A systematic review of endovascular management of chronic iliofemoral venous thrombosis


Department of Vascular Surgery, Democritus University of Thrace, Alexandroupolis, Greece

Abstract:

**Introduction.** Although endovascular management of acute iliofemoral venous thrombosis has been reported as a promising and effective treatment option in recently published societal guidelines, its role on chronic venous disease (CVD) management has not been adequately justified.

**Methods.** A retrospective systematic review was performed for the efficacy of endovascular stenting in patients with chronic post-thrombotic syndrome in terms of venous patency and QoL measurement of these patients in relevant studies.

**Results.** We identified 22 observational cohort studies reporting a total of 2288 participants. Primary outcome measures were technical success, primary, primary-assisted and secondary patency rates of the endovascular intervention of the lesions. Secondary outcome measure was improvement of QoL of life scales before and after the procedure. Primary patency rates at the 1st, 2nd and 3rd year of follow up ranged from 57% to 98%, 65% to 91% and 43% to 96% respectively. Similarly, primary-assisted patency rates ranged from 71% to 99%, 68%-90% and 65%-90% at 1st, 2nd and 3rd year of follow up respectively. Secondary patency rates ranged from 85% to 100%, 79% to 95% and 75% to 94% at the 1st, 2nd and 3rd year respectively. QoL measurements were improved after the intervention compared to preoperative values.

**Conclusion.** Our study indicated that the use of endovascular stenting is associated with a high patency rates and a trend towards a reduced incidence of post-thrombotic syndrome. More well-designed randomized clinical trials will clarify and strengthen the efficacy of endovascular stenting in CVTs.

**Key-words:** iliofemoral thrombosis, venous stenting, stent patency, QoL measures/

INTRODUCTION

Chronic iliofemoral venous thrombosis (CVT) is a major health problem worldwide, frequently resulting in chronic venous insufficiency and in the development of the post-thrombotic syndrome (PTS), at the same time having a great economic social and psychological impact worldwide. Chronic venous disease is associated with various etiologic factors including external pressure, anatomical diversities (May-Turner syndrome), acute or chronic deep venous thrombosis (DVT) whereas the symptomatology depends on the cause, extent and duration of the disease. Among the most serious complications of the disease is the development of the PTS which appears in 20% to 100% of patients despite contemporary treatment, having a negative influence on the Quality of Life (QoL) of involved patients. Historically, surgical venous thrombectomy firstly described by Leriche in 1948, represented an alternative treatment choice compared to conservative treatment with controversial short-term results regarding the recanalization of the iliofemoral venous segment and the improvement of the post thrombotic syndrome. Therapeutic anticoagulation for CVT currently represents the gold-standard treatment and is a globally accepted as the treatment of choice despite high morbidity rates. Although endovascular management of acute iliofemoral venous thrombosis has been reported as a promising and effective treatment option in recently published societal guidelines its role on CVT management has not been adequately justified. In the present study, we conducted a systematic review and meta-analysis of the current literature for the efficacy of endovascular stenting in CVT in terms of venous patency and its effect on the QoL of these patients.

METHODS

**Design and study selection**

This review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards. We included observational studies and case series including more than five patients who underwent endovascular intervention for iliofemoral CVT suffering from PTS. Studies had to report at least one of the outcomes of interest: technical success and patency rates.
Search strategy
A systematic review of relevant studies between January 1992 and December 2018. Searches of the Ovid Medline, Scopus and Cochrane Library were performed using a combination of the following search terms: venous thrombosis with either iliofemoral, endovascular, stenting and post-thrombotic syndrome to identify articles published in English language. In relevant studies we calculated Quality-of-Life (QoL) measurements with the SF-36 and VEINES-QOL questionnaires whereas clinical examination was also recorded according to the C of the CEAP classification (scores C4-6), the Venous Clinical Severity Score (VCSS) and the Villalta scale.

