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The Effect of Stenting on Venous Hypertension: Results Using a Treadmill Stress Test with Invasive Pressure Measurements in Patients with Iliofemoral Venous Obstruction

Ralph L.M. Kurstjens [a,b,c,*], Mark A.F. de Wolf [a,b], Helena W. Konijn [a], Irwin M. Toonder [a], Patricia J. Nelemans [d], Jorinde H.H. van Laanen [a], Rick de Graaf [e], Cees H.A. Wittens [a,b,f]

[a] Department of Vascular Surgery, Maastricht University Medical Centre, Maastricht, The Netherlands
[b] Cardiovascular Research Institute Maastricht, Maastricht, The Netherlands
[c] Department of Obstetrics & Gynaecology, Haga Teaching Hospital, The Hague, The Netherlands
[d] Department of Epidemiology, Maastricht University Medical Centre, Maastricht, The Netherlands
[e] Department of Radiology, Maastricht University Medical Centre, Maastricht, The Netherlands
[f] Department of Vascular Surgery, University Hospital Aachen, Aachen, The Netherlands

WHAT THIS PAPER ADDS

This prospective observational study using invasive pressure measurements during a treadmill stress test demonstrates that ambulatory venous hypertension, caused by post-thrombotic iliofemoral venous obstruction, can be significantly reduced by stenting. It also shows that this is associated with a reduction in venous claudication and a significant improvement in quality of life. These results substantiate the use of stenting in patients suffering from post-thrombotic iliofemoral venous obstruction that is resistant to conservative treatment.

Objectives: The primary aim was to investigate whether stenting of post-thrombotic iliofemoral obstruction reduces venous hypertension. The secondary aim was to establish whether improvement in haemodynamic parameters impacts on quality of life.

Methods: In this prospective observational study, 12 participants with unilateral post-thrombotic obstruction of the iliac and/or common femoral veins (CFVs) underwent a treadmill stress test with invasive pressure measurements in the CFVs and dorsal foot veins of both affected and non-affected limbs. This was performed the day before and 3 months after stenting the obstructed tract. Paired sample *t*-tests were used to compare the treatment effect and univariable linear regression analysis to determine the association with improvement in quality of life.

Results: Before treatment, CFV pressure increased 34.8 ± 23.1 mmHg during walking in affected limbs compared with 3.9 ± 5.8 mmHg in non-affected limbs. This pressure rise decreased to 22.3 ± 24.8 mmHg after 3 months follow up compared with a 4.0 ± 6.0 mmHg increase in non-affected limbs (−26.2 mmHg difference; 95% CI −41.2 to −11.3). No such effect was found in the dorsal foot veins. The VEINES-QOL increased 25.3 ± 11.3 points after stenting and was significantly associated with a decrease in CFV pressure rise during walking (regression coefficient 0.4; 95% CI 0.1–0.6).

Conclusion: Stenting of post-thrombotic iliofemoral obstruction significantly reduces venous hypertension in the common femoral vein and correlates with an improvement in the quality of life. Larger studies with a broader range of degree of obstruction need be performed to assess whether pre-stenting pressure measurements can predict post stenting clinical success.

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INTRODUCTION

Post-thrombotic syndrome (PTS) is a frequent disease with a prevalence of 20–70% among people who have suffered from deep vein thrombosis.[1–5] Patients with PTS report reduced quality of life (QoL), similar to diseases such as congestive heart failure, diabetes mellitus, and chronic obstructive pulmonary disease.[6,7] In a quarter of patients

* Corresponding author. Maastricht University Medical Centre, Department of Surgery, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands.
E-mail address: r.kurstjens@maastrichtuniversity.nl (Ralph L.M. Kurstjens).

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with deep vein thrombosis the iliac and common femoral veins (CFVs) are involved. When not properly recanalised, this can severely limit outflow, which can occur in up to 70% of patients with iliofemoral deep vein thrombosis.[5,8] Although PTS management usually consists of conservative treatment with therapeutic elastic stockings and mobilisation, percutaneous transluminal angioplasty (PTA) with stenting should be considered in the aforementioned subset of patients if conservative treatment is not sufficient.[9,10] In cases where post-thrombotic disease is extensive a hybrid approach including endophlebectomy can also be performed.[11]

