Venous thromboprophylaxis in gastrointestinal bleeding


OBJECTIVE: To study the use of venous thromboembolism (VTE) prophylaxis and the incidence of thrombotic events in patients with acute gastrointestinal (GI) bleeding.

METHODS: Individuals admitted with a primary diagnosis of a GI bleed along with any endoscopically confirmed source (over a two-year period) were included. Patient comorbidity and data regarding anticoagulation or antiplatelet agent use before hospitalization were collected, in addition to type of VTE prophylaxis and duration of treatment. The primary end point was the development of VTE (deep vein thrombosis or pulmonary embolism) within one year of presentation.

RESULTS: Data from 504 patients admitted with GI bleeding were eligible for review. The total number of VTE events was 20 (4%) while the mortality rate during hospitalization was 4.6%; 397 patients were not given VTE prophylaxis during their hospitalization. Of the patients who were given VTE prophylaxis, 68 received prophylactic heparin or heparin derivatives during their admission. One hundred sixty-five patients had at least one other significant risk factor for VTE including recent or subsequent surgery, past thrombotic event or malignancy. The incidence of thrombosis in those with significant risk factors for VTE was significantly higher than those without (8.5% versus 1.8%; P=0.0099). Overall, there was no significant difference in thrombotic events between individuals receiving pharmacological prophylaxis (1.2%) and those who did not (2.8%) (P=0.4).

CONCLUSION: Overall, VTE prophylaxis did not significantly affect thrombotic events in patients admitted for an active GI bleed.

Key Words: Gastrointestinal bleeding; Venous thromboembolism prophylaxis
Table 2 summarizes the distribution of anticoagulant and antiplatelet agents before admission. The vast majority of patients were on some form of antiplatelet therapy (64.7%), with acetylsalicylic acid as the most common agent (57.4%). For patients who were started on some form of VTE prophylaxis, the most common agents were heparin or low molecular weight heparin, as shown in Table 3. It should also be noted that some form of VTE prophylaxis, the most common agent (57.4%). For patients who were started on some form of antiplatelet therapy (64.7%), with acetylsalicylic acid as the most common agent (57.4%). For patients who were started on some form of VTE prophylaxis, the most common agents were heparin or low molecular weight heparin, as shown in Table 3. It should also be noted that no source of bleeding was identified. This left 504 patient charts eligible for the present study. The demographic characteristics of the study group are summarized in Table 1. A higher number of patients were found to have a lower GI bleed (69.4%) compared with an upper GI bleed source (30.6%). In addition, pharmacological prophylaxis against VTE was only given in a minority (21.2%) of cases.

Demographic data comprised patient age in addition to information regarding comorbidities that may have contributed to a thrombotic event including known history of thrombotic events, recent surgery (within three months), and diagnosis of malignancy or cirrhosis. Documenting anticoagulation status included antiplatelet agents, vitamin K antagonists, direct thrombin inhibitors, as well as heparin and heparin derivatives at the time of admission while hospitalized and after discharge. Any of these agents were considered to be protective against the development of thrombosis even if they were discontinued for a portion of the hospital stay.

The primary outcome was the incidence of VTE up to one year after discharge based those who received anticoagulant therapy for prophylaxis against VTE during hospitalization. The potential role of hypercoagulable states (malignancy, cirrhosis, recent surgery and past thrombosis) as risk factors for thromboembolic disease was used as a secondary outcome.

Statistical analysis
Standard descriptive analysis was performed to determine the source of GI bleeding along with the modality of endoscopic intervention most used for diagnosis. The frequency of VTE development, in addition to anticoagulation and hypercoagulable states, was also documented. Fisher’s exact test with two-tailed P value using SAS/Stat Software version 9.1.3 (SAS Institute Inc, USA) was performed to analyze the primary outcome of VTE in those who received pharmacological prophylaxis compared with those who did not. A subgroup analysis was performed to investigate the outcome of pharmacological prophylaxis in those with significant risk factors likely predisposing to thromboembolic complications.

RESULTS
After initial review, 1045 potential charts were identified. Of these, 419 had a primary diagnosis other than GI bleed leading to admission (Figure 1). Further screening found that 43 patients had no endoscopic procedure or imaging to confirm their diagnosis. Seventy-nine investigations were completed, but no source of bleeding was identified. This left 504 patient charts eligible for the present study. The demographic characteristics of the study group are summarized in Table 1. A higher number of patients were found to have a lower GI bleed (69.4%) compared with an upper GI bleed source (30.6%). In addition, pharmacological prophylaxis against VTE was only given in a minority (21.2%) of cases.

