Comparison of vein valve function following pharmacomechanical thrombolysis versus simple catheter-directed thrombolysis for iliofemoral deep vein thrombosis

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Background: **Successful catheter-directed thrombolysis (CDT) for iliofemoral deep vein thrombosis (IFDVT) reduces post-thrombotic morbidity and is a suggested treatment option by the American College of Chest Physicians for patients with IFDVT. Pharmacomechanical thrombolysis (PMT) is also suggested to shorten treatment time and reduce the dose of plasminogen activator. However, concern remains that mechanical devices might damage vein valves. The purpose of this study is to examine whether PMT adversely affects venous valve function compared to CDT alone in IFDVT patients treated with catheter-based techniques.**

Methods: **Sixty-nine limbs in 54 patients (39 unilateral, 15 bilateral) who underwent catheter-based treatment for IFDVT form the basis of this study. Lytic success and degree of residual obstruction were analyzed by reviewing postprocedural phlebograms. All patients underwent bilateral postprocedure duplex to evaluate patency and valve function. Phlebograms and venous duplex examinations were interpreted in a blinded fashion. Limbs were analyzed based on the method of treatment: CDT alone (n = 20), PMT using rheolytic thrombolysis (n = 14), and isolated pharmacomechanical thrombolysis (n = 35). The validated outcome measures were compared between the treatment groups.**

Results: **Sixty-nine limbs underwent CDT with or without PMT. The average patient age was 47 years (range, 16-78). Venous duplex was performed 44.4 months (mean) post-treatment. Of the limbs treated with CDT with drip technique, 65% demonstrated reflux vs 53% treated with PMT ($P = .42$). There was no difference in long-term valve function between patients treated with rheolytic and isolated pharmacomechanical thrombolysis. In the bilateral group, 87% (13/15) demonstrated reflux in at least one limb. In the unilateral group, 64% (25/39) had reflux in their treated limb and 36% (14/39) in their contralateral limb. There was no correlation effect of residual venous obstruction on valve function, although few patients had >50% residual obstruction.**

Conclusions: **In patients undergoing catheter-based intervention for IFDVT, PMT does not adversely affect valve function compared with CDT alone. A higher than expected number of patients had reflux in their uninvolved limb. (J Vasc Surg 2012;56:1351-4.)**

Iliofemoral deep venous thrombosis (IFDVT) is associated with the most severe post-thrombotic morbidity, reflected by reduction in quality of life, 15% of patients developing venous ulcers within 5 years, and 40% having venous claudication.[1-3] Comerota et al[4] recently demonstrated that successful thrombus removal with the use of catheter-based techniques is not only safe but also reduces post-thrombotic syndrome (PTS), and others have shown that the addition of pharmacomechanical thrombolysis (PMT) to a strategy of catheter-directed thrombolysis (CDT) improves overall lysis, shortens treatment time, reduces the dose of recombinant tissue plasminogen activator (rt-PA), and reduces intensive care unit and hospital stay.[5-7] The 2008 American College of Chest Physicians (ACCP) practice guidelines recommended a strategy of thrombus removal for patients with extensive deep vein thrombosis (DVT) and suggested the use of PMT to shorten the treatment time of CDT.[8] However, concern remains that PMT may harm venous valve function compared with CDT drip infusion. The purpose of this study is to evaluate the effect of PMT techniques on venous valve function compared with standard CDT drip technique for the management of patients with extensive DVT.

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METHODS

Patients. Fifty-four consecutive patients with symptomatic acute IFDVT were treated between September 2002 and November 2009 with catheter-based techniques using rt-PA. Fifteen patients had bilateral IFDVT, resulting in 69 lower extremities treated, which form the basis of this retrospective study. The study was approved by the institu-

tional review board. DVT was diagnosed on duplex ultrasonography and confirmed with phlebography at the time of thrombolysis.

Twenty limbs were treated with CDT alone when only CDT was available. Forty-nine underwent PMT. Within the PMT group, 14 limbs were treated with the AngioJet catheter (MEDRAD Interventional, Warrendale, Pa) and 35 limbs were treated with the Trellis catheter (Covidien, Mansfield, Mass) when these technologies became available. The method of PMT chosen was at the discretion of the treating interventionalist. The mean age of the patient population was 48 years (range, 16-78). Forty-six percent were male and 54% female. Twenty-four patients had left lower extremity involvement, 15 had right lower extremity involvement, and 15 were bilateral.

