

Endovascular treatment of proximal lower extremity deep vein thrombosis – experience of a center

Miguel Queirós, Duarte Rego, Rui de Almeida 

Centro Hospitalar Universitário de Santo António, Porto, Portugal

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ABSTRACT

INTRODUCTION: Proximal lower extremity deep vein thrombosis (DVT) occurs in 5-10/10000 patients annually. Left untreated, there's a notable risk of pulmonary embolism development and the onset of long-term limb complications linked to post-thrombotic syndrome (PTS). Traditionally, these patients were treated with conservative therapy, namely anticoagulation and compression stockings. Nowadays, new and more aggressive treatments have emerged. Endovascular therapies, such as thrombectomy devices, catheter-directed thrombolysis (CDT), percutaneous transluminal angioplasty (PTA), and stent placement, provide a highly effective treatment option with minimal patient risk of complications.

METHODS: We retrospectively studied all patients with proximal lower extremity DVT who were treated with endovascular therapy in our center between the years of 2018 and 2021. We choose as primary outcomes symptoms of PTS (Villalta Score) and quality of life (VEINES-QoL/Sym questionnaire) and as secondary outcomes treatment efficacy (grade of thrombolysis), treatment safety, and primary patency.

RESULTS: A total of 20 patients were treated by endovascular treatment. The majority of these patients were women (95%); 60% of them had DVT of the left limb, and 30% had *phlegmasia alba dolens*. Seven patients were treated with the Angiojet™ system (35%), four with the Penumbra™ system (20%) and nine with CDT alone (45%).

Two patients presented with mild PTS symptoms, and the mean VEINES-QoL/Sym questionnaire score was 84.8% +/- 13.6%. There were no cases of major bleeding or pulmonary embolism after the procedure. Two patients had small vein ruptures with no need for additional treatment. The average length of stay in a high surveillance unit for vigilance was 2.2 days. At the end of treatment, 75% of the patients had complete thrombolysis, 15% had partial thrombolysis (50–99% thrombus removal), and 10% showed minimal or no thrombolysis (< 50% thrombus removal). The primary patency rate was 88% after 12 months.

CONCLUSION: Our experience has shown that endovascular therapy for acute proximal lower extremity DVT is a safe and effective treatment associated with a very low incidence of PTS and recurrent venous thromboembolism. However, life-threatening complications such as major bleeding can occur. As such, while under treatment, close monitoring of these patients in a high surveillance unit is mandatory.

Keywords: Deep vein thrombosis; endovascular thrombectomy; post-thrombotic syndrome.



INTRODUCTION

Proximal lower extremity deep vein thrombosis (DVT) occurs in 5-10/10000 patients annually. A proximal DVT is defined as a thrombus involving iliac, femoral, and/or popliteal veins. DVT frequently affects the lower limb, with proximal vessels being common sites affected: common femoral (20%), femoral (20%), popliteal (16%), and iliac (4%). Distal veins comprise 40% of all cases. Left untreated, there's a notable risk of pulmonary embolism development and the onset of long-term limb complications linked to post-thrombotic syndrome (PTS).^[1-5] Post-thrombotic syndrome is a frequent complication affecting up to 50 % of patients after ilio-femoral DVT, even with proper anticoagulation. PTS develops from venous obstruction and insufficiency, causing a variety of symptoms, ranging from mild signs and symptoms like heaviness and paraesthesia to more severe expressions such as tissue edema, subcutaneous fibrosis, and subsequent ulceration. PTS negatively affects the quality of life (QoL). Therefore, appropriate therapy is mandatory in preventing and reducing the incidence of PTS.^[6-9]

The mainstay of treatment for DVT is medical therapy, which involves anticoagulation for a minimum period of three months, along with the use of compression therapy to help prevent PTS in the long term. Gradually, more aggressive endovascular therapies, including catheter-directed thrombolysis (CDT), pharmaco-mechanical catheter-directed thrombolysis (PCDT), percutaneous transluminal angioplasty (PTA) and stent placement, have emerged and these modalities have advantages compared to conservative anticoagulation therapies. Many individual trials and randomized control trials (RCTs) have shown that patients with proximal DVT managed with medical therapy alone have an increased risk of PTS development when compared to patients treated with endovascular therapy.^[4,10-17]

As a result, some patients with proximal DVT may benefit from endovascular interventional treatment, as medical therapy alone does not offer a thrombolytic effect. This enables early thrombus removal, thereby improving vessel patency and restoring function, which helps with the long-term outcome. However, many complications associated with intervention have been described, with vein rupture associated with major bleeding, pulmonary embolism, and intracranial bleeding being the most critical among them.^[4,10,11]

METHODS

We conducted a retrospective analysis of all patients with an unprovoked proximal lower extremity DVT that were treated with endovascular therapy in our centre between the years of 2018 and 2021. Patients with DVT caused by iliac stent thrombosis were excluded from the study. The following data were retrospectively analyzed: sex, age, surgery date, presence of *phlegmasia alba dolens*, affected limb (laterality), extension of thrombosis, and presence/type of symptoms. Data were collected through hospital reports and by direct patient questioning through phone calls.

