Periprocedural Anticoagulation Management of Patients With Venous Thromboembolism

Robert D. McBane, Waldemar E. Wysokinski, Paul R. Daniels, Scott C. Litin, Joshua Slusser, David O. Hodge, Nicole F. Dowling, John A. Heit

Objective—Patients with venous thromboembolism (VTE) often require temporary warfarin interruption for an invasive procedure. The incidence of thromboembolism and bleeding related to periprocedural anticoagulation management of such patients is unknown.

Methods and Results—In a protocol-driven, inception cohort design study, all VTE patients (n=775) referred for periprocedural anticoagulation management (1997–2007) were followed-up to estimate the 3-month cumulative incidence of thromboembolism and bleeding. Patients were stratified by thrombus acuity (acute, <30 days; subacute, 31–90 days; or chronic ≥91 days). Decisions to provide “bridging” low-molecular-weight heparin were based on estimated thromboembolism and bleeding risk. Low-molecular-weight heparin was more often administered in acute (87%) and subacute (81%) VTE compared to chronic VTE (59%; P<0.001). The 3-month cumulative incidence of thromboembolism (1.8%), major hemorrhage (1.8%), and mortality (1.7%) were low and did not differ by management strategy. Active cancer was the only independent predictor of thrombotic recurrence (HR, 4.86; 95% CI, 1.6–14.5; P=0.005), major hemorrhage (HR, 6.8; 95% CI, 2.1–21.7; P=0.001), and death (HR, 32.7; 95% CI, 4.3–251.2; P=0.0008).

Conclusion—Thromboembolism, bleeding, and death among VTE patients in whom anticoagulation is temporarily interrupted for an invasive procedure is low. Cancer patients require particular care given their propensity for both clotting and bleeding. (Arterioscler Thromb Vasc Biol. 2010;30:442-448.)

Key Words: anticoagulation ▪ deep vein thrombosis ▪ pulmonary embolism

Venous thromboembolism (VTE) is the fourth leading cause of death in western society and the third leading cause of cardiovascular death after myocardial infarction and stroke.¹–³ The 30-day mortality of patients experiencing a thrombotic event is 30%, and 20% of patients with pulmonary embolism die suddenly. Furthermore, VTE is a recurrent disease and 30% will have recurrent VTE within 10 years. Anticoagulation is the primary treatment for acute VTE, with the main objectives including prevention of thrombus propagation and embolization.⁴ Management of VTE is conceptually divided into 2 stages. The initial stage encompasses the first 3 months of anticoagulation after diagnosis when the risk of recurrence and mortality is the highest. Beyond 3 months, continued anticoagulation is referred to as secondary prophylaxis. Chronic oral anticoagulation with warfarin reduces the rate of recurrent VTE and mortality with an acceptably low rate of major hemorrhage.⁵–⁸ The need for temporary interruption of warfarin therapy so patients may safely undergo an invasive procedure is a common dilemma. With anticoagulation discontinuation, particularly after an unprovoked VTE, the rate of venous thrombosis recurrence increases sharply, irrespective of the duration of anticoagulation provided before its discontinuation.⁶ Moreover, invasive procedures have an increased propensity for venous thrombosis that is directly related to the extent of tissue injury associated with the procedure. The extent of tissue injury also directly impacts the likelihood of major bleeding. Standardizing periprocedural anticoagulation management for VTE patients has not been adequately defined by either randomized, controlled trial data or observational cohorts. A number of strategies have been proposed, ranging from simple warfarin discontinuation 5 days before surgery with prompt reinitiation postoperatively to “bridging” therapy with either intravenous unfractionated heparin or subcutaneous low-molecular-weight heparin (LMWH).

The current guidelines for periprocedural anticoagulation management of VTE patients include warfarin interruption 5 days before the anticipated procedure to allow adequate time for initial heparinization and proper reversal of heparinization before surgery. Anticoagulation should be reinitiated promptly after the procedure. More recent guidelines for the management of thrombosis in cancer patients recommend use of LMWH during an invasive procedure followed by prompt reinitiation of warfarin after surgery. Warfarin should be started within 24 hours of surgery. Patients with recent surgery should have their heparin dose adjusted based on the results of their preoperative PT/INR test. If the PT/INR is >2.5, the heparin dose should be reduced by 50%. If the PT/INR is >3.5, the heparin dose should be reduced by 75%.