PTA and stenting has been investigated in large case series and case control studies with good clinical results and followup as long as 10 years.[12–17] Primary patency rates for post-thrombotic obstructions treated by stenting vary from 50% to 90% and secondary patency rates of up to 100% are reported.[13,17] This is accompanied by a significant improvement in clinical severity scores and QoL.[12,16,18] However, ulcer healing rates are reported as low as 56% and oedema only improves in about 50% of patients.[12,17] Moreover, little is known about the haemodynamic impact of venous stenting. Recent insights have demonstrated that pressure in the CFV can vastly increase during exercise, though it is unknown whether recanalisation of the obstructed tract can mitigate this venous hypertension and potentially reduce the risk of complications such as venous ulcers.[19]

Despite positive study results, up to 25% of patients show only minor to no improvement in complaints after successful stenting.[16] Therefore, a better understanding of the pathophysiology of this condition and the effect of its treatment is warranted in order to identify patients who would truly benefit from PTA and stenting.

The primary aim of this study was to investigate whether stenting of iliofemoral deep venous obstruction reduces venous hypertension. The secondary aims were to establish whether the improvement in haemodynamic parameters has an impact on QoL and to determine whether preoperative pressure measurements can predict treatment outcome, as measured by change in QoL.

METHODS

Study design and participants

In this prospective observational study, pressures in the CFV and dorsal foot vein of participants with unilateral post-thrombotic deep venous obstruction were compared with pressures in their healthy contralateral limbs as a control, before and after PTA and stenting. This study was approved by the institutional review board of Maastricht University Medical Centre (METC 13-2-027) and followed the principles of the 2013 revised declaration of Helsinki. Informed consent was obtained from all participants (Clinical Trial Registration: https://clinicaltrials.gov/show/NCT01846780).

Between December 2013 and June 2015, 24 participants were recruited from the tertiary outpatient clinic of our hospital. Baseline data of this group of patients, including the participants with complete data available for analysis in the present paper, have been published before.[19] Participants with unilateral post-thrombotic obstruction of the iliac veins and/or CFV, possibly with lesions extending into the popliteal—femoral tract, willing to undergo PTA and stenting were eligible for this study. Post-thrombotic obstruction was diagnosed by duplex ultrasound, characterised by intraluminal synechiae and flow division, and magnetic resonance venography, characterised by low signal intraluminal changes indicative of trabeculation. The extent of stenosis was established by comparing the functional lumen with the healthy contralateral side. Exclusion criteria were obstruction of the inferior vena cava and/or contralateral deep veins, peripheral arterial disease, pregnancy, a life expectancy of $<$6 months, and age younger than 18 years. Participants requiring endophlebectomy (surgical unblocking of the CFV) and the creation of a temporary arteriovenous fistula (AVF) were not excluded from this study as these procedures are only necessary to (temporarily) improve inflow of the CFV and prevent early stent occlusion.[11]

Procedures

Two tests were performed: one on the day before intervention and one 3 months after PTA and stenting. During a test session, both femoral veins were cannulated under ultrasound guidance and a 4F sheath (PreludoPRO; Merit Medical Systems, South Jordan, UT, USA) was placed with its tip in the CFV. Bilateral cannulation of a dorsal foot vein was performed using an 18, 20, or 22 gauge Vasofix Safety IV Catheter (B. Braun, Melsungen, Germany), depending on vein size. All pressures were measured continuously to compare affected with non-affected limbs, using TruWave pressure transducer sets (Edwards Lifesciences, Irvine, CA, USA) attached to a Hewlett Packard M1165A patient monitoring system (Philips Medical Systems, Best, The Netherlands).

Pressures were first measured in the supine position. Subsequently, the participant was asked to stand with the support of a frame. After stable pressures were observed, the participant was instructed to perform a stress test on a treadmill. The speed was set at 3.2 km/hour on a 0% slope, increasing 2% every 120 s until participants indicated they had to stop walking because of pain. Pain free and maximum walking times were registered. Participants were not coerced during the stress test and the test was ceased when participants indicated they had to stop or at a maximum of 26 minutes.

The day after the first test session, participants were treated by PTA and stenting of the iliac veins and/or CFV. Access to the femoral vein of the affected limb was obtained under ultrasound guidance and a 5F sheath (PreludoPRO; Merit Medical Systems) was inserted. Venography was performed and recanalisation of the obstructed tract was performed using a hydrophilic guidewire (Radifocus M; Terumo Interventional Systems, Somerset, NJ, USA). Subsequently, PTA was performed using non-compliant balloons with sizes varying from 12 to 16 mm (Powerflex and

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