Eligibility criteria
We excluded studies involving endovascular intervention relating to acute iliofemoral venous thrombosis and those with mixed groups of acute and chronic venous disease in cases that relevant data could not be safely extracted. Furthermore, we excluded patients from studies who underwent endovascular intervention due to other venous pathologies such as iliac vein compression syndromes (May-Turner Syndrome) or non-thrombotic etiology of venous occlusion. The detailed search is provided in figure 1.

Study records
Primary outcome measures were technical success, primary, primary-assisted and secondary patency rates of the endovascular intervention of the lesions. Secondary outcome measure was improvement of QoL of life scales before and after the procedure. Post-operative (30-day) complications as well as stent thrombosis were recorded. All data were calculated as ratios. Major complications included death and major bleeding whereas minor complications were minor bleeding, back pain persisting after stent deployment and venous perforation caused by catheter or guidewire injury. Eligibility assessment of identified studies was performed by two review authors (CA, LM). We developed a data extraction sheet, pilot tested it in randomly selected studies that met our inclusion criteria and refined it accordingly. One author (CA) extracted relevant information from selected studies. A second review author (GG) cross-checked the data that were extracted from the studies. We collected study-related information, such as study design and year of publication; baseline demographics and clinical characteristics of the entire screened population (Table 1).

Figure 1. Study flow diagram showing the number of studies that were screened, assessed for eligibility and included/excluded from the systematic review (along with reasons for exclusion)
RESULTS

Our search identified 1300 articles. After duplicate (n=563) and non-relevant (n=463) studies were excluded, we screened 274 studies which were considered eligible for inclusion. Finally, we identified 22 observational cohort studies reporting a total of 2288 participants (709 men and 1579 women) (Figure 1). The mean age of participants ranged across the studies from 18 to 85 years. Mean follow up was 18 months and positive thrombophilia screen was noted in 35% of included patients. Mean intervention time of endovascular intervention was 7.3 years, technical success ranged from 93% to 97%, 30-day stent occlusion and stent restenosis rates ranged from 3% to 5% and 14% to 18% respectively. Primary patency rates at the 1st, 2nd and 3rd year of follow up ranged from 57% to 98%, 65% to 91% and 43% to 96% respectively. Similarly, primary-assisted primary patency rates ranged from 71% to 99%, 68%-90% and 65%-90% at 1st, 2nd and 3rd year of follow up. Secondary patency rates ranged from 85% to 100%, 79% to 95% and 75% to 94% at the 1st, 2nd and 3rd year respectively. (Table 2). Six studies, reported QoL measurements and these represented 55.5% of the overall patient pool. QoL measurements were improved after the intervention compared to preoperative values but did not reach statistical significance (p<.05). Clinical venous scales were not calculated to the heterogeneity of the data.

There were no major 30-day post-operative complications (major bleeding, death due to operation-related causes) reported. Minor complications were recorded, including venous perforation occurring in 23% of recorded patients, back pain with restricted retroperitoneal bleeding in 37% of reported cases, Posto-operative (30-day) stent thrombosis occurred in 2.8% (42/1503) of the overall stent placement.

NR; not reported, Pts; patients, RT; retrospective study, SC; Single-center study, Yrs; years