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From Mayo Clinic Thrombophilia Center, Gonda Vascular Center (R.D.M., W.E.W., P.R.D., S.C.L., J.A.H.), and Division of Biostatistics (D.O.H.), Department of Health Sciences Research, Mayo Clinic, Rochester, Minn; Division of Blood Disorders (N.F.D.), National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Ga.
R.D.M. and W.E.W. contributed equally to this manuscript.
Correspondence to Robert D. McBane II, MD, Gonda Thrombophilia Clinic, Mayo Clinic, 200 First Street SW, Rochester, MN 55902. E-mail mcbane.robert@mayo.edu
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for the international normalized ratio (INR) to normalize.9 Whether preprocedural bridging therapy with LMWH is needed depends on the clinician’s assessment of thromboembolic risk for the specific patient. When the risk is deemed to be more than “low,” a therapeutic dose of a heparin is felt justified. When feasible, LMWH administered subcutaneously in the outpatient setting is preferred. According to these guidelines, low-dose LMWH remains an option even in patients at low risk. These recommendations reflect the preference of the guideline authors for preventing thromboembolism in contrast to limiting bleeding. Postprocedural warfarin is then reinitiated 12 to 24 hours after surgery, once adequate hemostasis is ensured. Depending on the bleeding risk of the procedure, postprocedural heparin is delayed between 24 and 72 hours. These guidelines are primarily based on expert opinion, with evidence grading ranging from 1C to 2C. Data supporting these recommendations therefore are admittedly limited.10–12 To address these limitations, consecutive VTE patients referred to the Mayo Clinic Thrombophilia Center for periprocedural anticoagulation management over the 10-year period (1997–2007) were followed-up to determine the 3-month cumulative incidence of thromboembolism, bleeding, and all-cause mortality. The relationship between bleeding and thrombotic outcomes and the timing of procedure relative to the VTE diagnosis (acute, <30 days; subacute, 31–90 days; or chronic, ≥91 days) was also assessed.

Subjects and Methods

Study Population, Design, and Setting

The Thrombophilia Clinic had its inception in 1997 to facilitate the outpatient delivery of the then newly available anticoagulant, LMWH. Consecutive, anticoagulated VTE patients who were referred to the Mayo Clinic Thrombophilia Center for periprocedural anticoagulation management over the 10-year period, January 1, 1997 to December 31, 2007, were eligible for inclusion; 97% consented to participate. Patients were excluded from this analysis if they had indications beyond VTE for chronic anticoagulation therapy (eg, atrial fibrillation, mechanical heart valves, or vascular bypass grafts). All patients were followed-up for 3 months from the date of the Thrombophilia Center consultation. Patients (or families members for deceased patients) who did not return for a clinic visit were mailed a questionnaire or contacted by telephone for any symptoms or signs of thromboembolism or bleeding in the 3 months after the Thrombophilia Center consultation and for vital status. The local medical records of patients reporting thromboembolism or bleeding and death certificates and autopsy reports for deceased patients were obtained and reviewed by the study end point adjudication committee. Two experienced study nurse abstractors reviewed the complete inpatient and outpatient medical records for each patient. The study was approved by the Mayo Clinic Institutional Review Board.

Periprocedural Anticoagulation Management

Patients were referred to the Thrombophilia Center for periprocedural anticoagulation management recommendations between 4 and 7 days before the anticipated procedure. Each patient was evaluated for the patient-specific risk of thromboembolism and the procedure-specific risk of major bleeding. The risk of VTE recurrence was estimated based on the presence of both acquired and congenital risk factors.13,14 For patients requiring outpatient dental or other minor procedures associated with either a low risk of bleeding or easy access for physical hemostasis, the intensity of warfarin anticoagulation was reduced to the lower limit of the therapeutic range (INR = 2.0). For patients undergoing a nonminor procedure who were otherwise deemed to be at low risk for recurrent VTE, warfarin was stopped 5 days before surgery and resumed as soon as possible after surgery, starting with the patient’s usual daily warfarin dose. For nonminor procedures in patients deemed to be at moderate to high risk for VTE recurrence, warfarin was stopped 5 days before surgery and the patient was “bridged” with LMWH as an outpatient when the INR was anticipated to be below the lower limit of the therapeutic range. The last LMWH injection was administered 24 hours before the procedure at 50% of the calculated daily dose. For those high-risk patients requiring postoperative therapeutic dose LMWH, the first dose administration was delayed 24 to 48 hours. Warfarin and LMWH therapy were overlapped for at least 5 days and until the INR exceeded the lower limit of the therapeutic range for at least 24 hours. Over the 10-year time period, 3 successive LMWH (ardeparin, dalteparin, and enoxaparin) were on the Mayo Clinic formulary and were used for periprocedural anticoagulation therapy (Table 1). All patients received aggressive deep vein thrombosis (DVT) prophylaxis postoperatively. The current guidelines for DVT prophylaxis are both patient-specific and procedure-specific, and recommendations vary depending on these variables in combination. Recommendations included use of both mechanical (sequential compression devices and graduated compression stockings) and pharmacological DVT prophylaxis, depending on patient-specific and procedure-specific variables. Aspirin was stopped 1 week before the procedure and restarted after the procedure when hemostasis was assured.

