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Venous Thromboembolism in Patients with:

Inflammatory Bowel Diseases: A case-control study of risk factors

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Abstract

Introduction—Inflammatory bowel disease is a well known risk factor for venous thromboembolism (VTE). Existing guidelines for thromboprophylaxis in hospitalized patients do not extend to other clinical scenarios that may also be associated with VTE risk. Our aim was to estimate the fraction of VTE events in IBD patients that could be prevented.

Methods—A retrospective analysis assessed all IBD patients diagnosed with VTE at a single academic medical center from 2002–2012. Confirmed cases were analyzed for VTE risk factors, inpatient status, the use of DVT prophylaxis, and when applicable the reason for omission of prophylaxis. IBD VTE cases were compared with age- and sex-matched non-IBD VTE controls with regards to risk factors and potential opportunities for VTE prevention.

Results—There were 204 IBD patients (108 UC, 96 CD) diagnosed with VTE (110 DVT, 66 PE, 27 intra-abdominal thromboses, 1 other). One third of the VTE events occurred in hospitalized patients. Two-third of the medical inpatients and 44% of surgical in-patients who developed VTE did not receive prophylaxis. Importantly, 129 VTE events occurred in outpatients. The proportion of outpatients hospitalized within 4 weeks of developing venous thrombosis was higher in IBD patients than non-IBD controls (33 vs. 15%, $p=0.0003$). One-third of patients (36%) were experiencing ambulatory disease flares at the time of VTE diagnosis.

Conclusions—A substantial portion of VTE events in IBD patients occurred in clinical scenarios not routinely recommended for thromboprophylaxis. Further investigation of primary prophylaxis for IBD patients in high risk outpatients may be warranted.

Keywords

celiac disease; Crohn's disease; ulcerative colitis; thrombosis; prophylaxis

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INTRODUCTION

Inflammatory bowel diseases (IBD; Crohn's disease (CD), ulcerative colitis (UC)) are a well recognized risk factor for venous thromboembolism (VTE)¹⁻⁷. In population based cohort studies, patients with IBD have a 1.5-3 fold increase in risk of venous thromboembolism^{1, 2, 8, 9}. Furthermore, VTE in such patients is associated with considerable morbidity and mortality with higher rates of death from pulmonary embolism in IBD patients than the general population^{5, 10}. The reason for the increased risk of VTE in patients with IBD is unclear, but may be multifactorial⁴. Many studies identified no increase in frequency of thrombophilias in IBD patients compared to non-IBD controls^{4, 6}. Ongoing active inflammation in IBD itself appears to be a significant factor determining VTE risk. Disease flares are associated with an increased risk of VTE, with the highest absolute risk in those requiring hospitalization^{2, 11}. Consequently, the recommendation for routine thromboprophylaxis in hospitalized patients with active disease has become part of the standard guidelines of care¹²⁻¹⁴.

Despite evidence that prophylactic anticoagulation is safe and effective⁸, the rates of inpatient VTE prophylaxis in IBD patients remain low¹⁵. Furthermore, current guidelines do not extend to other clinical scenarios such as post-hospitalization states and ambulatory disease flares that may also be associated with an increased absolute and relative risk of VTE^{2, 11}. Thus, in addition to existing literature demonstrating infrequent use of VTE prophylaxis in hospitalized IBD patients, it is equally important to estimate not only the fraction of VTE events in IBD patients that may have been prevented by wider adoption of current guidelines, but also identify their frequency of occurrence in clinical settings that fall outside the scope of the present recommendations⁴.

Thus, we performed this study with the following aims: (1) To estimate the fraction of VTE events in IBD patients that could be prevented by wider adoption of the current guidelines (i.e. VTE events occurring during inpatient status); (2) To examine the need to expand recommendations for VTE prophylaxis in IBD patients to other clinical settings not covered by current guidelines for prophylaxis by defining the proportion of VTE events among IBD patients that occur in such settings; and (3) to compare the proportion of potentially preventable VTE events in IBD patients compared to a matched non-IBD cohort.

