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Outcome of central venous catheter associated upper extremity deep vein thrombosis in cancer patients

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ABSTRACT

Introduction: Data on efficacy and safety of using low molecular weight heparin in cancer patients with catheter-related upper extremity deep vein thrombosis is scarce and the risk of recurrent venous thromboembolism after discontinuation of anticoagulation is unknown.
Material and methods: We conducted a retrospective cohort study including consecutive cancer outpatients assessed for the management of symptomatic central venous catheter-associated proximal upper extremity deep vein thrombosis.
Results: Of 99 included patients, 89 were treated with one month of full therapeutic weight-adjusted dose of low molecular weight heparin followed by an intermediate dose. Median duration of anticoagulation was 124 days (range 40 to 1849). No recurrent venous thromboembolism and two major bleeding episodes occurred during the first 3 months of treatment. Eighty patients were followed-up after anticoagulation discontinuation for a median of 632 days (range 6 to 2495). Central venous line was pulled in all patients in remission and in 26 of the 29 patients (89.6%) with active cancer. Five recurrences were observed during follow-up. The cumulative probability of recurrent venous thromboembolism was higher in patients whose cancer was active at the time of anticoagulation discontinuation as compared with those in remission (22.2% (95% CI: 0 to 40.6) *vs.* 2.3% (95% CI: 0 to 6.7)).
Conclusion: The risk of venous thromboembolism recurrence in patients whose central venous catheter has been pulled out and cancer is in remission appears low following anticoagulation discontinuation and after a minimum of 3 months of full/intermediate dose.

Introduction

Central venous catheters are used in cancer patients to facilitate chemotherapy, transfusions and parenteral nutrition deliverance, and to provide readily available venous access for laboratory testing. However, upper extremity deep vein thromboses (UEDVT) are a frequent complication and occur in approximately 2-6% of cancer patients with a central venous catheter [1]. Vessel injury caused by the catheter insertion, venous stasis caused by indwelling catheter, and cancer-related hypercoagulability all contribute to the development of UEDVT [2]. Anticoagulation with low molecular weight heparin (LMWH) for a minimum of 3 months is the currently recommended treatment for catheter-related UEDVT in cancer patients [3,4]. Data on efficacy and safety of LMWH in this setting are scarce and current recommendations are extrapolated from efficacy data for the management of deep vein thrombosis of the lower extremity [5].

Initiating therapeutic anticoagulation allows keeping a functioning catheter in place with little risk of recurrent venous thromboembolism (VTE) or extension of the UEDVT [6]. Recommendations suggest that as long as the line is functional and required for ongoing therapy, anticoagulation should be continued [3,4,7]. Following catheter removal and a minimum of three months of anticoagulant therapy, the risk of recurrence of VTE is likely to be low and it might be reasonable to discontinue anticoagulant therapy. However, there are no data available to support this hypothesis. Therefore, we sought to address these important knowledge gaps and assess the efficacy and safety of LMWH for the treatment of catheter-related UEDVT in cancer patients and determine the risk of recurrence of VTE after discontinuation of anticoagulation.

Materials and Methods

Design and Setting

We conducted a retrospective cohort study of consecutive cancer outpatients seen in our centre between July 2008 and December 2012

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for management of a symptomatic central venous catheter related proximal UEDVT. A standardized case report form (CRF) was used to record relevant patient demographics and outcomes of interest. The protocol was approved by The Research and Ethics Board of our institution. Patients were included if they had: 1) documented active malignancy (receiving therapy (chemotherapy or radiotherapy) or with metastatic disease); 2) no on-going anticoagulation; and 3) objectively proven episode of symptomatic central venous catheter DVT of upper extremity involving the axillary vein or a more proximal vein. Treatment type and duration was left at discretion of the attending physician.

Study Outcomes

Venous thromboembolism was defined and reported as recommended by the International Society on Thrombosis and Haemostasis (ISTH) SSC Haemostasis & Malignancy [8]. Recurrent DVT was defined as a new non-compressible site or proximal extension from a previously non-compressible site. Recurrent pulmonary embolism was defined as a new mismatched segmental or greater perfusion defect on V/Q scan or a new intraluminal filling defect in a segmental or larger pulmonary artery on computed tomographic pulmonary angiography. Major bleeding episode was defined as per the ISTH criteria [9].

Statistical Analysis

Baseline summary statistics were reported as mean and standard deviation (SD) for continuous variables and as number (%) for categorical variables. Comparisons were made by Student t-test for quantitative variables and Fisher exact test for qualitative variables. Median time of anticoagulation, between diagnosis of VTE and recurrence for patients who did not discontinue anticoagulation, and median time between anticoagulation discontinuation and VTE recurrence or last day of follow-up free of event were determined. Kaplan-Meier estimates and 95% confidence intervals (CIs) were calculated to assess the probability of VTE recurrence. Recurrence distributions were compared by the log-rank test.

