Stenting for Chronic Post-thrombotic Vena Cava and Iliofemoral Venous Occlusions: Mid-term Patency and Clinical Outcome

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KEYWORDS
Venous claudication;
Post-thrombotic syndrome;
Chronic venous occlusions;
Chronic venous insufficiency;
Self-expanding stents

Abstract
Objectives: The aim of this study was to determine the mid-term patency and the clinical outcome after stenting of chronic occluded caval and iliofemoral venous segments.
Design: Observational study.
Material/methods: During the period 2000 and 2009, 2400 patients with chronic venous insufficiency (CVI) were evaluated, and 34 with chronic venous occlusions after deep venous thrombosis (DVT) were selected for endovascular treatment. The median age was 41 (range 15–63) years, and 19 were female. The following investigations were undertaken: colour duplex ultrasound (CDU), ascending venography (AV), venous occlusion plethysmography (VOP), venous pressure gradient (VPG) and CT venography or trans-femoral/popliteal venography. The major symptoms were venous claudication, oedema, pain and ulcer. All patients were treated by stenting occluded segments. Self-expanding stents were deployed in 22 iliofemoral, nine iliac and one caval-iliac-femoral. Twenty-one procedures required stenting across the inguinal ligament.
Results: Primary recanalisation was accomplished in 32/34 (94%). The median follow-up was 33 months (1–96) with clinical examination, CDU and VOP. Two-year primary patency was 14/21 (67%), primary-assisted patency 16/21(76%), and secondary patency was 19/21 (90%). Venous claudication and oedema resolved in those successfully recanalised. Four of the seven ulcers healed.
Conclusion: Stenting to treat venous claudication, oedema and recurrent venous ulcer caused by post-thrombotic chronic venous occlusions has positive clinical outcome and good mid-term patency.

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The standard treatment for deep venous thrombosis (DVT) is anti-coagulation with low molecular weight heparin followed by oral warfarin. The fact that removal of thrombus is not one of the effects accomplished by anti-coagulation may have a severe impact in the long-term disability caused by DVT. Post-thrombotic syndrome (PTS) characterised by reflux and/or obstruction will develop in as many as 40% of patients suffering a DVT. Venous claudication and/or leg ulceration are serious clinical consequences experienced by at least 15% of patients developing PTS. The pattern of spontaneous recanalisation after DVT varies according to the affected anatomical segment as shown by colour duplex ultrasound (CDU) studies. While recanalisation occurs in up to 90% of the femoro-popliteal veins after one year, this is rarely the case (<5%) after iliofemoral thrombosis. Persistent, chronic venous outflow obstruction in the iliofemoral veins leads to the development of venous claudication in about 43% of these patients. Surgical treatment of chronic venous obstruction has produced variable results with very few available reports of long-term follow-up.

The development of percutaneous endovascular techniques has made possible the recanalisation and stenting of chronic venous occlusions with successful clinical outcomes and low morbidity.

The long-term consequences of DVT occurred in terms of the development of PTS. The latter represents a reduction in quality of life, and it incurs large costs to society if this condition remains untreated. There are few reports in the literature analysing the effect of endovascular treatment in patients with severe symptoms due to venous outflow post-thrombotic chronic occlusions.

The aim of this study was to assess the mid-term patency and clinical outcome after recanalisation and stenting of post-thrombotic chronically occluded vena cava and iliofemoral venous segments.

**Material and Methods**

During the period 2000–09, 2400 patients with severe CVI were initially evaluated with colour duplex ultrasound (CDU) and ambulatory venous pressure measurement. Fifty-nine patients with severe symptoms including venous claudication, oedema, pain and leg ulcer suggestive of venous outflow impairment were further investigated with ascending venography (AV), venous occlusion plethysmography (VOP), venous pressure gradient (VPG) and CT venography or trans-femoral/popliteal venography. The severity of these symptoms rendered these patients incapable of functioning at work and/or in other physical activities, representing a clear indication to attempt endovascular treatment. Twenty-five patients were found unavailable for endovascular treatment due to the extension of the post-thrombotic occlusion to the popliteal level that precluded adequate restoration of venous blood flow. The other 34 patients had chronic venous occlusions after DVT with open popliteal and distal femoral veins, and were chosen for treatment. This group constitutes the patients included in our study, who were then categorised according to the CEAP (clinical—etiological—anatomical—pathophysiological) classification for chronic venous insufficiency. The severity of the symptoms was assessed using the venous clinical severity score (VCSS) (Table 1).