Outcomes

The primary outcomes evaluated were the incidence and severity of PTS after surgery defined using the Villalta scoring system of PTS. The Villalta scoring system can diagnose and categorize the severity of PTS and divides severity into five categories: < 5 as none; 5-9 as mild; 10-14 as moderate; > 14 as severe.^[6]

Quality of life was evaluated using the VEINES-QoL/Sym questionnaire, adapted and validated for Brazilian Portuguese. VEINES-QoL/Sym questionnaire is a well-known and extensively used questionnaire valid and reliable for use as a measure of QoL and symptoms in patients with acute DVT. The questionnaire includes 26 items, including symptoms related to venous disease, limitations and changes in daily activities and psychological impact of the venous disease. To calculate the VEINES-QoL score, 25 items are used (question related to the most symptomatic time of the day is excluded) and to calculate VEINES-Sym score only ten items related to symptom severity are used. The total score was calculated and converted to a maximum of 100% according to the authors' indications, with higher scores indicating better QoL.^[18] Villalta scoring and VEINES-QoL/Sym questionnaires were accessed after a minimum of six months post procedure.

Secondary outcomes included treatment safety, primary patency 12 months after the procedure and treatment efficacy. Treatment efficacy was defined as thrombus removal grading after the end of the procedure, through venography evaluation. It was evaluated as complete thrombolysis (100% thrombus removal rate with no residual clots), partial thrombolysis (50–99% thrombus removal rate), and minimal or no thrombolysis (<50% thrombus removal rate). Thrombus removal higher than 50% was considered clinical success.

RESULTS

A total of 20 patients were included. Most of these patients were women (95%) with a mean age of 41y +/- 15. All patients presented with iliac vein thrombosis. The most common type of DVT was ilio-femoral-popliteal (55%) followed by ilio-femoral thrombosis (45%). 60% of patients had DVT of the left limb, and 30% had *phlegmasia alba dolens*. Seven patients were treated with the Angiojet™ system (35%), four with the Penumbra™ system (20%) and nine with CDT alone (45%). Mean follow-up time was 29.7 +/- 11.41 months.

All patients except for two were treated with CDT (alteplase 0.5-1.0 mg/h) for at least 48 hours. These two patients were treated with the Angiojet™ system with posterior stenting and did not receive further thrombolytic treatment, given the excellent immediate result. Seven patients received complementary treatment with stenting. All patients received, after discharge, a therapeutic dosage of anticoagulation therapy (apixaban 5 mg bid or rivaroxaban 20 mg id) for a minimum period of three months.

Primary Outcomes

PTS symptoms were evaluated using Villalta scoring system, with only two patients (10%) presenting with mild PTS (score 5-9). All other patients did not present with symptoms or symptom severity to be classified as PTS. Our population

Table 1. Description of complementary treatment and treatment efficacy of the different types of treatment applied for deep venous thrombosis patients

	Complementary treatment				Treatment efficacy		
	PTA/Stenting	PTA/Stenting + CDT	CDT	None	Complete Thrombolysis	Partial Thrombolysis	Minimal/ no thrombolysis
AngioJet™ (n=7)	29% (2)	57% (4)	14% (1)	-	86% (6)	14% (1)	-
Penumbra (n=4)	-	-	100% (4)	-	75% (3)	25% (1)	-
CDT (n=9)	-	22% (2)	88% (7)	-	67% (6)	11% (1)	22% (2)

scored a mean of 84.8 % +/- 13.6 % in the VEINES-QoL/Sym questionnaire.

Secondary Outcomes

At the end of treatment, 75% of the patients had complete thrombolysis, 15% had partial thrombolysis and 10% showed minimal or no thrombolysis. A clinical success of 90% was achieved. Both Angiojet and Penumbra achieved a clinical success of 100%. On the other hand, CDT achieved only 79%. A more detailed description of the treatment efficacy is described in Table 1. Primary patency rate was 88% after 12 months (100% for Angiojet, 75% for Penumbra and 75% for CDT).

There were no cases of major bleeding or pulmonary embolism after the procedure. Two patients had small vein ruptures with no need for additional treatment. The average length of stay in a high-dependency unit for vigilance was 2.2 days.