METHODS

Study population

We performed a retrospective analysis of all IBD patients diagnosed with VTE at a single academic medical center. The study included all patients with either CD or UC diagnosed with a VTE event (deep venous thrombosis (DVT), pulmonary embolism (PE), portal or mesenteric vein thrombosis, or other venous thrombosis) between January 2002 and December of 2012. Eligible patients were identified from the Partners Healthcare Research Practice Data Registry (RPDR)¹⁶. This is an electronic database of all patients receiving inpatient or outpatient care at Massachusetts General Hospital in Boston, a tertiary referral academic hospital serving over 4 million patients in the Greater Boston area. The RPDR has been utilized to identify eligible patients in prior studies from our center^{17, 18} and

incorporates information dating to 1989 from a variety of sources including electronic medical records, billing, laboratory tests, patient scheduling, and other administrative sources. Potential cases were identified first by the co-occurrence of an International Classification of Diseases, 9th edition, clinical modification (ICD-9-CM) code for either CD (555.x) or UC (556.x) in conjunction with codes for venous thromboembolic events (415.1, V125.1, 451.1–451.8, 453.0–453.9, 671.5, 325.0, 437.6, 671.9) ^{2, 5}. Medical records were reviewed for all eligible patients to confirm both the IBD and VTE diagnosis, yielding a total of 204 IBD patients with VTE events. Patients with VTE diagnosed prior to the diagnosis of IBD as well as those where both the IBD and VTE diagnosis could not be confirmed were excluded. To compare the fraction of VTE events in IBD patients that are preventable compared to non-IBD controls, we selected a control population from the same data source, matching each case by age (± 5 years) and gender. This included 204 patients without an underlying diagnosis of IBD with a confirmed diagnosis of VTE. To identify IBD related risk factors, we additionally selected a set of IBD controls that were matched 1:1 to each VTE case by inpatient or outpatient status as well as history of recent hospitalization.

Variables

Demographic information including ages at diagnosis of VTE and IBD, gender, duration and type of IBD, and type of VTE were recorded. IBD activity at the time of VTE was categorized as active or inactive from chart review based on documentation of symptoms of active disease at the time of medical encounter for VTE, assessment during recent gastroenterology visits, or recent endoscopic or radiologic evidence of active disease. Known risk factors for VTE including prior VTE, oral contraceptive or hormone replacement therapy use, pregnancy, clotting disorders, malignancy, smoking status, recent immobilization, recent surgery (within 3 months), current or recent hospitalization within one month and steroid use were all noted. IBD medications at the time of VTE diagnosis were also retrieved by chart review.

For patients hospitalized at the time of diagnosis or within 4 weeks of diagnosis, the dates of hospitalization and reason for hospitalization were gathered. For all patients, the use of anticoagulant medications at therapeutic or prophylactic doses at the time of diagnosis was obtained from review of medical records as well as prescription ordering data. RPDR contains information on all inpatient and outpatient medication orders written at our hospital and affiliated outpatient clinics. For all patients who were not on prophylactic or therapeutic anticoagulation available documentation was reviewed for a reason of omission. Reasons for prophylaxis omission were categorized as active bleeding, ambulatory patient, refusal, surgical contraindications, underlying coagulopathy (i.e. thrombocytopenia), other, and unknown/not recorded. For patients with active disease, information on disease severity including albumin, C-reactive protein (CRP), and hemoglobin were obtained. For patients with recent hospitalization, the duration of hospitalization, length of time from discharge to VTE diagnosis, and pharmacologic VTE prophylaxis use during the hospitalization were obtained.

Statistical Analysis

All analysis was performed using Stata 12.0 (StataCorp, College Station, TX). Categorical variables were reported using percentages and compared using the chi square test with Fisher's exact test applied when appropriate. Continuous variables were reported using means and standard deviations and compared using the t-test. The study was approved by the institutional review board at Massachusetts General Hospital.