The median patient age was 41 (range 15–63) years, and 19 were women. The time elapsed following the previous episode of DVT varied widely with a median of 108 (range 9–420) months. Seventeen patients (50%) had a thrombophilia (APC resistance, protein C or S deficiency and homocysteinaemia). The major symptoms were venous claudication in 27 patients, oedema in 24, pain in 21 and leg ulcer in seven. Eighteen out of 34 (53%) patients were on sick leave, and 6/34 (18%) patients on welfare at the time of diagnosis.

In addition to venous outflow obstruction, reflux was detected in the femoro-popliteal veins along with high levels of ambulatory venous pressure (AVP) in 18/34 (53%) patients. Air plethysmography and/or VPG measurement were positive in only 17/34 (50%) patients.

All 34 patients were planned for treatment using endovascular techniques by recanalisation and stenting. In two cases, recanalisation was not possible. In three cases, complementary open surgery was required during the same procedure: two A-V fistulas, and one vein plasty.

Self-expanding stents (Wallstent) were placed in the iliofemoral segment in 22 cases, in the iliac segment alone in nine cases, and in one case, in the caval-iliofemoral segment. Twenty-one procedures required stenting across the inguinal ligament to secure adequate inflow.

Anti-coagulation was administered pre-, per- and post-operatively, first, using low molecular weight heparin (LMWH), dalteparin 100 IE/kg/twice daily, and then using warfarin. Patients with a proven thrombophilia received lifelong anti-coagulation. The others were evaluated individually in conjunction with a haematologist, according to the other risk factors.

**Investigations**

Colour duplex ultrasound (CDU) was used to evaluate axial reflux in the different anatomical segments of each venous

<table>
<thead>
<tr>
<th>CEAP</th>
<th>No. patients</th>
<th>Only obstruction</th>
<th>Reflux + obstruction</th>
<th>Higha AVP</th>
<th>VOPb</th>
<th>VPGc</th>
<th>VCSSd</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>27</td>
<td>16</td>
<td>11</td>
<td>11</td>
<td>15</td>
<td>15</td>
<td>9 (5–12)</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>0</td>
<td>7</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>21 (18–29)</td>
</tr>
</tbody>
</table>

a High ambulatory venous pressure levels median 72 mmHg (64–72).

b Abnormal values of venous occlusion plethysmography.

c Abnormal values of venous pressure gradient.

d Venous clinical severity score, median and range.
system. Morphological post-thrombotic changes of the vein, such as, wall thickening, trabeculae and the lack of colour or Doppler signal were also assessed.

AVP measurement was used to assess the global venous reflux, which is a function of the veno-muscular pump and the severity of venous hypertension. AVP provides information about a pressure drop with ambulation (a measure of the venous pump function), ambulatory pressure and recovery time. Both CDU and AVP are described in the detail in our previous publications.\(^{16,17}\)

To evaluate the haemodynamic significance of a post-thrombotic vein occlusion, two additional investigations were performed:

VOP was performed to exclude persistent venous outflow obstruction by using an air plethysmograph (MacroLab, E. Stranden). In the recumbent position, venous occlusion and recording cuffs were applied proximally to the patella and at the calf, respectively. An occlusive cuff pressure of 50 mmHg was maintained during 1 min. This permits uninhibited arterial flow into the limb, while the venous outflow is compromised, resulting in an increased leg volume. On decompression of the thigh cuff, the leg volume decreases rapidly when the venous outflow is normal. In case of the presence of a functional venous obstruction, the leg volume will decrease slowly.

VPG was obtained by comparing venous pressure measurements before and after a reactive hyperaemia test of the lower extremity. An inflatable tourniquet was applied to the thigh, and venous pressure was recorded in a superficial leg vein. With the patient in supine position, a basal measurement was done. The thigh tourniquet was then inflated to 300 mmHg of pressure and sustained for 3 min. After releasing the tourniquet, reactive hyperaemia increases arterial flow and thus venous outflow. A venous pressure increase above 8 mmHg may indicate an outflow obstruction.