DISCUSSION

Patients with ilio-femoral deep venous thrombosis have a risk of up to 50% of developing post-thrombotic syndrome one to two years after DVT even with proper anticoagulation. Endovascular treatment for proximal DVT may reduce the incidence of PTS and increase QoL in these patients.^[2,6,18]

We found that the incidence of PTS after endovascular treatment was 10%. Özcan Gür et al. compared the effects of endovascular treatment and medical therapy in patients with acute proximal deep vein thrombosis (DVT) on the risk of development of PTS. At 12-month follow-up, the number of patients treated with endovascular treatment with a Villalta score of ≥ 5 was 6.25% in a total of 128 patients, which is very close to our findings. On the other hand, at 12-month follow-up, the number of patients treated with anticoagulation alone with a Villalta score of ≥ 5 was 81 (67.5%) in 120 patients.^[2,13-18]

The CaVenT and the ATTRACT are two major randomized controlled trials (RCTs) that compared endovascular treatment of proximal DVT to conservative treatment with anticoagulation. The CaVenT study compared CDT in addition to anticoagulant therapy with anticoagulant treatment alone. The study demonstrated a significant reduction in PTS in the interventional group, with an absolute risk reduction of developing PTS of 14.4% at 24 months. The ATTRACT study was a multicentre RCT that evaluated PCDT and CDT for the prevention of PTS in patients with femoral or more proximal DVT compared with standard therapy with oral anticoagulants alone. This study did not find any difference in the proportion of patients who developed PTS between the two treatment

groups (47% with CDT/ PCDT vs. 48% with standard therapy; RR 0.96, 95% CI 0.82 e 1.11, $p = 0.56$). However, despite not reducing the incidence of PTS intervention significantly reduced PTS severity scores and significantly reduced the development of moderate to severe PTS (18% with PCDT vs. 24% with standard therapy; RR 0.73, 95% CI 0.54 e 0.98, $p = 0.035$ over 24 months of follow up.^[11,12]

In our analysis, we found an average score of 84.8% +/- 13.6% in the VEINES-QoL/Sym questionnaire, which seems to demonstrate not only the efficacy of endovascular therapy in QoL impact but also the correlation between the lower incidence and severity of PTS with a higher QoL in these patients. Özcan Gür et al. found a significant difference ($p < .001$) in QoL in patients treated with endovascular treatment vs anticoagulation alone, which goes in hand with our findings. On the other hand, the ATTRACT study found that endovascular treatment, despite reducing leg pain and swelling up to 30 days after intervention, did not significantly improve QoL from baseline to 24 months.^[2,11-19]

Treatment efficacy was defined as thrombus removal grading after the end of the procedure through venography evaluation. Indeed, over the past few years, there has been a notable increase in the utilization of intravascular vascular ultrasound (IVUS), offering numerous advantages as an adjunct to venography. IVUS offers a 360-degree two-dimensional grayscale ultrasound image of lumen and vessel wall structures in major axial veins. Its application in patients with DVT enables superior visualization and assessment of venous disease. IVUS enhances the differentiation between acute and chronic thrombus, identifies external compression, fibrosis, residual thrombus, and grades stenosis more accurately. Consequently, IVUS facilitates a more precise and effective treatment approach.

Unfortunately, two patients did not achieve clinical success, despite treatment efforts. It's important to highlight that both individuals exhibited symptoms over a week before hospital admission. This late presentation may have contributed to a more organized thrombosis, thereby reducing the effectiveness of fibrinolysis in these cases.

There are very few studies concerning technical success of these thrombectomy systems. Xu He et al. studied the efficacy of thrombectomy using the AngioJet system and achieved clinical success, defined as thrombus removal higher than 50% of 100%. Both AngioJet and Penumbra systems achieved a higher clinical success (100%) than CDT alone (79%). These systems provide mechanical thrombectomy that CDT doesn't have, which leads to a higher success rate.^[20] Primary patency after 12 months

was 88%, demonstrating the excellent ability of immediate thrombus removal and the ability to maintain patency.

Treatment safety and the time needed in a high surveillance unit are also important points to consider when choosing between intervention and conservative treatment. We did not have any cases of major bleeding or pulmonary embolism after the procedure. However, major bleeding rates with CDT are reported to range from 2.2% to 3.3% and 1.7% in patients treated with PCDT. These complications lead to further intervention and a more extended hospital stay. Even though hospital admission is needed for endovascular treatment, patients treated with the AngioJet system may not require a lengthy hospital stay. According to the PEARL study (Peripheral Use of AngioJet Rheolytic Thrombectomy with a Variety of Catheter Lengths; an industry sponsored device registry), about 70% of patients treated with the Angiojet system had their treatment completed within 24 hours, clearly faster than the two to three days with CDT. In our experience, two out of the seven patients treated with the Angiojet TM system did not require additional CDT. As such, there was no need to repeat venography and no need for further surveillance in a high dependency unit, providing a faster hospital discharge.^[20-24]

CONCLUSION

Our experience has shown that endovascular therapy for acute proximal lower extremity DVT is a safe and effective treatment associated with a very low incidence of PTS and recurrent venous thromboembolism. In association with a very low incidence of PTS, a high QoL score is achieved in these patients. However, although rare, life-threatening complications such as major bleeding can occur in a minority of patients. In our experience, there were no cases of major bleeding reported; nonetheless, most of these patients require close monitoring on a high dependency unit while under treatment.

Choosing between endovascular treatment and conservative management will always depend on the surgeon's experience. However, in young patients with extensive proximal thrombosis or the presence of phlegmasia alba dolens, the probability of PTS is increased, so choosing endovascular treatment may be the best treatment.

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