RESULTS

Our study included 204 IBD patients (108 UC, 96 CD) diagnosed with VTE (110 DVT, 66 PE, 27 intra-abdominal thrombosis, 1 cerebral vein thrombosis) and an equal number of matched non-IBD controls with VTE diagnosed during the same follow-up period (Table 1). IBD patients had a mean age of 54 years; 48% were male. IBD patients had a higher proportion of patients with abdominal vein thrombosis than non-IBD controls (13% vs. 3%, $p=0.0002$) and a lower fraction of VTE events presenting with pulmonary embolism (34% vs. 45%, $p=0.02$). Three IBD patients (2 with PE and one with cerebral vein thrombosis) died as a result of thromboembolic disease. Three controls without IBD also died as a result of pulmonary embolism.

Risk Factors for VTE

One hundred and thirty-three (65%) IBD patients had at least one risk factor for VTE (hospitalization, surgery within 90 days, cancer, indwelling catheter, known thrombophilia, use of OCP or hormone replacement therapy) which was similar to the proportion among age- and gender-matched controls ($n=144$, 71%, $p=0.29$). IBD patients had higher proportions of total events associated with surgery within 90 days (37% vs. 21%; $p=0.0004$), steroid use (42% vs. 8%; $p<0.0001$), and a smaller proportion of events associated with clotting disorders (2% vs. 8%; $p=0.02$) and cancer (16% vs. 33%; $p=0.0001$). One-third of the VTE events occurred in hospitalized IBD patients (37%, $n=75$), equally split between medical ($n=40$) and surgical ($n=35$) hospitalizations. A significantly higher proportion of IBD patients were hospitalized at the time of developing venous thrombosis than age- and sex-matched controls (37% vs. 18%, $p<0.0001$).

Disease Activity and Treatment

More patients were categorized as having active IBD in the VTE affected than control IBD populations (111 vs. 81 $p=0.004$). At the time of VTE, 60 (29%) patients were being treated with 5-ASA compounds, 26 (13%) with azathioprine/6MP, 3 (1%) with methotrexate, 13 (6%) with anti-TNF agents, and 86 (42%) with systemic steroids. IBD patients without VTE had higher proportions of treatment with anti-TNF agents (16% vs. 6%, $p=0.003$) and 5-ASA compounds (46% vs. 29%, $p=0.001$) and were less likely to be on systemic steroids (23% vs. 42%, $p=0.0001$).

Inpatient VTE events

Two-thirds of medical inpatients and 44% of surgical in-patients who developed VTE did not receive prophylaxis. These proportions were similar to that in the non-IBD population (64% of medical and 40% of surgical patients VTE events occurred in the setting of no

prophylaxis). The most common reason cited for not receiving prophylaxis in IBD patients were GI bleeding (21% of inpatients with prophylaxis held) followed by ambulatory status (7%) (Table 2).

VTE in outpatients

Despite a known strong association between hospitalization status and VTE risk, the majority of VTE events occurred in outpatients (n=129 in IBD patients). Interestingly, a higher proportion of VTE events occurred in the outpatient setting in the non-IBD population as well ($p < 0.05$) (Table 3). IBD outpatients also had a higher proportion of total events associated with surgery in the past 90 days (29% vs. 15%, $p=0.0008$) and steroid use (35% vs. 7%, $p<0.0001$), but a smaller proportion of events associated with cancer (17% vs. 34%, $p=0.0009$) than non-IBD outpatient VTE matched controls.

