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Factors Associated with Long-Term Outcome in 191 Patients with Ilio-Femoral DVT Treated With Catheter-Directed Thrombolysis

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WHAT THIS PAPER ADDS

The present study demonstrates, for the first time, that outcome in terms of competent veins after catheter-directed thrombolysis in ilio-femoral deep venous thrombosis is better in patients with symptom duration <14 days compared with patients with longer symptom duration.

Objective: To identify factors associated with long-term treatment success after catheter-directed thrombolysis (CDT) for acute deep venous thrombosis (DVT) involving the ilio-femoral vein.

Material and methods: This was a non-randomised observational cohort study. From 1999 to 2013, 191 consecutive patients (203 limbs) attending a tertiary vascular centre at Gentofte University Hospital, Denmark underwent CDT. All patients had ultrasonically verified acute ilio-femoral DVT with open distal popliteal vein and calf veins. Patients were seen in the outpatient clinic 6 weeks, 3, 6, and 12 months, and annually thereafter following the DVT. Successful outcome was defined as patent deep veins without reflux on Duplex ultrasound scanning (DUS). Data were collected prospectively as per protocol and analysed retrospectively.

Results: Median age was 27 years (range 14–74 years) and overall median lysis time was 56 h (range 22–146 h). A stent was placed in 106 limbs (52%). Six patients had major bleeding. The median follow-up was 5 years (range 1 month–14.3 years). The cumulative rate of patients with deep patent veins without reflux at 7 years was 79%. Multivariate Cox regression analyses showed that symptom duration >2 weeks (hazard ratio (HR) 2.78, 95% CI 1.14–6.73) and chronic post-thrombotic lesions (HR 19.3, 95% CI 7.29–51.2) were significantly associated with poorer outcome, while the pulse-spray technique (HR 0.15, 95% CI 0.05–0.48) was associated with better outcome. Age, gender, side, IVC atresia, stenting, and lysis duration did not affect outcome.

Conclusion: In this observational study of CDT for ilio-femoral DVT it was demonstrated that symptom duration less than 2 weeks, absence of chronic post-thrombotic lesions and use of the pulse-spray technique for CDT resulted in better primary patency including normal valve function in the long term.

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INTRODUCTION

Patients suffering from acute deep venous thrombosis (DVT) with involvement of the ilio-femoral vein segment have the worst outcome in terms of post-thrombotic syndrome (PTS) and Quality of life (QoL) if treated with anticoagulation (AC) only.[1,2] An ilio-femoral DVT involves the iliac and the common femoral veins with or without involvement of any additional vein segment.[3,4] The venous return from the femoral and/or the deep femoral vein is significantly impaired because of the poor rate of recanalisation and poor collateral development in the pelvic region. The thrombus may involve vein segments central and peripheral to the ilio-femoral vein.

Over the years, different methods for thrombus removal have been introduced to restore patency, save valve function, and reduce the occurrence of PTS. CDT has been practiced for the last 20 years and is considered to be a minimally invasive procedure.[4–7] A meta-analysis based on four studies comparing anticoagulation and CDT found a statistically significant reduction in the risk of venous obstruction (RR 0.38; 95% CI 0.18–0.37; $I^2 = 46\%$), PTS (RR 0.19; 95% CI 0.07–0.48; $I^2 = 64\%$) and a trend for reduction

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in the risk of venous reflux (RR 0.39; 95% CI 0.16—1.00; $I^2 = 92\%$) in patients who had CDT.[8] The Norwegian RCT (CaVenT study) including 176 patients demonstrated a 28% absolute risk reduction in PTS after 5 years as the most important result.[9]

During the last 16 years, the Vascular Clinic at Gentofte University Hospital, Denmark has offered CDT for patients with acute ilio-femoral DVT as part of a treatment algorithm. Data on safety, long-term patency results, valve function, PTS, and QoL based on this cohort, have been reported previously.[7,10—12] The cohort now contains a substantially larger number of patients, followed for a considerably longer time. The aim of this study was to identify factors associated with long-term treatment success using multivariate analysis.

