Pathways for lower extremity superficial vein thrombosis management in an academic medical center

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ABSTRACT

There is currently no established management pathway for lower extremity superficial vein thrombosis (SVT), leading to significant uncertainty among front-line providers. This study aimed to assess prescribing practices and patient outcomes for the initial treatment of lower extremity SVT. This descriptive retrospective cohort study in a single center included consecutive patients with radiographically diagnosed acute lower extremity isolated SVT between January 1, 2016 and December 31, 2021. Exclusions were chronic SVT, concomitant deep vein thrombosis or pulmonary embolism, required anticoagulation for another indication, or no documented SVT treatment plan. This 6-year study included 265 patients. The majority received conservative therapy as the SVT management strategy (n=188, 70.9%), while 23% (n=61) received anticoagulation therapy. Few patients received no treatment (n=13, 4.9%) or surgery (n=3, 1.1%). The most common strategy in those utilizing anticoagulation was a VTE treatment-dose DOAC, but the duration varied considerably (11.5% 30 days or less, 37.7% 31-45 days, 21.3% for 46-90 days, and 24.6% >90 days). Ninety-day progression to VTE occurred in 8 patients (3.1%, 2 in the anticoagulation therapy group and 6 in the conservative therapy group). Bleeding occurred in 6 patients (2.3%, 4 in the conservative therapy group and 2 in the anticoagulation group). Over a six-year period, there were varying pathways of managing acute lower extremity SVT without a concerning signal in adverse events with any single treatment approach. Future study should focus on which patients benefit from anticoagulation therapy *vs* conservative therapy and clarifying the optimal anticoagulation treatment intensity and duration.

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Introduction

Superficial vein thrombosis (SVT) of the lower extremities is a common condition that presents significant challenges in clinical management due to the absence of a definitive treatment pathway. Management strategies for SVT vary widely in practice, contributing to uncertainty among front-line providers.[1] This is further complicated by the heterogeneity of clinical trials on SVT, which often employ differing methodologies, treatment regimens, and outcome measures. As a result, drawing conclusions on the most effective management strategies remains difficult. Treatment options for SVT include conservative approaches such as observation, topical or compressive therapies, and serial imaging, as well as pharmacologic interventions, including non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulants, and even surgical interventions. The American College of Chest Physicians (ACCP) updated its guidelines on venous thromboembolism (VTE) in 2021, recommending anticoagulation for 45 days in patients at risk of clot progression, particularly those with extensive SVT, proximal involvement, or a history of VTE, among other risk factors. This recommendation includes the use of prophylactic-dose fondaparinux or rivaroxaban as alternatives, although the evidence supporting this approach remains of low certainty. Given that direct oral anticoagulants (DOACs) are widely recommended as first-line therapy for deep vein thrombosis (DVT) and pulmonary embolism (PE),[2,3] there is increasing interest in their use for SVT management as well. This

study aimed to explore institutional prescribing practices for DOACs in the initial treatment of lower extremity SVT and to evaluate the associated patient outcomes.

Materials and Methods

In this descriptive retrospective cohort study, we included consecutive patients with radiographically diagnosed acute lower extremity isolated SVT within the University of Utah Health (UUH) system between January 1, 2016, and December 31, 2021. Patients were excluded if they had chronic SVT, concomitant DVT or PE, were already receiving anticoagulation for another indication at the time of diagnosis, or had no documented SVT management plan. Manual chart review was conducted to characterize the initial SVT treatment pathway into a conservative therapy group (defined as compression, heat, elevation, oral non-steroidal anti-inflammatory drugs, or topical pain relievers), an anticoagulation therapy group (defined as either with VTE treatment dosing or prophylactic dosing), surgery, or no therapy. Duration of the chosen therapy was also stratified. Clinical adverse events up to 90 days from the acute SVT diagnosis were assessed and these included progression of SVT to either DVT or PE, major bleeding, or clinically relevant nonmajor bleeding.

Results

A total of 526 patients were screened for eligibility and 265 patients met inclusion criteria. The mean age was 51.5 years (SD=15.3), 148 (55.8%) were female, and 215 (81.1%) were Caucasian. Of the ACCP 2021-cited risk factors for thrombus extension, the most prevalent were SVT length >5 cm (n=158, 59.6%), GSV location (n=142, 53.6%), prior history of VTE (n=78, 29.4%), active cancer (n=29, 10.9%), and thrombus <3 cm from the saphenofemoral junction (n=26, 9.8%).

The majority of patients in this cohort received conservative therapy as their SVT management strategy (n=188, 70.9%). Sixty-one patients (23.0%) received anticoagulation therapy, 13 (4.9%) received no therapy, and 3 (1.1%) underwent surgery. In the 61 patients prescribed anticoagulation therapy, 7 patients (11.5%) were treated for 30 days or less, 23 patients (37.7%) were treated for 31-45 days, 13 patients (21.3%) were treated for 46-90 days, 15 patients were treated for >90 days (24.6%), and we could not determine duration of therapy for 3 patients (4.9%). DOACs were preferred (n=41, 67.2% of patients) with 22 (36.1%) receiving apixaban and 19 (31.1%) rivaroxaban, and the remaining patients received enoxaparin monotherapy (n=13), enoxaparin bridged to warfarin (n=6), or fondaparinux (n=1) (Figure 1). VTE treatment dosing was prescribed in 40 patients