One-third of IBD patients who developed VTE as an outpatient were experiencing symptoms of a disease flare for a median of 5 weeks prior to VTE diagnosis. The majority of such patients (80%) had required systemic steroid initiation. Additionally, at the time of VTE event, 13 (28%) were on 5-ASA, 7 (15%) on azathioprine, 1 (0.8%) on methotrexate, 7 (15%) on anti-TNF agents, and 5 (7%) on antibiotics. This cohort had a mean C-reactive protein level of 49.9 mg/L, mean hemoglobin of 10.1 g/dL, and mean albumin of 2.99 g/dL. Outpatient IBD controls without VTE had a similar proportion of active disease (n=49 vs. 46) than those with VTE.

A similar proportion, one-third (33%, n=43, had been hospitalized within 4 weeks prior to the VTE event. The mean duration of hospitalization in such IBD patients was 8 days and the mean time between hospital discharge and VTE was 11 days. Interestingly, two-thirds of such patients had received prophylaxis while in the hospital. The proportion of patients who were hospitalized within 4 weeks of developing venous thrombosis was higher in IBD patients than non-IBD controls (33% vs. 15%, $p=0.0003$). Control patients with recent hospitalization had similar characteristics with a mean duration of hospitalization of 6 days and mean time between hospital discharge and VTE of 12 days ($p=NS$). Fifteen were medical hospitalizations and 10 surgical hospitalizations of which only 44% had documented prophylaxis use.

DISCUSSION

Inflammatory bowel disease is well recognized as a risk factor for VTE leading expert guidelines to recommend routine VTE prophylaxis during hospitalization^{1, 2, 4, 5, 11, 12, 19, 20}. However, the proportion of VTE events that can be prevented by wider adoption of current guidelines is unknown making it difficult to estimate the impact of wider adoption of such guidelines on overall VTE-related morbidity. Furthermore, whether a larger fraction of such VTE events in IBD are potentially preventable compared to the non-IBD population has not been examined previously. In this study including all patients with IBD who were diagnosed with VTE at a tertiary referral-center, we demonstrate that (1) two-thirds of VTE events in both IBD and non-IBD populations were associated with possible traditional risk factors, but distribution of such risk factors varied; (2) a larger fraction of VTE events in IBD patients occur in the inpatient

setting compared to age- and gender-matched non-IBD controls; and (3) despite current low rates of thromboprophylaxis for IBD inpatients, the majority of burden of VTE in IBD still occurs in the outpatient setting, with a third of such events occurring within a month of recent hospitalization, and a similar proportion during an ambulatory flare; and (4) Compared to non-VTE IBD patients, those who developed VTE were more likely to be current users of corticosteroids and less likely to be on anti-TNF therapy.

A few other studies have noted that the majority of VTE events occur in outpatients. Similar to our study, a recent study by Papay *et al.* with a smaller number of VTE events (n=157) showed that only 35% of venous thrombosis in IBD patient's occurred in hospitalized patients²¹. This outpatient predominance is not unique to IBD with other studies demonstrating that inpatients account for 18% to 30% of VTE occurring in the general population^{22–24}. However the fact that twice the VTE burden in the IBD population occurs in the inpatient setting (compared to non-IBD matched controls) suggests that a larger fraction of VTE may thus be 'preventable' in those with IBD.

Despite our finding that the majority of VTE events occur in IBD outpatients, developing recommendations for prophylaxis in this setting has been challenging for several reasons. Though the relative risk of VTE associated with IBD in the outpatient setting may be higher, the absolute risk remains lower than during the hospitalized period². Consequently, routine prophylaxis becomes a cost-ineffective intervention²⁵. Based on the limited data available, a recent decision analysis predicted that prophylaxis in outpatient flare may increase unadjusted life years (47.76 yrs vs. 46.67 yrs) and decrease lifetime risk of VTE (6.2% versus 9.3%), however may not be cost-effective if applied widely²⁵. On the other hand, if there are discernible subgroups of patients who are at a particularly high risk of VTE in the outpatient setting, then tailored thromboprophylaxis in such patients may be of value. Nearly one-third of outpatient VTE events (one-quarter of all VTE events in IBD patients) in our institution occurred in patients experiencing significant flares requiring systemic steroids. Given the substantial proportion of events in our population more investigation is warranted, particularly with regards to quantifying the absolute risk of VTE during ambulatory flares. We were not able to estimate this from our analysis but this question merits further investigation.

