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Pulse-spray Pharmacomechanical Thrombolysis for Proximal Deep Vein Thrombosis

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Objective. *The aim of this study was to evaluate the efficacy, safety, and feasibility of pulse-spray pharmacomechanical thrombolysis to treat proximal deep vein thrombosis (DVT) in conjunction with the placement of a non-permanent IVC filter.*

Methods. *We studied 31 consecutive patients with acute proximal DVT defined as the inferior vena cava (IVC), iliac vein and/or femoral vein, who were diagnosed using duplex ultrasonography and/or contrast venography. All were treated with pulse-spray urokinase. Early success was assessed by comparing the pre- and post-treatment venographic severity score. Non-permanent IVC filters were used to reduce the risk of pulmonary thromboembolism.*

Results. *The average total urokinase dose was 1.71 million IU (range: 0.72–3.6 million IU) and the average duration of therapy was 2.4 days. The average percentage of thrombus lysed was 85% (range: 22–100%). A large thrombus trapped by the filter was detected using cavography before extraction of the filter in one patient. There was no major treatment-related adverse event.*

Conclusion. *The combination of pulse-spray pharmacomechanical thrombolysis and the prophylactic use of a non-permanent IVC filter was a safe and effective approach for treating acute proximal DVT.*

Keywords: Deep vein thrombosis; Clinical trials; Fibrinolytic therapy; Intravascular devices; Pulmonary embolism.

Introduction

Deep vein thrombosis (DVT) can cause both pulmonary thromboembolism (PTE) and post-thrombotic syndrome. DVT treatment aims to relieve the acute symptoms of limb swelling and pain, reduce the risk of PTE, and prevent long-term disability from chronic venous insufficiency including persistent limb pain and swelling, hyperpigmentation, venous claudication, and skin ulceration. Early thrombolysis seems to be important to preserve valvular function.[1,2] However, conventional treatment strategies, including anticoagulation and systemic thrombolytic therapy, do not lead to rapid resolution of proximal DVT. It has been reported that only 6% of patients treated with standard heparin anticoagulation alone for DVT of a lower extremity achieve clot lysis within 10 days of treatment,[3] and thrombus propagation is seen in up to 40% despite adequate anticoagulation.[4] Systemic thrombolysis is more effective than heparinization,[5] but seems less effective than catheter-directed thrombolysis probably because of poor penetration of thrombi by the drugs which have been used.[6] A recent report found that venous valvular function was better preserved in patients with iliofemoral DVT treated with catheter-directed thrombolysis than systemic thrombolysis.[7] Although catheter-directed thrombolysis can be effective,[8–21] the high daily dose of thrombolytic drug increases the risk of haemorrhage and can cause serious bleeding complications.[22]

Pulse-spray pharmacomechanical thrombolysis in which a highly concentrated fibrinolytic agent is injected directly into the thrombus as a brief high-pressure spray via multiple side hole ports in the catheter, has been used primarily to treat peripheral arterial occlusions. Pulse-spray pharmacomechanical thrombolysis for DVT appears superior to conventional catheter infusion thrombolysis in fragmenting and lysing the clot,[23–25] but only a few case reports have been published.[26–28] The routine use of an inferior vena cava (IVC) filter was not recommended for conventional catheter infusion thrombolysis for

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proximal DVT except for patients with poor cardiovascular reserve or patients with large, free-floating thrombi in the IVC.[16] However, a non-permanent IVC filter was used before pulse-spray pharmacomechanical thrombolysis in this study because of the potential risk of pulmonary thromboembolism due to fragmentation of thrombi.

The combination of pulse-spray pharmacomechanical thrombolysis and non-permanent IVC filter placement should theoretically maximize the likelihood of successful thrombolysis while minimizing the risk of PTE and bleeding complications. The purpose of this study was to evaluate the efficacy, safety and feasibility of pulse-spray pharmacomechanical thrombolysis in conjunction with the placement of a non-permanent IVC filter for treating proximal DVT.