Definition of Outcomes

The primary efficacy outcome was symptomatic arterial or venous thromboembolism occurring from 5 days before the first day that warfarin was stopped) to 3 months after the procedure or surgery. VTE recurrence was defined as DVT or pulmonary embolism as previously described.13,14 Arterial thromboembolism was defined as ischemic stroke, transient ischemic attack, amaurosis fugax, unstable angina, myocardial infarction, or other peripheral artery thromboembolism. Criteria for unstable angina, myocardial infarction, stroke, and transient ischemic attack were adapted from those of the American Heart Association.15 Peripheral artery embolism was defined as acute ischemia of an extremity or any organ other than the brain and arterial thromboembolus confirmed by either embolectomy or direct imaging.

The primary safety end point was major bleeding. Major bleeding was defined as overt bleeding plus a hemoglobin decrease of ≥2 g/dL after the procedure or transfusion of ≥2 units of packed red blood cells, or intracranial, intraspinal, intraocular, retroperitoneal, pericardial, or fatal bleeding.16 Minor bleeding was defined as overt bleeding that did not meet criteria for major bleeding.

All events were adjudicated using a priori study criteria by a committee comprising 4 Thrombophilia Center physicians blinded to patient name and health care provider. To determine whether there was any relationship between bleeding and thrombotic outcomes and the timing of the procedure relative to the VTE diagnosis, patients were divided into 1 of 3 groups (acute, <30 days; subacute, 31–90 days; or chronic, ≥91 days).
Table 2. All VTE Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Bridging Heparin (N=261)</th>
<th>Bridging Heparin (N=514)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD</td>
<td>64.6±14.3</td>
<td>59.4±15.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>115 (44%)</td>
<td>275 (54%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Acute/nonacute VTE, N (%)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute VTE</td>
<td>6 (2%)</td>
<td>47 (9%)</td>
<td></td>
</tr>
<tr>
<td>Subacute VTE</td>
<td>19 (7%)</td>
<td>92 (18%)</td>
<td></td>
</tr>
<tr>
<td>Chronic VTE</td>
<td>231 (89%)</td>
<td>360 (70%)</td>
<td></td>
</tr>
<tr>
<td>Unable to categorize</td>
<td>5 (2%)</td>
<td>15 (3%)</td>
<td></td>
</tr>
<tr>
<td>VTE, location N (%)</td>
<td></td>
<td></td>
<td>0.50</td>
</tr>
<tr>
<td>PE: DVT</td>
<td>129 (49%)</td>
<td>226 (44%)</td>
<td></td>
</tr>
<tr>
<td>Lower extremity</td>
<td>110 (42%)</td>
<td>235 (46%)</td>
<td></td>
</tr>
<tr>
<td>Upper extremity</td>
<td>10 (4%)</td>
<td>22 (5%)</td>
<td></td>
</tr>
<tr>
<td>Abtypical location</td>
<td>12 (5%)</td>
<td>31 (6%)</td>
<td></td>
</tr>
<tr>
<td>Active cancer</td>
<td>56 (22%)</td>
<td>155 (30%)</td>
<td>0.011</td>
</tr>
<tr>
<td>Chemotherapy, N (%)</td>
<td>10 (11%)</td>
<td>58 (27%)</td>
<td>0.003</td>
</tr>
<tr>
<td>IVC filter, N (%)</td>
<td>29 (11%)</td>
<td>71 (14%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Bleeding history, N (%)</td>
<td>37 (14%)</td>
<td>101 (20%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Aspirin, N (%)</td>
<td>34 (13%)</td>
<td>54 (11%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Thrombophilia, N (%)</td>
<td>57 (22%)</td>
<td>137 (27%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Aggressive thrombophilia, N (%)</td>
<td>11 (4%)</td>
<td>45 (9%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Previous nonembolic stroke/TIA, N (%)</td>
<td>18 (7%)</td>
<td>52 (10%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

PE indicates pulmonary embolism; TIA, transient ischemic attack.