Table 1. Demographics
A systematic review of endovascular management of chronic iliofemoral venous thrombosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Mean Intervention time range (yrs)</th>
<th>Technical success % (pts/L)</th>
<th>Primary patency (%)</th>
<th>Primary assisted patency (%)</th>
<th>Secondary patency (%)</th>
<th>Stent size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ye, 2014&lt;sup&gt;12&lt;/sup&gt;</td>
<td>range 1-40</td>
<td>95(112/118 L)</td>
<td>3yr (70)</td>
<td>3yr (90)</td>
<td>3yr (94)</td>
<td>D 4-16 L 60-220</td>
</tr>
<tr>
<td>Sang, 2014&lt;sup&gt;13&lt;/sup&gt;</td>
<td>range 12-36</td>
<td>94(63/67 pts)</td>
<td>1yr (87.9)</td>
<td>3yr (70.7)</td>
<td>NR</td>
<td>1yr (93.3) L 82.8</td>
</tr>
<tr>
<td>Rosales, 2010&lt;sup&gt;14&lt;/sup&gt;</td>
<td>NR</td>
<td>94(32/34 pts)</td>
<td>2yr (67)</td>
<td>2yr (76)</td>
<td>2yr (90)</td>
<td>NR</td>
</tr>
<tr>
<td>Raju, 2009&lt;sup&gt;15&lt;/sup&gt;</td>
<td>NR</td>
<td>83(139/167 limbs)</td>
<td>1yr (57)</td>
<td>2yr (68)</td>
<td>1yr (85)</td>
<td>NR</td>
</tr>
<tr>
<td>Falcoz, 2016&lt;sup&gt;16&lt;/sup&gt;</td>
<td>2 (range 1.8-5)</td>
<td>100 (21/21pts)</td>
<td>1yr (90.5)</td>
<td>NR</td>
<td>NR</td>
<td>D 8-18 L 40-80</td>
</tr>
<tr>
<td>Raju, 2002&lt;sup&gt;17&lt;/sup&gt;</td>
<td>100(292/292pts)</td>
<td>1yr 71</td>
<td>1yr 71</td>
<td>1yr 97</td>
<td>D 14-16</td>
<td></td>
</tr>
<tr>
<td>Neglen, 2007&lt;sup&gt;14&lt;/sup&gt;</td>
<td>NR</td>
<td>94(32/34 pts)</td>
<td>1yr (90)</td>
<td>1yr (95)</td>
<td>1yr (95)</td>
<td>D 10-20 L 40-260</td>
</tr>
<tr>
<td>Hartung, 2009&lt;sup&gt;17&lt;/sup&gt;</td>
<td>NR</td>
<td>98 (87/91pts)</td>
<td>1yr (89)</td>
<td>1yr (94)</td>
<td>1yr (96)</td>
<td>D 12-16 L 40-90</td>
</tr>
<tr>
<td>de Wolf, 2015&lt;sup&gt;18&lt;/sup&gt;</td>
<td>6 (1-37)</td>
<td>100 (75/75pts)</td>
<td>1yr (90)</td>
<td>1yr (99)</td>
<td>1yr (100)</td>
<td>NR</td>
</tr>
<tr>
<td>Catarinella, 2015&lt;sup&gt;26&lt;/sup&gt;</td>
<td>NR</td>
<td>2yr 65</td>
<td>2yr 78</td>
<td>2yr 89</td>
<td>2yr 89</td>
<td>NR</td>
</tr>
<tr>
<td>Alenari, 2014&lt;sup&gt;19&lt;/sup&gt;</td>
<td>8.8 (2-48)</td>
<td>2yr 74</td>
<td>2yr 87</td>
<td>2yr 89</td>
<td>2yr 89</td>
<td>D 12-24</td>
</tr>
<tr>
<td>Kurkisnisky, 2012&lt;sup&gt;27&lt;/sup&gt;</td>
<td>NR</td>
<td>1yr 81</td>
<td>1yr 94</td>
<td>1yr 95</td>
<td>1yr 95</td>
<td>NR</td>
</tr>
<tr>
<td>George, 2014&lt;sup&gt;18&lt;/sup&gt;</td>
<td>NR</td>
<td>1yr 94</td>
<td>1yr 97</td>
<td>NR</td>
<td>D 6-24</td>
<td></td>
</tr>
<tr>
<td>Ruihua, 2017&lt;sup&gt;21&lt;/sup&gt;</td>
<td>7.8 (2-35)</td>
<td>77/81 (95)</td>
<td>2yr (81.5)</td>
<td>2yr (91.4)</td>
<td>2yr (93.8)</td>
<td>D 10-12</td>
</tr>
<tr>
<td>Kolbel, 2009&lt;sup&gt;29&lt;/sup&gt;</td>
<td>NR</td>
<td>59/62 (92)</td>
<td>5yr (70)</td>
<td>5yr (73)</td>
<td>5yr (80)</td>
<td>D 12-22</td>
</tr>
<tr>
<td>Nayak, 2012&lt;sup&gt;20&lt;/sup&gt;</td>
<td>5±5.9</td>
<td>39/44 (89)</td>
<td>NR</td>
<td>NR</td>
<td>D 12-16</td>
<td></td>
</tr>
<tr>
<td>Oguzkurt, 2008&lt;sup&gt;28&lt;/sup&gt;</td>
<td>1 (2-5)</td>
<td>1yr 80</td>
<td>NR</td>
<td>NR</td>
<td>D 12-16</td>
<td></td>
</tr>
<tr>
<td>Lou, 2009&lt;sup&gt;31&lt;/sup&gt;</td>
<td>NR</td>
<td>1yr 93</td>
<td>2yr 86</td>
<td>3yr 75</td>
<td>D 40-80</td>
<td></td>
</tr>
<tr>
<td>Blattler, 1999&lt;sup&gt;21&lt;/sup&gt;</td>
<td>mean 18.3 (range 1.7-46)</td>
<td>25/42(60)</td>
<td>1yr 11(79)</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>O’Sullivan, 2013&lt;sup&gt;22&lt;/sup&gt;</td>
<td>mean 0.5 (range 1-15)</td>
<td>1yr 93.9</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Sarici, 2013&lt;sup&gt;19&lt;/sup&gt;</td>
<td>NR</td>
<td>52/52 (100)</td>
<td>NR</td>
<td>NR</td>
<td>D 6-14</td>
<td></td>
</tr>
<tr>
<td>Meng, 2011&lt;sup&gt;15&lt;/sup&gt;</td>
<td>NR</td>
<td>285/296 (96)</td>
<td>1yr 98</td>
<td>NR</td>
<td>L 40-80</td>
<td></td>
</tr>
</tbody>
</table>