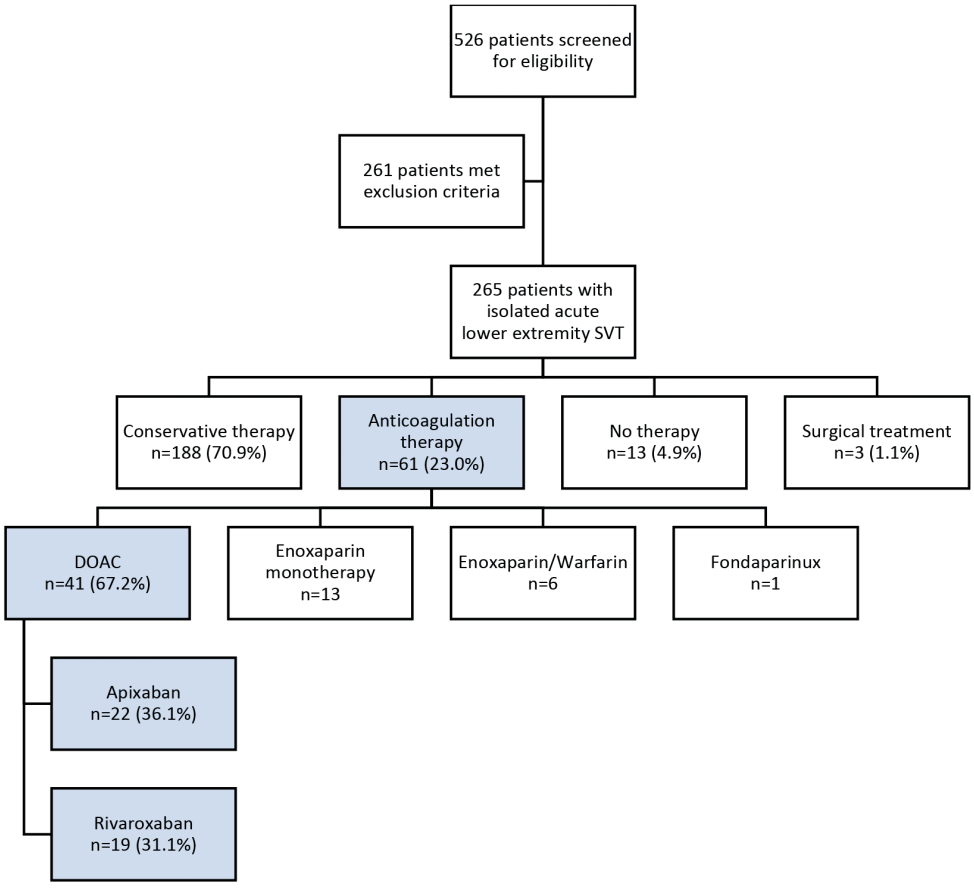

Figure 1. Lower extremity superficial vein thrombosis management pathways: DOAC focus. DOAC, direct oral anticoagulant; SVT, superficial vein thrombosis.

(65.6%), and 21 patients (34.4%) received prophylactic dosing.

Progression from SVT to VTE occurred in 8 patients (3.1%), including 5 patients with DVT, 2 with PE, and one patient with both DVT and PE. Two thrombotic events occurred in the anticoagulation therapy group (2/265, 0.75%) and 6 (6/265, 2.3%) in the conservative therapy group. Bleeding occurred in 6 patients (2.3%), 4 in the conservative therapy group and 2 in the anticoagulation therapy group – all receiving prophylactic dose anticoagulation. Of these, 5 (1.9%) were clinically relevant non-major bleeding events (3 in the conservative therapy group and 2 in the anticoagulation group), and one major bleeding event (0.5%) occurred in a patient managed with conservative therapy.

Discussion

In this cohort study of 265 patients within an academic medical center who had radiographically diagnosed lower extremity isolated SVT, the majority received conservative management, with only just under a fourth receiving anticoagulation therapy. Two-thirds of anticoagulated patients received either apixaban or rivaroxaban, predominantly with the acute VTE treatment dosing regimen. We hypothesize that the low utilization of fondaparinux (suggested for SVT treatment over other therapies in the 2021 ACCP VTE guideline[2,4] due its having the largest randomized controlled trial for SVT) is multifactorial: i) patient preference for an oral *vs* an injectable anticoagulant; ii) the relatively higher cost for fondaparinux and poor prescription insurance formulary uptake *vs* DOACs in the United States. Duration of anticoagulation therapy for the management of SVT was variable, with just over half of patients receiving anticoagulation for 1-3 months, likely reflecting provider uncertainty.

Ninety-day clinical adverse events were relatively uncommon in this cohort and there were no concerning signals in any of the SVT management approaches, indicating that a variety of approaches may be acceptable. Specifically, 3.1% of patients experienced progression to VTE during the 90 days following SVT diagnosis. These progression rates are lower than the composite outcomes in the fondaparinux SVT randomized trial (0.9% for fondaparinux and 5.9% for placebo).[4] Bleeding outcomes were similarly infrequent. A limitation of the study is that clinical adverse events diagnosed external to UUH were not captured.

Conclusions

In summary, these data reflect that there are likely numerous acceptable pathways for management of isolated lower extremity SVT. Questions for future study include a comparison of which patients with SVT may truly benefit from conservative therapy *vs* DOAC therapy, anticoagulant prophylactic dosing *vs* treatment dosing, and clarifying the minimum and maximum beneficial duration of anticoagulation therapy.

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