Statistical Analyses

Continuous numeric variables were reported as means with SD. Frequencies were reported when appropriate. Continuous variables were compared between the groups treated and not treated with LMWH (bridging heparin and no bridging heparin) using the Wilcoxon rank-sum test. Categorical factors were compared between these groups using the χ² test for independence. The 3-month cumulative incidence rates for first events of thromboembolism, major and minor bleeding, were estimated using the Kaplan-Meier method. Recurrence rates were calculated per patient as opposed to per procedure. Cox proportional hazard models were constructed for each of 4 outcomes (VTE, any thrombotic event, major bleeding, and all-cause mortality).

Results

Patient Demographic

During the 10-year study period, 775 patients receiving chronic warfarin therapy for the sole indication of VTE (50% women; mean age, 61±15 years) were referred to the Thrombophilia Center for periprocedural anticoagulation management. Ninety-day follow-up data were available for all but 5 (0.6%). Three-hundred thirty-three patients had a history of >1 episode of venous thrombosis. Baseline patient characteristics are provided in Table 2 separated by whether bridging heparin therapy was provided. The majority of venous thrombotic events were provoked (70%); however, contributing mechanisms could not be firmly defined in 23 cases. Of the 775 patients in our study, 43 had venous thrombosis at “atypical” sites, including hepatic (n=1), portal (n=10), mesenteric (n=14), renal (n=4), cerebral (n=1), and multisegmental (n=13). Patients receiving bridging therapy with LMWH were younger, with a greater percentage of these patients being women. Patients with active cancer and those currently receiving chemotherapy were also more likely to have received LMWH bridging therapy. Conversely, bridging strategy did not differ by the location of the original thrombotic event. Other variables, including presence of an inferior vena cava (IVC) filter, history of major bleeding, current aspirin therapy, or presence of a defined thrombophilia, did not differ by bridging strategy. Aggressive thrombophilia was defined as patients with either homozygous or compound heterozygous mutations of factor V Leiden and the prothrombin G20210A mutations. Protein C, protein S, antithrombin mutations, and lupus anticoagulant/antiphospholipid antibody syndrome were also within this definition. Of the 275 patients tested for antiphospholipid antibody syndrome, 10 had positive results (7 primary and 3 secondary). These patients more frequently had bridging.

Of the total cohort, 53 (7%) patients had their VTE diagnosed within 30 days and it was designated acute. Of the remainder, VTE was deemed subacute in 111 (15%) patients and chronic in 591 (78%) patients. Patients with either acute (87%) or subacute (81%) thrombosis were more likely to receive bridging LMWH compared to those with chronic VTE (59%; P<0.001). Patients with acute VTE were younger (55±17 years) compared to those with subacute (59±15 years) or chronic (62±15 years) VTE (P<0.001). Patients with acute and subacute groups had greater percentages with active cancer (48% vs 48% and 22%, respectively; P<0.001) and were more frequently receiving chemotherapy (31% vs 34% and 18%, respectively; P=0.018) relative to chronic VTE patients.

These 775 patients underwent a total of 779 procedures (Table 3). Fifteen patients had a procedure scheduled that ultimately was not performed. The timing of warfarin cessation, reinitiation, and the mean duration off warfarin, as well as the timing and duration of bridging heparin therapy, are shown in Table 4.

One hundred patients had an IVC filter. Of these, 90 were permanent filters (most commonly Greenfield or Venatech devices) and 10 were optional (temporary or retrievable).
filters. Only 4 IVC filters were placed as part of the periprocedural bridging strategy. Two of these 4 filters were permanent devices placed in patients with chronic thromboembolic pulmonary hypertension scheduled to undergo pulmonary thrombectomy. The other 2 patients had acute proximal thrombi requiring urgent surgery.