Endovascular and Surgical Procedure

The procedures were performed in a hybrid suite, under general anaesthesia. Access was gained by ultrasound-guided puncture of the popliteal vein \((n = 19)\), femoral vein \((n = 13)\). (Fig. 1). In two cases, the access was combined with jugular puncture, in one, due to vena cava involvement, and in the other, to be able to catheterise the profunda femoral vein. Once access was established, baseline venography was performed to determine the extent of the post-thrombotic occlusion, both cranially and caudally (Fig. 2). By using hydrophilic guide wires (Terumo\(^{23}\)), the occluded segment was passed through. Pre-dilatation angioplasty was carried

Figure 1  Puncture of the popliteal vein is performed with ultrasound guidance.

Figure 2  Baseline venography showing occlusion of the left iliac and femoral veins, with pelvic, paravertebral and suprapubic collaterals.

Figure 3  Pre-dilatation is recommended. This picture illustrates how resilient a stenosis/occlusion can be in a post-thrombotic vein and the obvious need for stenting.
out before large diameter (16–12 mm) self-expanding stents (Wallstent®) were deployed (Fig. 3). After implantation, the stents were dilated with appropriate size balloons. Cranially, the stent was placed well into the vena cava (1–2 cm) and caudally enough to secure inflow (Fig. 4). Crossing the inguinal ligament was often necessary to secure adequate inflow as described by other authors (Figs. 5 and 6). Successful recanalisation was defined as the free flow of contrast medium through a stented venous segment emptying into the vena cava without collaterals. Slow flow and/or post-thrombotic changes caudally were criteria to consider the construction of an arterio-venous fistulae.

Pneumatic sequential pumps were used post-operatively (Lympha Press®) to promote flow through the stented segments of the vein.18

**Follow-up**

Patients were followed-up after 3, 6 and 12 months and yearly, thereafter. The resolution/recurrence of clinical signs and symptoms was recorded by using the venous disability score (VCSS) and related to the patient’s ability to function at work/home. CDU was performed to visualise the stent segment recording flow and looking for morphological changes suggesting stenosis (>50% diameter reduction) with Doppler and spectral analysis. If the findings of CDU were inconclusive, venography was carried on. VOP was performed routinely in all patients looking for early haemodynamic signs of re-obstruction.
Data Collection and Statistical Analysis

This is an observational study of patients with post-thrombotic chronic venous occlusions resulting in severe disability due to venous claudication, oedema and pain resolved in those successfully recanalised. Four ulcers healed after 3 months (Table 2). The clinical improvement recorded by using the VCSS score was statistically significant for both C III and C VI groups ($p = 0.0001$ and $p = 0.002$, respectively). Reconstructive deep venous surgery in the form of venous valve transplantation was needed at a later stage to accomplish ulcer healing in three. Despite a clear clinical picture of venous claudication preoperatively, haemodynamic evidence of outflow impairment by using VOP and VPG was shown in only 18/34 patients.

Post-operatively haemodynamic improvement in outflow (VOP and VPG), after successful stenting, was recorded in only four of these 17. Reflux and high AVP persisted unchanged in 16 patients after successful stenting.

The median follow-up was 33 months (1–96) with clinical examination, CDU and VOP. VCSS was assessed at 3 months follow-up to establish the clinical outcome. Symptom recurrence occurred in 13 patients and was investigated with both CDU and trans-popliteal venography. In two cases, a significant stenosis compromising the inflow was discovered. New stenting was performed in both, and the construction of an A-V fistula was necessary in one. In six occlusions, catheter-based thrombolysis (CBT) and further stenting was performed with construction of an A-V fistula in three. In five other occlusions, re-intervention was considered not to be indicated due to poor inflow conditions (Table 3).

The 2-year primary patency rate was 14/21 (67%), primary-assisted patency of 16/21 (76%) and secondary patency was 19/21 (90%). By comparing Kaplan–Meier survival curve analysis, we attempted to identify factors that could influence patency. Stents deployed above the inguinal ligament showed a better primary patency, but no difference was recorded on the secondary patency. In those patients with thrombophilia, the patency was no different when compared with those with normal coagulation (Figs. 7–9).