Residual obstruction calculation. Mewissen et al described a method to determine the degree of clot lysis following CDT.[9] This was modified by Martinez et al[5] to further estimate the degree of successful thrombolysis. Although this method quantifies the degree of thrombolysis of the acute thrombus, it does not quantify residual obstruction from a persistent luminal stenosis. Serial phlebography was obtained to monitor resolution of thrombus during treatment. The final post-thrombolysis phlebogram was used to measure degree of residual luminal obstruction, which was calculated by measuring the luminal diameter in the area of maximal residual stenosis in the iliofemoral segment. To best obtain an estimated normal luminal diameter at the segment with residual stenosis, the normal-appearing venous segment above and below this segment was measured and averaged. This average was then used as the denominator to calculate residual venous obstruction. All patients with typical left common iliac vein stenosis due to right iliac artery compression (May-Thurner syndrome) had correction with venoplasty and stenting.

Venous valve function measurement. Patients who were not treated by the authors were contacted and returned to have the necessary follow-up noninvasive studies. The majority of patients had noninvasive venous evaluations performed as a routine part of follow-up care, which averaged 44 months, with a median of 41 months. Venous valve function was determined using venous duplex ultrasonography, with venous valve closure times used as the end point.[10,11] Patients were placed in a steep reverse Trendelenburg position. Valve closure times in the common femoral, femoral, and popliteal vein segments were measured following manual compression. Deep venous reflux was defined as a valve closure time ≥1 second.[11]

Statistical analysis. The Student *t*-test was used to assess differences in valve function and residual iliofemoral obstruction between all treatment groups. The R-square between valve function and residual iliofemoral obstruction is based on a linear trend for a 10% range of residual iliofemoral obstruction vs the mean number of limbs with reflux in the corresponding range. R-square was also used to compare valve function between the CDT and PMT treatment groups.

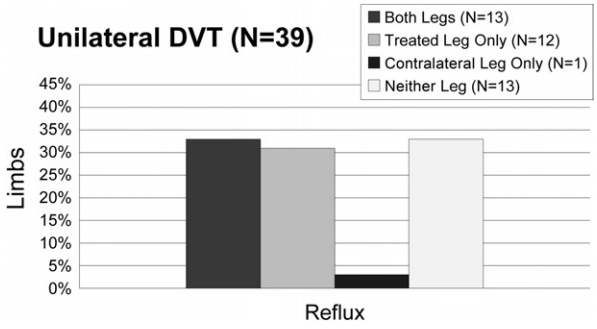

Fig 1. Detailed analysis of valve function in legs of patients with unilateral deep vein thrombosis (*DVT*).

RESULTS

Residual obstruction. Only 20% of limbs had >50% residual obstruction in the iliofemoral venous segment on completion phlebogram, and of these, 75% had obstruction within the common femoral segment or external iliac vein just above the inguinal ligament. In limbs treated with CDT alone, 25% had >50% residual luminal obstruction vs 18% of limbs treated with PMT.

Valve function. Fifty-seven percent of treated limbs had reflux in the common femoral, femoral, or popliteal venous segment as measured on post-treatment duplex ultrasound. In the group of patients with bilateral DVT, 87% (13/15) demonstrated reflux in at least one limb, 53% (8/15) had reflux in both limbs, and 13% (2/15) had no reflux.

In the unilateral patient group, 12 of the 39 patients (31%) had valvular reflux in their treated limb only, one (3%) in the contralateral limb only, and 13 (33%) had reflux in both of their limbs. Thirteen patients (33%) demonstrated no reflux in either limb (Fig 1). None of the patients with unilateral IFDVT had a history of contralateral DVT.

Limbs treated with CDT alone had a reflux rate of 65% vs 53% in those treated with PMT ($P = .42$) (Fig 2). Those treated with the Trellis catheter had a reflux rate of 57%, whereas limbs treated with the AngioJet demonstrated a reflux rate of 43%. Further analysis between treatment groups is illustrated in Fig 3.

Of the patients with >50% residual obstruction and unilateral IFDVT, 70% (7/10) had reflux of their treated limb compared to 45% (13/29) reflux with ≤50% residual obstruction ($P = .056$).

DISCUSSION

Following acute DVT, post-thrombotic morbidity in patients treated with anticoagulation alone is reported to occur in 25% to 46% of patients at 10 years.[12,13] These numbers are derived from all patients with acute DVT, not just those with IFDVT. Patients with IFDVT have a higher risk for developing PTS and suffer the most severe PTS.[1,2,14] The iliofemoral segment represents the single outflow channel for the entire lower limb, and acute thrombotic occlusion results in severe venous hypertension.[15]