Results

A total 116 patients with catheter associated proximal UEDVT were identified (Fig. 1). Seventeen patients were excluded from analysis due to missing data about treatment (n = 8), or lost to follow-up (n = 9). (See Fig. 2.)

Thus, a total of 99 patients were included in the analyses. Baseline characteristics are depicted in Table 1. Sixty nine percent of patients were women and the mean age was 57.3 (± 12.8 years). Twenty four (24%) patients had metastatic disease and 79 had a PICC line inserted (Table 1). All patients had a symptomatic UEDVT event at presentation. Overall, patients were followed-up for a median of 604 days (range: 62 to 2601).

The most common treatment regimen was one month of full therapeutic weight-adjusted dose of LMWH (dalteparin 200 units/kg daily, tinzaparin 175 units/kg daily, or enoxaparin 1 mg/kg twice daily) followed by intermediate dosing (75 to 80% of the full therapeutic weight adjusted dose) (n = 89). A preventive dose of LMWH was given after 3 (n = 8), 6 (n = 4), or 12 (n = 1) months of intermediate dosing of LMWH (Fig. 1). One patient was initially treated with LMWH and then switched to rivaroxaban due to skin reaction at injection sites. No patients received thrombolytic therapy.

Safety and Efficacy of Anticoagulation

The median duration of anticoagulation was 124 days (range: 40 to 1849). Two patients had major upper gastrointestinal bleeding episodes that led to discontinuation of anticoagulation prior to completion of three months of treatment. The incidence of major bleeding episodes

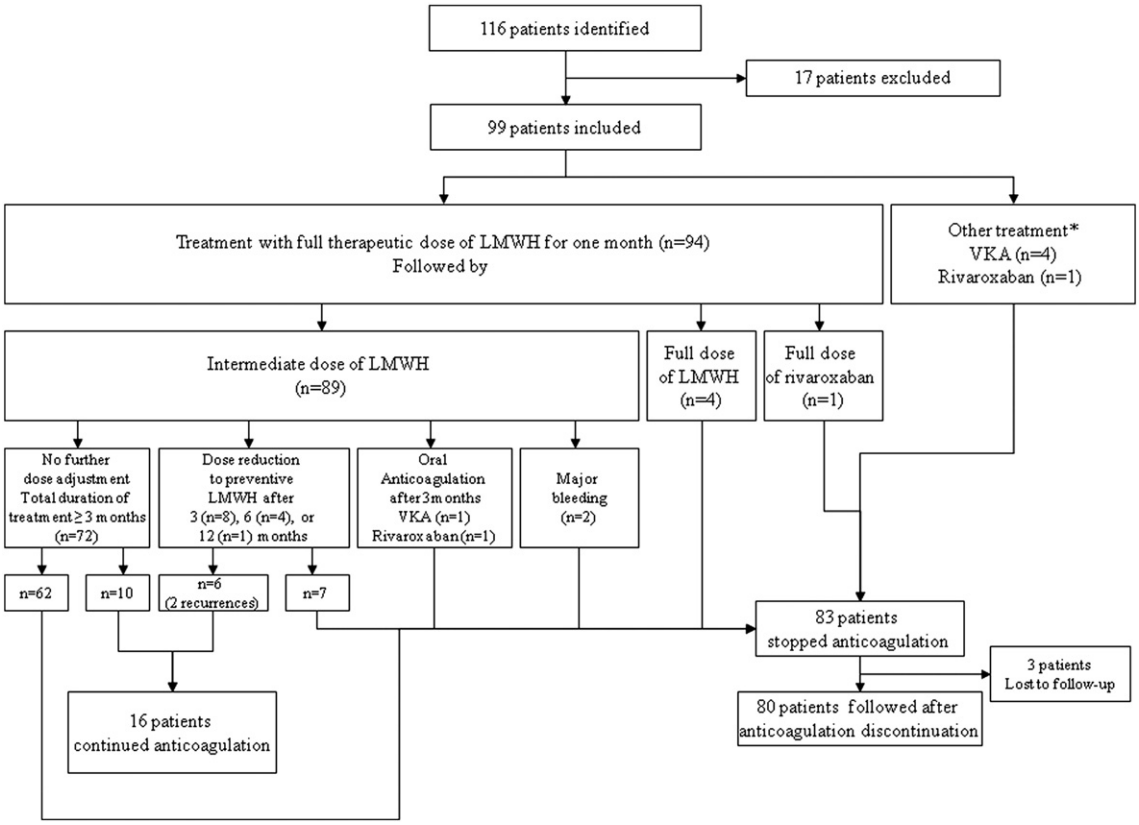

Fig. 1. Flow diagram. Figure legend: * for a median time of 104 days (range 70 to 149).