A second notable population of outpatients arose in our analysis. Similar to outpatients with active IBD, 21% of all thrombotic events seen in IBD patients occurred in outpatients who had been hospitalized within 4 weeks of the thrombosis. Extended post hospital prophylaxis has been studied in various other medical and surgical populations where mobility is likely decreased post hospitalization. Post hospital prophylaxis has not proven effective in general medical patients; however, prior studies have not looked at specific high-risk populations such as IBD²⁶. Post hospital prophylaxis has been used for some time in high-risk post surgical populations such as following orthopedic procedures²⁷. Post hospital prophylaxis has also been an area of interest in other high-risk populations such as bariatric surgery²⁸. IBD patients are known to be high risk for post operative DVT^{3, 29} and based on our findings this risk may extend to the post hospital period in both medical and surgical patients. This is an area that has not been explored in prior studies and also merits further investigation.

Our series demonstrates that the proportion of hospitalized patients who developed VTE while on prophylaxis was similar in IBD and non-IBD groups. Though investigated in the general inpatient population,³⁰ to our knowledge no study has looked at the effectiveness of commonly used prophylaxis regimens specifically in IBD patients. Our study suggests that efficacy and failure rates may be similar. However, of note, in our non-IBD population prophylaxis was frequently held for absolute contraindications (i.e. intracranial hemorrhage) while in the IBD population it was more frequently held at times when it could potentially be administered safely (i.e. minor rectal bleeding), as has been noted by others³¹.

The major strength of our study is that it evaluates a relatively large series of objectively confirmed thrombotic events. Access to inpatient and outpatient physician orders allowed us to objectively measure rates of thromboprophylaxis prescription, although it is important to note that it is challenging to measure patient refusal as a contributing factor since this is difficult to ascertain retrospectively in an EMR study. We also readily acknowledge several limitations to our study. Owing to our case-control design, we cannot determine the incidence or prevalence of these events. Second, our population was entirely from a single tertiary academic referral center and as such our population (both case and control) may be subject to a selection bias skewed towards more severe disease. Furthermore, the proportion of VTE events that occurred as an outpatient in our center may be influenced by the disease activity of patients seeking care at our referral center practices, and may not be generalizable to population-based cohorts. As healthcare seeking behaviors may be different in those with IBD compared to non-IBD controls with VTE, it is possible that different thresholds exist for triggering an evaluation for VTE between the two groups. However, given that a substantial portion of the non-IBD controls also had significant co-morbidity such as cancer, it is likely that they utilize healthcare frequently and similar to patients with IBD. Similarly, the higher proportion of intra-abdominal thrombosis in patients with IBD could, in part, be due to increased ascertainment as IBD patients are more likely to undergo abdominal imaging studies.

In conclusion, the majority of venous thromboembolic events in IBD patients occur in the outpatient setting. While this outpatient predominance is not unique to the IBD population, a substantial proportion of VTE events in IBD patients occur in settings that can be clinically defined as higher risk (i.e. following discharge from hospitalization, active disease flare, or post-operative outpatients). As the absolute risk of VTE in such settings is better defined, these may represent potential opportunities to expand current prophylaxis guidelines. Further investigation on the potential benefits of targeted thromboprophylaxis in such settings and the cost-effectiveness of extending prophylaxis to those settings is warranted.