Thromboembolism
Three-month follow-up data were available for all but 5 patients, including symptomatic thromboembolism, bleeding, and vital status (Table 5). Over this time period, there were 14 patients with a total of 16 thromboembolism events for a 3-month cumulative thromboembolism incidence rate of 1.8% (95% CI, 0.9%–2.8%). These events included 10 VTE events, 1 acute coronary syndrome, and 5 cerebrovascular events. The thromboembolic events were evenly distributed between those individuals receiving and not receiving bridging LMWH therapy. The majority of the thromboembolic events (71%) occurred >30 days from the procedure (Figure 1A). These events did not differ by the acuity of the original thrombotic event (Figure 2A). Active cancer was the only independent predictor of thrombotic recurrence (HR, 4.86; 95% CI, 1.63–14.50; \(P=0.005\)). When thrombotic complications were restricted to VTE events, active cancer remained an independent predictor (HR, 8.04; 95% CI, 1.62–39.83; \(P=0.01\)).

Pulmonary embolism was a rare event, occurring in 4 patients (0.5%). Two of these 4 patients died as a result of their pulmonary embolism. Neither of these patients was from the acute VTE group. Both deaths occurred in patients who received “bridging” LMWH.

Bleeding
There was a total of 37 bleeding events, of which 14 were considered major bleeding as established by the criteria used in this study (Table 5; Figure 1B, 2B). The 3-month cumu-
Discussion

The major finding of this study is that the 3-month cumulative incidence of recurrent thromboembolism, major hemorrhage, and death among VTE patients requiring temporary interruption of chronic warfarin therapy for an invasive procedure is quite low. The current guidelines for periprocedural anticoagulation management of VTE patients is based on limited data. Most of the published data on periprocedural anticoagulation management come from studies of patients with either mechanical heart valves or chronic atrial fibrillation. One of largest and most recently published studies enrolled 1262 patients in a protocol-driven, multicenter, prospective, inception cohort design. Of these, however, only 16.6% were anticoagulated for the indication of VTE. These investigators stratified patients by thromboembolic risk, and those deemed at high risk were provided preoperative and postoperative LMWH at 70 anti-Xa U/kg twice daily. Those at moderate to low risk were administered once-daily prophylactic LMWH doses. Follow-up was limited to 30 days. Major bleeding was low (1.2%), as were thromboembolic events (0.4%). Another study enrolled 1024 patients, of whom only 14% were using warfarin for VTE. Like in the previous study, follow-up was also limited to 30 days. Thromboembolism was rare (0.7%) and occurred only in those patients not receiving periprocedural bridging therapy. Major hemorrhage (0.6%) and clinically significant nonmajor hemorrhage (1.7%) were also rare. Although helpful, these studies include a heterogeneous population of patients receiving anticoagulation for various indications. Whereas <15% of these patients had VTE as an indication for anticoagulation, it remains unclear whether these findings can be applied to this population. Without disease-specific outcome data for this practice, both clinicians and guidelines are left without sufficient knowledge of whether periprocedural anticoagulation recommendations for patients with 1 indication can be generalized to other indications. We now provide periprocedural data on 775 patients undergoing 779 procedures with VTE as the sole indication for anticoagulant therapy.

VTE is a unique disease entity among those requiring chronic anticoagulation therapy. Unlike atrial fibrillation or mechanical heart valves, patients with previous VTE are particularly prone to disease recurrence when subjected to major operative procedures. Major surgery is known to be one of the most aggressive acquired risk factors for this disease, with a hazard ratio exceeding 20. Unlike reports by others, our report has extended the duration of follow-up to 3 months. According to the guidelines, 3 months is the typical timeframe during which a thrombotic event occurs within the 3-month interval, then one can assume a causal relationship. Beyond this timeframe, causality can no longer be inferred. By truncating the follow-up to 1 month, important outcome events may be missed. In our experience, more than half of the thrombotic outcomes occurred between the 30- and 90-day time window (Figure 1A, 2A). Whereas extending the follow-up period to 3 months may not be important for atrial fibrillation and mechanical heart valves, it is preferable for studies of VTE recurrence. This is underscored in the guidelines that are increasingly extending the timeframe for postoperative DVT prophylaxis. Furthermore, these same
guidelines have designated 3 months as the necessary requirement for VTE “treatment.” Despite extending our follow-up period to 3 months, the frequency of hard outcomes did not differ from other reports.