Table 2

<table>
<thead>
<tr>
<th>CEAP</th>
<th>No. patients</th>
<th>Recanalised</th>
<th>Reflux</th>
<th>Pre-VCSS</th>
<th>Post-VCSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>27</td>
<td>25</td>
<td>9</td>
<td>9 (5–12)</td>
<td>1 (0–11)</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>21 (18–29)</td>
<td>7 (6–14)</td>
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</table>
Discussion

Chronic venous obstruction, after DVT, can be the cause of major disability and yet, it is an under-diagnosed condition, based on the prevalence and the anatomical distribution of DVT. According to the results in the present study, venous claudication and leg ulcer caused by chronic post-thrombotic total venous occlusions in the femoro-iliocaval segments can be effectively treated by percutaneous recanalisation and stenting. The preoperative duration of the occlusion process does not seem to influence the technical feasibility for recanalisation.

The use of the VCSS score showed significant clinical improvement after successful recanalisation and stenting; and we may remind the reader that the maximal score varies according to which CEAP clinical class it refers to; for C3 it is 12, while for C5 it is 30.

Our 2-year primary patency was 67%, primary-assisted patency of 76% and secondary patency was 90%. This is somewhat better than the one reported by Raju et al. in 2002, in a very similar series regarding aetiology and total occlusions.\textsuperscript{13} Other articles published address both stenosis (non-occlusive lesions) and occlusions; furthermore, there is a mixture of aetiology. Hartung et al. mid-term patency compares with ours, but this series included only 10/44 post-thrombotic cases.\textsuperscript{11} In the remarkable material published by Neglen et al. in 2007, 45% of 982 lesions were post-thrombotic, but only 6% were occlusions,\textsuperscript{9} and yet, their patency is comparable with ours at 24 months. Kölbl et al. published in 2009 results of a series where 66% was post-thrombotic with primary patency of 67%, assisted primary patency 75% and secondary patency 79%, at 2 years.\textsuperscript{12}

The size of our series may represent a certain lack of power, but when we look at the number of equivalent cases (total occlusions after DVT) in other publications and convert it to cases per year, the figure varies from 1 to 6 per year. We report 3.7 per year.

We found, as have other authors, that the haemodynamic tests for venous obstruction that are currently available lack accuracy and sensitivity, making difficult a correlation with clinical symptoms. Therefore, imaging techniques and clinical symptoms may constitute the main parameters to indicate treatment and to evaluate outcome during the follow-up period as of today, but this is an area that deserves further research.

Crossing the inguinal ligament (2/3 of our patients) is necessary in many cases and even though it may seem negatively to influence the primary patency, it is placing stents distally that yields to a better secondary patency\textsuperscript{19} (Fig. 8).

Survival of these patients after treatment is important to detect re-stenosis. Symptom recurrence seems to be a reliable sign that warrants prompt CDU examination. In

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Recurrence of symptoms occurred in 13 patients. In two re-stenosis was detected and treated. The other 11 events represented occlusions which were treated in only 6 patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events (13)</td>
<td>Procedures (8)</td>
</tr>
<tr>
<td>Re-stenosis (2)</td>
<td>Stent, stent + A-V fistula</td>
</tr>
<tr>
<td>Occlusions (3)</td>
<td>CBT + stent</td>
</tr>
<tr>
<td>Occlusions (3)</td>
<td>CBT + stent + A-V fistula</td>
</tr>
<tr>
<td>Occlusions (5)</td>
<td>None</td>
</tr>
</tbody>
</table>

Figure 7 Survival analysis (Kaplan–Meier) curves for primary, assisted primary and secondary patency after recanalisation and stenting of total venous occlusions (\(p = 0.0340\), Log rank test).

Figure 8 PP = primary patency. SP = secondary patency. Survival curves comparing patency of stents deployed above and below the inguinal ligament (\(p = 0.0063\), Log rank test).

Figure 9 PP = primary patency. SP = secondary patency. Survival curves showing that thrombophilia patients did not reach a significant different patency (\(p = 0.1340\), Log rank test).
cases of re-occlusion, immediate catheter directed thrombolysis and re-stenting is possible and may be durable, as suggested with our secondary patency rate. A good clinical outcome, combined with little morbidity and no mortality related to this procedure, supports the use of this technique.

Conflict of Interest

None.

References