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References

- 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; 85:430–4. [PubMed: 11307809]
- Kappelman MD, Horvath-Puho E, Sandler RS, Rubin DT, Ullman TA, Pedersen L, Baron JA, Sorensen HT. Thromboembolic risk among Danish children and adults with inflammatory bowel diseases: a population-based nationwide study. *Gut.* 60:937–43. [PubMed: 21339206]
- Merrill A, Millham F. Increased risk of postoperative deep vein thrombosis and pulmonary embolism in patients with inflammatory bowel disease: a study of National Surgical Quality Improvement Program patients. *Arch Surg.* 147:120–4. [PubMed: 22006853]
- Murthy SK, Nguyen GC. Venous thromboembolism in inflammatory bowel disease: an epidemiological review. *Am J Gastroenterol.* 106:713–8. [PubMed: 21407182]
- Nguyen GC, Sam J. Rising prevalence of venous thromboembolism and its impact on mortality among hospitalized inflammatory bowel disease patients. *Am J Gastroenterol.* 2008; 103:2272–80. [PubMed: 18684186]
- Novacek G, Weltermann A, Sobala A, Tilg H, Petritsch W, Reinisch W, Mayer A, Haas T, Kaser A, Feichtenschlager T, Fuchssteiner H, Knoflach P, Vogelsang H, Miehsler W, Platzer R, Tillinger W, Jaritz B, Schmid A, Blaha B, Dejaco C, Eichinger S. Inflammatory bowel disease is a risk factor for recurrent venous thromboembolism. *Gastroenterology.* 139:779–87. 787, e1. [PubMed: 20546736]
- Huerta C, Johansson S, Wallander MA, Garcia Rodriguez LA. Risk factors and short-term mortality of venous thromboembolism diagnosed in the primary care setting in the United Kingdom. *Arch Intern Med.* 2007; 167:935–43. [PubMed: 17502535]
- Yuhara H, Steinmaus C, Corley D, Koike J, Igarashi M, Suzuki T, Mine T. Meta-analysis: the risk of venous thromboembolism in patients with inflammatory bowel disease. *Aliment Pharmacol Ther.* 2013; 37:953–62. [PubMed: 23550660]
- Saleh T, Matta F, Yaekoub AY, Danescu S, Stein PD. Risk of venous thromboembolism with inflammatory bowel disease. *Clin Appl Thromb Hemost.* 17:254–8. [PubMed: 20211927]
- Jess T, Gamborg M, Munkholm P, Sorensen TI. Overall and cause-specific mortality in ulcerative colitis: meta-analysis of population-based inception cohort studies. *Am J Gastroenterol.* 2007; 102:609–17. [PubMed: 17156150]
- Grainge MJ, West J, Card TR. Venous thromboembolism during active disease and remission in inflammatory bowel disease: a cohort study. *Lancet.* 375:657–63. [PubMed: 20149425]
- Bitton A, Buie D, Enns R, Feagan BG, Jones JL, Marshall JK, Whittaker S, Griffiths AM, Panaccione R. Treatment of hospitalized adult patients with severe ulcerative colitis: Toronto consensus statements. *Am J Gastroenterol.* 2012; 107:179–94. author reply 195. [PubMed: 22108451]
- Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, Mitton S, Orchard T, Rutter M, Younge L, Lees C, Ho GT, Satsangi J, Bloom S. Guidelines for the management of inflammatory bowel disease in adults. *Gut.* 2011; 60:571–607. [PubMed: 21464096]
- Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol.* 2010; 105:501–23. quiz 524. [PubMed: 20068560]
- Baser O, Liu X, Phatak H, Wang L, Mardekian J, Kawabata H, Petersel D, Hamilton M, Ramacciotti E. Venous thromboembolism prophylaxis and clinical consequences in medically ill patients. *Am J Ther.* 2013; 20:132–42. [PubMed: 23466619]
- Nalichowski R, Keogh D, Chueh HC, Murphy SN. Calculating the benefits of a Research Patient Data Repository. *AMIA Annu Symp Proc.* 2006:1044. [PubMed: 17238663]
- Oxford EC, Nguyen DD, Sauk J, Korzenik JR, Yajnik V, Friedman S, Ananthakrishnan AN. Impact of coexistent celiac disease on phenotype and natural history of inflammatory bowel diseases. *Am J Gastroenterol.* 108:1123–9. [PubMed: 23419379]
- de Silva PS, Nguyen DD, Sauk J, Korzenik J, Yajnik V, Ananthakrishnan AN. Long-term outcome of a third anti-TNF monoclonal antibody after the failure of two prior anti-TNFs in inflammatory bowel disease. *Aliment Pharmacol Ther.* 36:459–66. [PubMed: 22784296]