MATERIAL AND METHODS

From 1999 to 2013, patients with acute ilio-femoral DVT were selected for CDT at the Vascular Clinic, Gentofte University Hospital, Denmark. Patients were referred from all regions of Denmark until 2010, when a second centre was established in the western part of the country. Inclusion criteria per protocol were first episode of ilio-femoral DVT, open distal popliteal vein and open calf veins, age <60 years for the first 60 patients and age <75 years thereafter, and symptom duration (assumed to be the best estimate of thrombus age) <14 days. During the study period a number of patients with symptom duration >14 days were also included. Exclusion criteria were previous ipsilateral DVT, pregnancy, malignancy, or other concomitant chronic or potentially life threatening disease, bleeding disorders, uncontrolled hypertension, recent surgery, and childbirth within the past week.[10] Approximately one in three patients referred for CDT were eligible. The remaining two thirds of the patients received anticoagulation according to national standards. This is in accordance with the findings of a recently published paper showing, that one third of patients with ilio-femoral DVT have open popliteal veins.[13]

Study design

The study prospectively included consecutive patients with ilio-femoral DVT referred to the Vascular Clinic at Gentofte University Hospital, who met the inclusion criteria per protocol. Medical records were reviewed for additional clinical data when necessary and at follow-up in 2014. No ethical approval was needed. Fifty predefined variables were kept on each patient in a local database of which 17 covariates (gender, age, side, stenting, number of stents, caval atresia, caval filter, caval extension of thrombus, thrombus extension below the inguinal ligament, treatment duration, use of pulse-spray, coagulopathy, child birth after initial thrombosis, use of low molecular weight heparin [LMWH] or heparin, symptoms >2 weeks, lifelong anticoagulation, underlying chronic post-thrombotic lesions) were selected. These 17 covariates were chosen as they were considered to be clinically or technically most relevant, and with a possible association with the outcome.

All patients were tested for thrombophilia (factor V Leiden mutation, prothrombin mutation 20210, protein C, protein S, antithrombin, plasminogen, anticardiolipin antibodies, lupus anticoagulant, and homocysteine).

Outcome as a surrogate marker for later PTS was defined as competent deep veins, defined as fully patent veins without evidence of reflux on duplex ultrasound scanning (DUS). Fully patent veins are compressible without any luminal echogenic appearance and with a normal flow pattern. A patent stent is characterised by no in-stent echoes, with a phasic flow pattern, and without any change in the colour mapping in the stent or in close proximity to it. Patency, in this context, is defined as an 85—90% open structure because DUS is unable to detect stenosis less than 10—15% in the vein or in the stent.

The CDT method

The distal popliteal vein was punctured under local anaesthesia using DUS guidance. A multiple side hole catheter with tip occlusion was placed in the thrombus. A bolus of 10 mg rtPA followed by rtPA 1.2 mg in 120 ml saline/h was administered using continuous infusion for the first 55 cases and thereafter using the pulse-spray infusion technique. In the first 129 patients, heparin was adjusted according to APTT (80—100 s). The following 62 patients had rtPA 1.2 mg/h mixed with LMWH adjusted by weight. All patients were treated with an intermittent pneumatic compression pump (IPC) during hospitalisation, and afterwards with a below knee class II graduated compression stocking (23—32 mmHg) and anticoagulation for at least 1 year. Radiological disappearance of thrombus in daily venograms accompanied by a decrease in D-dimer to values less than 10 mg/L was used as a marker for treatment success and determined the duration of lysis. Any remaining iliac obstruction (>10—15%) caused either by compression or in some cases by residual non-resolved thrombus material was stented. Venograms showing impenetrable occlusion, irregular and thickened vein walls, collaterals, and decreased flow were considered to be chronic post-thrombotic lesions.

Follow-up

All patients were seen in the outpatient clinic after 6 weeks, 3, 6, and 12 months, and annually thereafter. DUS was performed with the patient standing for assessment of valve function and in the supine position for assessment of vein (and stent) patency, as defined above. Femoral and popliteal vein reflux was defined as retrograde flow, following release of calf muscle compression, lasting more than 0.5 s, and in the common femoral vein lasting more than 1 s.

Statistical analyses

Continuous and interval variables are reported as median values with range. Per-protocol and intention-to-treat analyses were done. Associations between single variables and

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