received inpatient postoperative prophylaxis with subcutaneous heparin. The authors found the rate of postoperative PMVT to be 8.3%. It is important to note, however, that this rate comes only from those patients who had a postoperative abdominal CT scan for abdominal pain, and, again, not all patients had a routine postoperative CT scan, thereby limiting our understanding of the true rate of PMVT. Of note, all patients with a PMVT were treated with anticoagulation for 6 months, and following treatment, all patients had complete resolution of their PMVT. No patients had bowel infarction or required surgical intervention to address their PMVT. Although all patients did well, it remains challenging to answer if it is necessary to treat all cases of PMVT, and what the natural course of a PMVT is when left untreated.

When the authors assessed potential risk factors for PMVT, preoperative serum C-reactive protein (CRP) was found to be associated with postoperative PMVT. The authors determined that the optimal CRP cutoff for an association with PMVT was 45 mg/L. Thus, their recommendation was that patients with a preoperative CRP of >45 mg/L receive extended postoperative VTE prophylaxis. This finding is consistent with increased inflammation leading to an increase in hypercoagulability.[18] As most IBD patients have a CRP level

Received for publications June 15, 2019; Editorial Decision July 10, 2019.

From the Department of Colorectal Surgery, Cleveland Clinic, Cleveland, Ohio, USA

Conflicts of interest: Amy Lightner reports consultant fees from Takeda.

Address correspondence to: Amy L. Lightner, MD, Department of Colorectal Surgery, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195 (lightna@ccf.org).

doi: 10.1093/ibd/izz170
Published online 2 August 2019

before surgery, this could certainly be a practical and useful tool to risk-stratify patients to those who needed or did not need VTE prophylaxis. It would be worthwhile and important for future studies to look at the relationship of CRP and DVT/PE as well, as this is generally what drives the postoperative recommendations for VTE prophylaxis.

Interestingly, the mean time to VTE was nearly 2 months, underscoring that VTE is not just a phenomenon of the immediate perioperative period. Other studies have corroborated these findings with data of VTE up 6 months postoperatively.[19] This suggests that patients should be given prophylaxis for a duration longer than 30 days postoperatively, as the NCCN guidelines suggest for patients with colorectal cancer (REF). However, it is likely that compliance, especially with subcutaneous lovenox injections, would decrease with increasing time from the operative intervention.

The real challenges with understanding the relevance of PMVT are as follows: (1) Is the abdominal pain due to PMVT or another etiology? (2) What is the true incidence of PMVT? (3) If a PMVT were to go untreated, what would its natural course be? Thus, do we actually need to treat PMVT? Should we only treat when symptomatic?

To better answer the aforementioned questions, a prospective study that gets routine postoperative imaging on all patients would need to be performed. Then, asymptomatic patients with PMVT on abdominal imaging could be randomized to receive or not receive systemic anticoagulation to better understand whether it is necessary to treat all patients and decipher the natural history of untreated PMVT. Another important component of a prospective study is to document compliance with VTE prophylaxis. Studies on VTE are limited by a lack of information regarding whether a patient filled their prescription for VTE prophylaxis, which is uncommon,[20] and, when filled, whether the patient was compliant. Again, a well-designed prospective trial would help answer these questions. Until then, there remain significant gaps in our understanding of PMVT in postoperative IBD patients.

REFERENCES

1. Beckman MG, Hooper WC, Critchley SE, Ortel TL. Venous thromboembolism: a public health concern. *Am J Prev Med.* 2010;38:S495–S501.
2. Caprini JA. Risk assessment as a guide for the prevention of the many faces of venous thromboembolism. *Am J Surg.* 2010;199:S3–10.
3. MacDougall DA, Feliu AL, Boccuzzi SJ, Lin J. Economic burden of deep-vein thrombosis, pulmonary embolism, and post-thrombotic syndrome. *Am J Health Syst Pharm.* 2006;63:S5–15.
4. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(Suppl 2):e227S–e277S.
5. Yuhara H, Steinmaus C, Corley D, et al. Meta-analysis: the risk of venous thromboembolism in patients with inflammatory bowel disease. *Aliment Pharmacol Ther.* 2013;37:953–962.
6. Ali F, Al-Kindi SG, Blank JJ, et al. Elevated venous thromboembolism risk following colectomy for IBD is equal to those for colorectal cancer for ninety days after surgery. *Dis Colon Rectum.* 2018;61:375–381.
7. Brady MT, Patts GJ, Rosen A, et al. Postoperative venous thromboembolism in patients undergoing abdominal surgery for IBD: a common but rarely addressed problem. *Dis Colon Rectum.* 2017;60:61–67.
8. Gross ME, Vogler SA, Mone MC, et al. The importance of extended postoperative venous thromboembolism prophylaxis in IBD: a national surgical quality improvement program analysis. *Dis Colon Rectum.* 2014;57:482–489.
9. McKenna NP, Behm KT, Ubl DS, et al. Analysis of postoperative venous thromboembolism in patients with chronic ulcerative colitis: is it the disease or the operation? *Dis Colon Rectum.* 2017;60:714–722.
10. Alcalay A, Wun T, Khatri V, et al. Venous thromboembolism in patients with colorectal cancer: incidence and effect on survival. *J Clin Oncol.* 2006;24:1112–1118.
11. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest*. 2008;133(Suppl 6):381S–453S.
12. Fleming F, Gaertner W, Ternent CA, et al. The American Society of Colon and Rectal Surgeons clinical practice guideline for the prevention of venous thromboembolic disease in colorectal surgery. *Dis Colon Rectum.* 2018;61:14–20.
13. Wilson MZ, Connelly TM, Tinsley A, et al. Ulcerative colitis is associated with an increased risk of venous thromboembolism in the postoperative period: the results of a matched cohort analysis. *Ann Surg.* 2015;261:1160–1166.
14. Fleming FJ, Aquina CT. Extended-duration venous thromboembolism prophylaxis following colorectal surgery: ready for prime time? *Dis Colon Rectum.* 2018;61:273–274.
15. Allaix ME, Krane MK, Zoccali M, et al. Postoperative portomesenteric venous thrombosis: lessons learned from 1,069 consecutive laparoscopic colorectal resections. *World J Surg.* 2014;38:976–984.
16. Gorgun E, Sapci I, Onder A, et al. Factors associated with portomesenteric venous thrombosis after total colectomy with ileorectal anastomosis or end ileostomy. *Am J Surg.* 2018;215:62–65.
17. Singal AK, Kamath PS, Tefferi A. Mesenteric venous thrombosis. *Mayo Clin Proc.* 2013;88:285–294.
18. Branchford BR, Carpenter SL. The role of inflammation in venous thromboembolism. *Front Pediatr.* 2018;6:142.
19. Agnelli G, Bolis G, Capussotti L, et al. A clinical outcome-based prospective study on venous thromboembolism after cancer surgery: the @RISTOS Project. *Ann Surg.* 2006;243:89–95.
20. Merkow RP, Bilimoria KY, McCarter MD, et al. Post-discharge venous thromboembolism after cancer surgery: extending the case for extended prophylaxis. *Ann Surg.* 2011;254:131–137.