Patients and Methods

Between June 2002 and June 2004, patients were enrolled when they fulfilled the following three inclusion criteria: (1) DVT confirmed using duplex ultrasonography and/or contrast venography, (2) thrombus observed in proximal veins, including IVC, iliac vein, and femoral vein, (3) clinical symptoms (duration of $\leq$30 days) such as swelling and pain. Exclusion criteria were: (1) Limb ischemia, (2) previous DVT of the ipsilateral limb, (3) contraindications to contrast media, anticoagulation, or thrombolytic agents, and (4) refusal of the treatment by the patient. After duplex ultrasonography, enhanced computed tomography and/or contrast ascending venography were performed to evaluate the extent of the thrombus. Lung scan, multidetector computed tomography and/or pulmonary angiography was performed to establish the presence or absence of pulmonary embolism before the procedure. Non-permanent IVC filters (Neuhaus Protect filter (Neuhaus Laboratories Inc., Miami, FL, USA), Antheor filter (Boston Scientific Corp., Natick, MA, USA) and Günther tulip filter (William Cook Europe, Bjaeverskov, Denmark)) were used. In cases of DVT involving the femoral vein, the catheter was always inserted through a popliteal vein in the supine position with the knee slightly flexed, and the leg rotated. In cases of DVT limited to the IVC and iliac vein, the catheter was inserted through the ipsilateral femoral vein.

Pharmacomechanical thrombolysis was performed using a Fountain infusion catheter (Merit Medical Systems Inc., South Jordan, UT, USA) with 80–320 side holes at 1.25 mm intervals in a spiral pattern. A penetrating spray was emitted from the side holes by manual injection. The catheter was positioned with the aid of a guidewire so that the side holes contacted most of the thrombus; the most proximal side hole was placed at the proximal edge of the thrombus. The guidewire was exchanged for a tip-occluding wire, which was inserted to close the end hole of the catheter, and the catheter was connected with a Y-shaped adaptor to facilitate drug injections around the wire.

The urokinase dose was 720,000 IU/day. The thrombolytic solution was prepared by dissolving 240,000 IU of urokinase in 50 ml of saline, and 240,000 IU per injection was administered three times a day. To maximize penetration into the thrombus, approximately 50 forceful and rapid manual pulse injections of 0.5- to 1.0-ml with the Squirt fluid dispensing system (Merit Medical Systems Inc., South Jordan, UT, USA) were administered manually about every 10 s. Progress was assessed at 1 or 2 day intervals by venography through the catheter (Fig. 1). Thrombolytic therapy was terminated when recanalisation and brisk venous flow was obtained or no progress was observed.

All patients received concomitant continuously infused heparin during the procedure through the catheter or the side port of the introducer sheath. The heparin dose was adjusted to control the activated partial thromboplastin time twice the control value. After the procedure, heparin was continued until therapeutic anticoagulation with warfarin was achieved.

The extent of clot lysis was assessed using a scoring system based on pre- and post-treatment venography. All venographic images were read and the score was calculated independently by two trained observers blinded to the clinical data. As we considered that venous recanalisation is effective for early symptom relief such as limb pain and swelling, an original scoring system was adopted in this study to discriminate occluded segments from non-occluded segments post-treatment. The score was calculated for nine venous segments of the upper, middle and lower IVC; the common iliac vein; the external iliac vein; the common femoral vein; the proximal and distal portions of the femoral vein, and the popliteal vein. The score was classified into seven categories according to the extent and form of thrombus; 0: No thrombus, 1: Thrombus extended over 1/3 of the length of the venous segment without occlusion, 2: Thrombus extended over 2/3 of the length of the venous segment without occlusion, 3: Thrombus extending along the entire length of the venous segment without occlusion, 4: Thrombus extending over 1/3 of the length of the venous segment with