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embolic events compared with those who did not receive it (1.2% to 0.8%, respectively; P=0.2). Although there was no statistically significant difference, we were also able to demonstrate that VTE prophylaxis decreased the incidence of thromboembolic complications (1.2% with prophylaxis versus 6.7% without prophylaxis; P=0.0009). As shown in Table 5, the combined high/low risk group had a reduced incidence of thromboembolic complications (1.2%) with pharmacological prophylaxis, although not statistically significant (P=0.4). This difference was also observed in the subgroup of individuals with comorbidities, with the incidence of VTE being 1.8%.

DISCUSSION

It has been well established that acutely ill medical patients benefit from pharmacological prophylaxis for VTE (11). The difficulty in patients with evidence of GI bleed is the concern for recurrent bleeding and hemodynamic stability. Adding any antiplatelet or anticoagulant in these situations often increases concern among health care professionals, which was reflected in the present study by the low number of individuals who were given VTE prophylaxis (n=107). Interestingly, current evidence shows that there is no increase in mortality among patients with lower GI bleeding treated with VTE prophylaxis (10). However, there was a longer ICU stay and increased number of transfusions only within the first 24 h after admission (10). In a study investigating the clinical outcomes of patients with a recent diagnosis of VTE, 40% experienced a GI bleed 30 days previously (12). Three-month mortality was as high as 23%, which is a clinically important measure, indicating the importance of VTE prophylaxis.

Importantly, our study showed that thromboembolic complications do exist in patients admitted with a GI bleed. VTE is significantly more common among individuals with other risk factors predisposing them to hypercoagulable states (P=0.0009). Although not a statistically significant difference, we were also able to demonstrate that VTE prophylaxis decreased the incidence of thromboembolic events compared with those who did not receive it (1.2% versus 2.8%, respectively; P=0.4).

Other observational studies have reported that a large percentage of individuals with VTE were >65 years of age and had additional risk factors, including malignancy, for VTE (12). Patients in our study had a mean age of 70.5 years, with a mean length of hospitalization of 5.5 days. The most frequent comorbidities believed to confer additional risk for thromboembolism included malignancy (n=83), cirrhosis (n=45) and past thrombotic events (n=13).

Low-dose acetylsalicylic acid has been associated with an increased risk for upper GI bleeding (13). Our data indicate that antiplatelet therapy, specifically acetylsalicylic acid, was used most commonly (57.4%) by patients before presenting with upper or lower GI bleeding. Baseline demographic data showed that lower GI bleeds (69.4%) were more common than upper GI bleeds (30.6%). This supports the higher risk associated with acetylsalicylic acid therapy in lower GI bleeds documented in a recent prospective study (14).

The lack of a significantly lower incidence of VTE observed in our cohort was likely multifactorial. First, there were low event rates observed in both groups. The study period could have been extended to determine the longer-term incidence of DVT/PE. Second, our teaching centre has a large catchment area with a significant referral base. Confirmation of thromboembolic events required documented radiological evidence and, for patients transferred back to their local hospital, some would be lost to follow-up, which may have led to an understimation of our event rates.

Overall, it would be our recommendation to implement VTE prophylaxis on a case-by-case basis for patients admitted with an active GI bleed, particularly if they have other factors predisposing them to thrombosis. Further studies investigating complications of low-dose anticoagulant therapy are likely needed to adequately quantify the risk associated with therapy and to reassure future practice.

DISCLOSURES: The authors have no financial disclosures or conflicts of interest to declare.

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Patients (% of cohort)</th>
<th>P</th>
<th>OR (95%CI)</th>
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<tbody>
<tr>
<td>Malignancy</td>
<td>83</td>
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<tr>
<td>Past thromboembolic events*</td>
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<td>Recent surgery†</td>
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<td>Cirrhosis</td>
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| Table 5
Incidence of thromboembolic disease (deep vein thrombosis [DVT]/pulmonary embolism [PE])

Data presented as n. *Includes pulmonary embolism, deep vein thrombosis, aortic clot, apical thrombus and portal vein thrombosis; †Within three months

| Table 3
Pharmacological anticoagulation during hospital stay

Data presented n (%)
REFERENCES