Presence and degree of residual venous obstruction on serial duplex imaging is associated with increased risk of recurrence and progression of infrainguinal lower extremity deep venous thrombosis

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ABSTRACT

Objective: The role of follow-up venous duplex ultrasound (DUS) after acute lower extremity deep vein thrombosis (DVT) remains unclear, yet it is commonly performed. We aimed to clarify the role of follow-up DUS. Our primary objective was to determine the association between the presence of residual venous obstruction (RVO) on DUS and DVT recurrence or propagation (rDVT). Secondary objectives included finding risk factors associated with RVO and rDVT.

Methods: We conducted a retrospective study of patients diagnosed with DVT on DUS from January 1, 2011, to December 31, 2013, that received a follow-up DUS. Patient demographics, risk factors, medications, and DUS findings were recorded. Ten segments from the common femoral to distal calf veins were checked for the presence of RVO, DVT propagation, and recurrence. RVO was defined as any nonacute venous obstruction with more than 40% of luminal diameter remaining during compression or the presence of chronic post-thrombotic occlusive disease. rDVT was measured as either a new acute DVT in the previously involved segment, or involvement of a new segment in the same extremity.

Results: A total of 185 lower extremities representing 156 patients met the inclusion criteria. RVO was noted in 61.1% of limbs. The 3-year rDVT rate was 10.3%. Patients with recurrent venous thromboembolism or thrombophilia had a higher risk of developing RVO (odds ratio [OR], 2.89, $P < .01$; OR, 4.39, $P = .04$, respectively). Extremities with larger clot burden had an increased risk of RVO on follow-up DUS (OR, 1.25 per segment; $P < .01$). The presence and degree of RVO on follow-up DUS had an increased risk of rDVT on subsequent DUS (OR, 3.90, $P = .04$; OR, 1.21 per segment, $P = .04$, respectively). Limbs with complete resolution of DVT by DUS had a significantly decreased risk of rDVT (OR, 0.26; $P = .04$).

Conclusions: Extremities with larger initial clot burden exhibited an increased risk of subsequent RVO. The presence of RVO and, interestingly, the number of involved segments on follow-up DUS increased the risk of rDVT. Our results suggest that the presence of residual disease and increased RVO burden on follow-up DUS after an acute DVT may identify those patients who are at an increased risk for rDVT and may help guide the duration of anticoagulation therapy. (J Vasc Surg: Venous and Lym Dis 2018;■:1-8.)

Despite effective anticoagulation for prophylaxis and treatment, lower extremity acute deep venous thrombosis (DVT) remains a significant cause of morbidity and mortality. An estimated 900,000 people suffer from DVT annually, resulting in approximately 100,000 deaths in the United States alone.[1] In addition, after an episode of DVT, approximately half of all patients suffer from post-thrombotic syndrome, resulting in chronic swelling, pain, discoloration, skin changes of affected limbs, and diminished quality of life. In addition, unprovoked venous thromboembolism (VTE) is associated with a risk of recurrence as high as 30% within 5 to 10 years.[1]

The role of follow-up serial venous duplex ultrasound (DUS) in the management of DVT remains unclear. The American College of Chest Physician Evidence-Based Clinical Practice Guidelines recommends the standard treatment for VTE to be at least 3 months of anticoagulation therapy, with further assessment for extended anticoagulation, based on the risk-benefit ratio, particularly in patients with unprovoked VTE. Routine follow-up DUS is not recommended, except in the case of an acute

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This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. T.Y. was supported by the National Institutes of Health under the Ruth L. Kirschstein National Research Service Award, Advanced Research Training in Immunology for Surgery Trainees (ARTIST) from the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number NIH T32AI 106704-01A1. The content is solely the responsibility of the authors and does not necessarily represent the official views the National Institutes of Health.