NR; not reported, Pts; patients, RT; retrospective study, SC; single-center study, Yrs; years

Table 2. Results

**DISCUSSION**

Since 1990s, endovascular intervention for deep venous pathology has gained increased popularity in managing the severe clinical manifestations of post-thrombotic syndrome (PTS). Common manifestations of PTS include pain, calf swelling, heaviness, edema, skin pigmentation, or venous ulceration of the affected leg, with symptoms becoming apparent usually within the first 2 years after the thrombotic event. The present meta-analysis has demonstrated that endovascular treatment of chronic iliofemoral venous disease is a durable and effective option in treating symptomatic patients with PTS, having a high technical and clinical success. In particular, endovascular stenting has resulted in major symptom relief in patients with chronic venous disease however this was not consistently reflected in all aspects of QoL measurements and it nearly reached statistical significance (p<.051). In respect to the acute phase of deep venous thrombosis, the most recent CHEST guidelines state that “anticoagulation therapy alone is an acceptable alternative to Catheter-directed Thrombolysis (CDT) in all patients with acute lower extremity DVT,” citing unacceptable risk of bleeding. In contrast to the CHEST guidelines, the American Heart Association does recommend CDT as first-line therapy for patients at low bleeding risk with lower extremity DVT. The CaVenT study was the first randomised controlled trial to evaluate the clinically relevant effect of additional cathe-
ter-directed thrombolysis for proximal deep vein thrombosis. The results after 5 years of follow-up showed a continued and increased reduction in development of post-thrombotic syndrome in patients assigned to catheter-directed thrombolysis compared with those assigned to anticoagulation and compression therapy alone as well as reducing post-thrombotic syndrome after extensive DVT. The ATTRACT Trial was a 56 centre, randomised controlled trial (RCT) that evaluated pharmaco-mechanical catheter directed thrombolysis (PCDT) for prevention of PTS in patients with acute proximal deep vein thrombosis (DVT). The study found that PCDT did not prevent PTS over 2 years (primary outcome); increased major bleeding; did not influence health related quality of life (QOL) or recurrent venous thromboembolism; improved leg pain and swelling over 30 days; and reduced the severity of PTS. How-ever these randomized clinical trials included patients only in the acute phase of deep venous thrombosis whereas the recommendation for endovascular stenting of chronic deep venous thrombosis relies on low levels of evidence.