19. Koutroumpakis EI, Tsiolakidou G, Koutroubakis IE. Risk of venous thromboembolism in patients with inflammatory bowel disease. *Semin Thromb Hemost.* 39:461–8. [PubMed: 23629820]
20. Nguyen GC, Yeo EL. Prophylaxis of venous thromboembolism in IBD. *Lancet.* 375:616–7. [PubMed: 20149426]
21. Papay P, Miehsler W, Tilg H, Petritsch W, Reinisch W, Mayer A, Haas T, Kaser A, Feichtenschlager T, Fuchssteiner H, Knoflach P, Vogelsang H, Platzer R, Tillinger W, Jaritz B, Schmid A, Blaha B, Dejaco C, Sobala A, Weltermann A, Eichinger S, Novacek G. Clinical presentation of venous thromboembolism in inflammatory bowel disease. *J Crohns Colitis.* 7:723–9. [PubMed: 23127785]
22. Mean M, Righini M, Jaeger K, Beer HJ, Frauchiger B, Osterwalder J, Kucher N, Lammle B, Cornuz J, Angelillo-Scherrer A, Rodondi N, Limacher A, Trelle S, Matter CM, Husmann M, Banyai M, Aschwanden M, Egloff M, Mazzolai L, Hugli O, Bounameaux H, Aujesky D. The Swiss cohort of elderly patients with venous thromboembolism (SWITCO65+): rationale and methodology. *J Thromb Thrombolysis.* 2013
23. Maestre A, Sanchez R, Rosa V, Aujesky D, Lorenzo A, Barillari G, Monreal M. Clinical characteristics and outcome of inpatients versus outpatients with venous thromboembolism: findings from the RIETE Registry. *Eur J Intern Med.* 21:377–82. [PubMed: 20816588]
24. Spencer FA, Lessard D, Emery C, Reed G, Goldberg RJ. Venous thromboembolism in the outpatient setting. *Arch Intern Med.* 2007; 167:1471–5. [PubMed: 17646600]
25. 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; 19:2182–9. [PubMed: 23883960]
26. Sharma A, Chatterjee S, Lichstein E, Mukherjee D. Extended thromboprophylaxis for medically ill patients with decreased mobility: does it improve outcomes? *J Thromb Haemost.* 2012; 10:2053–60. [PubMed: 22863355]
27. Huo MH, Muntz J. Extended thromboprophylaxis with low-molecular-weight heparins after hospital discharge in high-risk surgical and medical patients: a review. *Clin Ther.* 2009; 31:1129–41. [PubMed: 19695383]
28. Ojo P, Asiyanbola B, Valin E, Reinhold R. Post discharge prophylactic anticoagulation in gastric bypass patient-how safe? *Obes Surg.* 2008; 18:791–6. [PubMed: 18386108]
29. Scarpa M, Pilon F, Pengo V, Romanato G, Ruffolo C, Erroi F, Elisa B, Frego M, Ossi E, Manzato E, Angriman I. Deep venous thrombosis after surgery for inflammatory bowel disease: is standard dose low molecular weight heparin prophylaxis enough? *World J Surg.* 34:1629–36. [PubMed: 20177681]
30. Dentali F, Douketis JD, Gianni M, Lim W, Crowther MA. Meta-analysis: anticoagulant prophylaxis to prevent symptomatic venous thromboembolism in hospitalized medical patients. *Ann Intern Med.* 2007; 146:278–88. [PubMed: 17310052]
31. Sam JJ, Bernstein CN, Razik R, Thanabalan R, Nguyen GC. Physicians' perceptions of risks and practices in venous thromboembolism prophylaxis in inflammatory bowel disease. *Dig Dis Sci.* 58:46–52. [PubMed: 23053902]