Intuitively, one might feel compelled to place an IVC filter in patients with acute or subacute VTE requiring anticoagulation cessation in order to perform an invasive procedure. Of the 775 patients in this study, 13% had an IVC filter in place at the time of referral. Despite placing only 4 filters as part of the “bridging” strategy (2 for chronic thromboembolic pulmonary hypertension anticipating surgical pulmonary endarterectomy), pulmonary embolism was a rare event occurring in 4 patients (0.5%). Of these however death due to pulmonary embolism occurred in 2. Could either of these 2 deaths been anticipated? Both patients had active cancer yet neither patient had an acute VTE at the time of consultation. Furthermore, both patients were provided peri-procedural “bridging” LMWH therapy. Anticipating these rare yet disastrous outcomes remains problematic because limited tools currently are available for their prediction. Therefore, in keeping with the current guidelines, IVC filter placement appears unwarranted and should not be a routine procedure as part of the “bridging” strategy in these patients.

By multivariate analysis, active cancer was the only significant predictor of bad outcomes. As noted in the multivariate analysis, much if not all of these recurrent thrombotic events occurred in patients with active cancer. Not previously evaluated by either our group or others, active cancer was associated not only with recurrent thromboembolic events but also with major hemorrhage. Active cancer is associated with an increased propensity for VTE, which is compounded by treatment with chemotherapy. Major surgery for cancer-related disease remains one of the greatest risk factors for postoperative thrombotic events. Furthermore, thrombocytopenia and hepatotoxicity-related complications of chemotherapy and the disease itself predispose the individual to hemorrhagic outcomes, further complicating the use heparin therapies. Liver disease and fluctuating diet complications treatment with vitamin K antagonists. Whether these outcomes reflect complications of anticoagulation management, cancer-related treatments, or simply the natural history of the disease itself is unclear. All of these variables underscore the complexity of managing such patients.

The impact of a defined congenital or acquired thrombophilia was also assessed in the periprocedural management of these patients. To our knowledge, the impact of these variables on periprocedural outcomes has not previously been reported. Of the 775 patients in this cohort, 194 (25%) had a defined thrombophilia (Table 2). Of these, 137 received bridging LMWH, whereas the remainder did not. Fifty-seven had an aggressive thrombophilia, of which 71% were “ bridged” with LMWH. By multivariate analysis, neither thrombophilia nor aggressive thrombophilia was associated with a thrombotic outcome. It would therefore appear that the mere presence of either acquired or congenital thrombophilia does not in and of itself mandate the use of periprocedural LMWH therapy in patients with previous VTE.

The location of the original venous thrombus (lower or upper extremity DVT, pulmonary embolism, or atypical) did not appear to influence the likelihood of recurrent events. Recurrent events during the periprocedural time interval therefore are not adequately predicted by the nature or location of the original event. There were 13 deaths occurring during the 3-month period of this study, all in patients with active cancer. Five of these deaths occurred suddenly, and pulmonary embolism must remain a possible though unproven mechanism of death in these patients. These deaths occurred despite LMWH bridging in 4 and IVC filter placement in 1. Whereas the original thrombotic event in 3 of these patients was a DVT only, it is not clear that these deaths could have been predicted or prevented short of foregoing the invasive procedure.

Several limitations of this study should be noted. First, the delivery of LMWH was not assigned randomly. Careful patient stratification based on perceived risks and benefits of LMWH by the attending physicians may have contributed to both the low rate of bleeding and thromboembolic complications observed. Moreover, because this was not designed as an intention-to-treat trial, patient preferences may have also contributed to these outcomes, both favorably and unfavorably. Second, although referral to the Mayo Clinic Thrombophilia Center was open to all VTE patients, we cannot exclude the possibility of referral bias. For example, VTE patients with a perceived high or low risk for thromboembolism may not have been referred to our center, which could have caused an underestimation or overestimation of the true thromboembolic and bleeding rate, respectively. This variable, however, may be less pronounced for this disease as compared to that of patients with mechanical heart valves, for example.

Among VTE patients referred to our Thrombophilia Clinic and managed according to our protocol, the 3-month cumulative incidence of thromboembolism during temporary anticoagulation interruption for an invasive procedure was low. Our current practice is to limit postprocedural heparin to prophylaxis doses only as outlined by the guidelines. Warfarin is restarted as soon as feasible once the patient is able to use oral medications. For patients with remote history of VTE, it appears to be safe to simply hold warfarin for the periprocedural interval without preoperative bridging heparin therapy. Patients with active malignancy require careful attention to limiting bleeding outcomes while maximizing thromboprophylaxis. Further studies are warranted to better define best practices for cancer patients requiring anticoagulant interruption for an invasive procedure. A randomized, controlled trial is currently underway to better define the utility of bridging therapy with LMWH in patients with atrial fibrillation. A similar trial enrolling patients with VTE is also warranted.

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Disclosure
None.
References


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