On the other hand, several reviews and meta-analyses have postulated the effectiveness of endovascular stenting on CVD and PTS. However these studies have included data of patients with CVD due to thrombotic and non-thrombotic etiology, thus limiting the clarity of the results since these different groups of patient diseases have been associated with different outcomes and results due to different pathological mechanisms. In the present meta-analysis, only patients with post-thrombotic syndrome due to thrombotic occlusion of the iliofemoral segment were included. Based on this parameter, the fact that the relief rate of PTS in these patients from the QoL scales did not reach statistical significance could partly be attributed to two reasons. Firstly, patients with PTS due to valvular insufficiency could maintain symptoms of leg edema and pain even if venous obstruction would have improved by stenting. Second, the recanalization of a completely thrombosed venous segment is highly dependent on distinct venous disease pathogenesis, on the degree of vein collaterals and venous recanalization, on the quality of inflow and outflow and rigor of anticoagulant treatment resulting in distinct clinical outcomes in each of the treated patients.

The results of our study show a high technical success of the endovascular intervention and high primary, primary-assisted and secondary patency rates. These results further support the trend of endovascular stenting as an option in patients with CVD suffering from PTS despite the wide application of alternative conservative measures such as pharmacologic treatment, compression therapy and exercise therapy. Technical factors limiting or altering the technical success and stent patency results of the present meta-analysis are venous stenting extending below the inguinal ligament and iliofemoral thrombosis of non-thrombotic etiologies. Indeed, in numerous studies, extension of the stenting below the level of the inguinal ligament has been associated with worse patencies whereas other studies have not shown this correlation. Other anatomical criteria playing a substantial role in the management and outcome of the disease are the location of the venous occlusion and the disease pathology. Neglen et al in their study have shown that stent patency was better correlated with the disease pathology, better patency achieving patients with non-thrombotic iliac vein lesions compared to chronic total occlusions. Limitations of the study include the statistical gaps in categorizing and estimating values of QoL tools and the fact that no QoL tools exist specifically for estimating venous diseases. Duration of follow-up and outcomes for the QoL measures was inconsistently reported. We made no attempt to compare group of patients with different disease pathogenesis due to the fact that most studies were retrospective and single centres and additionally pooled data were insufficient as to reach any definitive conclusions or suggestions. Furthermore, quality of the results are possibly hindered by the fact that different stent sizes and designs were used making impossible the comparator from the reported data. Patient characteristics, physician experience and periprocedural protocols used in each center are possible confounders influencing the credibility of outcomes. Quality results for the homogeneity of the included studies are lacking.

CONCLUSION

Endovascular management of chronic iliofemoral venous thrombosis is an emerging therapeutic option in managing patients with chronic iliofemoral venous thrombosis and PTS and should be considered an attractive option to alternative management strategies since it combines safety, technical success and negligible morbidity rates. However, in terms of QoL scales, possibly further studies could further support the efficacy in the improvement if the patient’s symptoms.

REFERENCES
6 O’Donnell Jr TF, Passman MA, Marston WA, Ennis WJ, Dlasing M, Kistner RL. Management of venous leg ulcers:
A systematic review of endovascular management of chronic iliofemoral venous thrombosis

175


18 Hartung O, Loundou AD, Barthelemy P, Arnoux D, Boufi M, Alimi YS. Endovascular management of chronic disa-