Author conflict of interest: none.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X

https://doi.org/10.1016/j.jvsv.2017.12.059

isolated distal DVT; a follow-up DUS in 2 weeks is recommended if anticoagulation is not given.[2] Previous studies have shown that routine surveillance after an acute DVT for residual venous obstruction (RVO) may help in determining the risk of DVT recurrence and, therefore, may be useful to guide the duration of anticoagulation.[3,4] However, other studies demonstrate conflicting results, making its clinical utility debatable.[5,6] Therefore, we conducted this study with the primary objective of determining if the presence of RVO by DUS predicted ipsilateral recurrent/propagative DVT (rDVT). Our secondary objective was to determine risk factors that are associated with RVO.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective single-center study
- **Take Home Message:** In 185 lower extremities of 156 patients with acute deep vein thrombosis (DVT), follow-up duplex ultrasound demonstrated residual venous obstruction (RVO) in 61.1%; larger initial clot burden was associated with an increased risk of RVO. Recurrent DVT was associated with the presence and degree of RVO, and limbs with no RVO had a decreased risk of recurrence or progression.
- **Recommendation:** The authors suggest using follow-up duplex ultrasound in patients with DVT to identify those at an increased risk for recurrence or progression and help guide the duration of anticoagulation therapy.

METHODS

Data source and patient characteristics. After approval by the Ohio State University Institutional Review Board, including waiver of consent, and in accordance with the Declaration of Helsinki, we conducted a retrospective study of patients diagnosed with DVT by DUS at our institution between January 1, 2011, and December 31, 2013. We searched for patients by Current Procedural Terminology codes for lower extremity US 93970 and 93971 with concurrent diagnosis of acute DVT by International Classification of Diseases, Ninth Revision, code 453.40. For each patient record, detailed clinical variables were collected including age, sex, ethnicity, body mass index, known risk factors including recent trauma (within 3 months, managed surgically or nonoperatively), recent surgery (within 3 months), pregnancy, oral contraceptive use, history of VTE, presence of central venous catheter, active malignancy, current chemotherapy, or history of congenital/acquired thrombophilia (Congenital: factor V Leiden gene mutation, prothrombin gene mutation, antithrombin III deficiency, protein C deficiency, or protein S deficiency; Acquired: persistently positive lupus anticoagulant or elevated antiphospholipid antibodies). We broadly categorized the index acute DVT as provoked or unprovoked based on the presence of these risk factors (Table I). We recorded the type and duration of anticoagulation, including warfarin, low-molecular-weight heparin, direct oral anticoagulants, antiplatelet agents (aspirin, clopidogrel), and statin use. Extended duration of anticoagulation was defined by continued anticoagulation past the study follow-up period of 3 years. Given alternative management of iliofemoral DVT with direct thrombolysis at our institution, patients with iliofemoral DVT were excluded from the study.

DUS analysis. A trained general surgery resident or vascular surgeon reviewed all duplex studies with Vascupro vascular lab software (Consensus Medical Systems, Richmond, BC, Canada). All studies were performed with the Philips iU22, General Electric Logiq E, and Zonare Z ultrasound machines. Ten infrainguinal lower extremity venous segments (common femoral, profunda femoris, proximal femoral, mid femoral, distal femoral, popliteal, peroneal, posterior tibial, soleal, gastrocnemius) were checked for the presence of RVO and DVT propagation or recurrence by comparison of follow-up DUS with initial DUS. RVO was defined as any nonacute venous obstruction with more than 40% of the luminal diameter remaining during compression (Fig), or the resence of chronic-appearing thrombus and wall thickening when luminal diameter was not reliably measurable.[3,4] rDVT was defined as either new acute DVT in the previously involved segment, or involvement of a new segment in the same extremity.

Statistical analysis. Variables were compared using Student's *t*-test for normally distributed data. Univariate comparisons between groups were made using Fischer's exact test, χ^2 test, logistic regression, and multivariate analysis using STATA version 14.1 (StataCorp, College Station Tex). Power analysis was performed using STATA. Statistical significance was defined by $\alpha = 0.05$. Our study power was 0.9, calculated with one-way binomial power analysis, $\alpha = 0.05$, $d = 0.10$.

RESULTS

Patient characteristics. We identified a total of 543 lower extremities DUS representing 518 total patients with acute DVT on DUS performed between January 1, 2012, to December 31, 2013. Of those patients with acute DVTs, 30.1% underwent one or more follow-up scans making up our cohort of 185 extremities in 156 patients. The mean age of the 156 patients was 58.0 years (range, 19-90 years), and 57.1% (n = 89) were men. A total of 78 patients (50.0%) had provoked DVT, and 57 patients (36.5%) had a history of VTE. Fourteen patients (9.0%) had confirmed congenital/acquired thrombophilia. Warfarin was the main form of anticoagulation (n = 100; 64.1%). Three patients (1.9%) with isolated calf vein DVT were not