Table 1

Characteristics of IBD and Non-IBD patients who developed VTE

Demographics	IBD Patients (n=204) [N(%)]	Non-IBD controls (n=204) [N(%)]	p-value
Age at VTE diagnosis (in years) (Mean(SD))	54 (19)	55 (18)	0.59
Sex			1.00
Female	106 (52)	106 (52)	
Male	98 (48)	98 (48)	
Mean IBD duration (in years) (Mean(SD))	13 (14)	-	-
Type of VTE			
DVT	110 (54)	105 (51)	0.69
PE	66 (34)	92 (45)	0.01
Intra-abdominal thrombosis	27 (13)	7 (3)	0.001
Other thrombosis	1 (0.40)	0 (0)	-
Current smoker	17 (8)	28 (14)	0.11
Hospitalization status at time of VTE			< 0.0001
Inpatient	75 (37)	37 (18)	
Outpatient	129 (63)	167 (82)	
Traditional VTE risk factors			
Cancer	33 (16)	67 (33)	< 0.001
Line Associated	21 (10)	11 (5)	0.10
Pregnancy	3 (1)	6 (3)	0.50
Clotting Disorder	5 (2)	16 (8)	0.02
Prior VTE	20 (10)	9 (4)	0.05
Steroid Use	86 (42)	16 (8)	< 0.001
OCP/HRT	10 (5)	12 (6)	0.83
Surgery within 90 days	75 (37)	42 (21)	< 0.001

VTE – venous thromboembolism, OCP – oral contraceptive pills, HRT – hormone replacement therapy

Table 2

Reasons documented for withholding prophylaxis in IBD and control patients during 1) admission resulting in venous thrombosis or 2) an admission within one month of venous thrombosis

	IBD		Non-IBD controls	
	Admission resulting in VTE	Admission within 1 month prior to VTE	Admission resulting in VTE	Admission within 1 month prior to VTE
Bleeding	11	4	10	2
Intracranial	0	0	4	0
GI bleeding	11	3	3	2
Other	0	1	3	0
Ambulatory	4	2	2	2
Surgical contraindication	5	0	4	4
Pre-op	2	0	3	1
Post-op	2	0	1	3
Coagulopathy/Thrombocytopenia	1	2	2	0
Unknown/No reason documented	16	4	3	6

Table 3
Characteristics of IBD and Non-IBD controls who developed venous thrombosis as outpatients

	IBD (n=129) [N(%)]	Controls (n=167) [N(%)]	p-value
Age (in years) [mean (SD)]	54.6 (19.0)	54.7 (18.8)	0.96
Sex			0.82
Male	63 (49)	79 (47)	
Female	66 (51)	88 (53)	
Recent Admission (<4 weeks)	43 (33)	25 (15)	<0.001
Recent admission by type			0.31
Medical	19 (15)	15 (9)	
Surgical	24 (12)	10 (6)	
Outpatient Active Disease	46 (36)	-	
Cancer	22 (17)	57 (34)	0.001
Line Associated	7 (5)	8 (5)	0.80
Pregnancy	3 (2)	6 (7)	0.74
Clotting Disorder	4 (3)	15 (9)	0.05
Prior VTE	12 (9)	7 (4)	0.09
Steroid Use	35 (35)	11 (7)	<0.0001
OCP/HRT	8 (6)	10 (6)	1.00
Surgery within 90 days	37 (29)	25 (15)	0.001
Prophylaxis use	1 (1)*	3 (2)#	0.63