World Journal of Surgery and Surgical Research

Research Article
Published: 05 Feb, 2019

Endovascular Management for Chronic Obstructive Iliofemoral Deep Vein Thrombosis, Mid-Term Result

Chiu-Yang Lee[1,2]*

[1]Department of Surgery, Taipei Veterans General Hospital, Taiwan

[2]Department of Senior Citizen Service Management, Chia Nan University of Pharmacy and Science, Taiwan

Abstract

Background: The purpose of this study was to assess the result of endovascular intervention including angioplasty alone (control group) or angioplasty plus stenting (stent group) in treating chronic obstructive iliofemoral Deep Vein Thrombosis (DVT). Methods: All the patients treated with endovascular interventions between January 2009 and October 2014 were examined for primary patency, assisted patency, and midterm venous functional outcomes.

Results: The overall success rate of endovascular technique was 88.9% (71 of 82 patients).No mortality, but minimal complications like ecchymosis and hematoma at puncture sites were found. 36-month primary patency rate and 36-month assisted patency rate were 63.9% and 72.2% of the stent group, and 17.6% and 26.4% of the control group, respectively. The survival analysis of the Kaplan-Meier curves and life table indicating the cumulative primary and assisted patency rate after 36 months in both angioplasty and stent groups are presented in Figure 1A (Log-rank test, P<0.001) and B (Log-rank test, P<0.001). Femoral valvular incompetence was observed in 58.3% and 82.4% of stent and control patients (P=0.028). The median (IQR) Villalta scores after 36 months, were 5.5 (3.3 to 7.0) and 7 (5 to 8) in stent and control patients (P=0.022), respectively. Post-Thrombotic Syndrome (PTS) were found in 50% and 79.4% of stent and control groups (P=0.01), respectively. Bleeding events during therapy were found in 27.8% and 17.6% of stent and control patients (P=0.313), respectively. Recurrent DVT was found in 19.4% and 52.9% of stent and control patients (P=0.003) at twenty-four follow-up. Using a univariate and multivariate Cox regression, recurrent DVT, DVT duration and treatment method were principal predicting factors of the 24-month primary patency (Duration of DVT, HR=5.13, 95% CI: 1.68 to 15.7, P=0.004; Recurrent DVT, HR=0.35, 95% CI: 0.17 to 0.72, P=0.004; Treatment method, HR=0.5, 95% CI: 0.26 to 0.96, P=0.036) after adjustment of gender and age and BMI.

Conclusion: This study suggests treatment method, DVT duration and recurrent DVT may be primary factors influencing vein patency. Endovascular intervention with stenting should be considered early for obstructive iliofemoral DVT because of a high technical success rate and acceptable mid-term, functional outcomes. A larger and randomized trial needs to be conducted in the future.

OPEN ACCESS

Correspondence:
Chiu-Yang Lee, Department of Surgery, Division of Cardiovascular Surgery, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, Tel: 886228757495; Fax: 886228757656; E-mail: davidlee0501@gmail.com.tw

Received Date: *16 Jan 2019*
Accepted Date: *03 Feb 2019*
Published Date: *05 Feb 2019*

Citation:
Lee C-Y. Endovascular Management for Chronic Obstructive Iliofemoral Deep Vein Thrombosis, Mid-Term Result. World J Surg Surgical Res. 2019; 2: 1099.

Introduction

Deep Vein Thrombosis (DVT) is a potentially progressive disease with complex chronic sequelae. The most common late complication of DVT is Post Thrombotic Syndrome (PTS), which results from sustained venous hypertension because of persisting venous obstruction and/or valvular incompetence. Although long-term anticoagulant therapy and supplementary compression stockings are the current standard of care for chronic proximal DVT, they only inhibit thrombus propagation, prevent Pulmonary Embolism (PE), and temporally relive symptoms. However, they neither prevent chronic post thrombotic complications nor remove existing thrombus. Bypass surgery (Palma bypass) was the treatment of choice for symptomatic obstructive iliofemoral DVT before the development of balloon angioplasty and stenting. Some papers state that iliofemoral venous obstructions can be corrected with this bypass surgery [1-3]. However, the majority of studies lack reliable follow-up results. Recently, there has been great interest in the clinical use of endovascular management with pharmacomechanical thrombectomy, angioplasty, and stenting. Several recent literatures suggested early removal of thrombus was a first choice in patients with acute iliofemoral DVT. However, ten years ago, most of these patients were treated with traditional anticoagulation, and later developed complications such as recurrent DVT, pulmonary embolism,

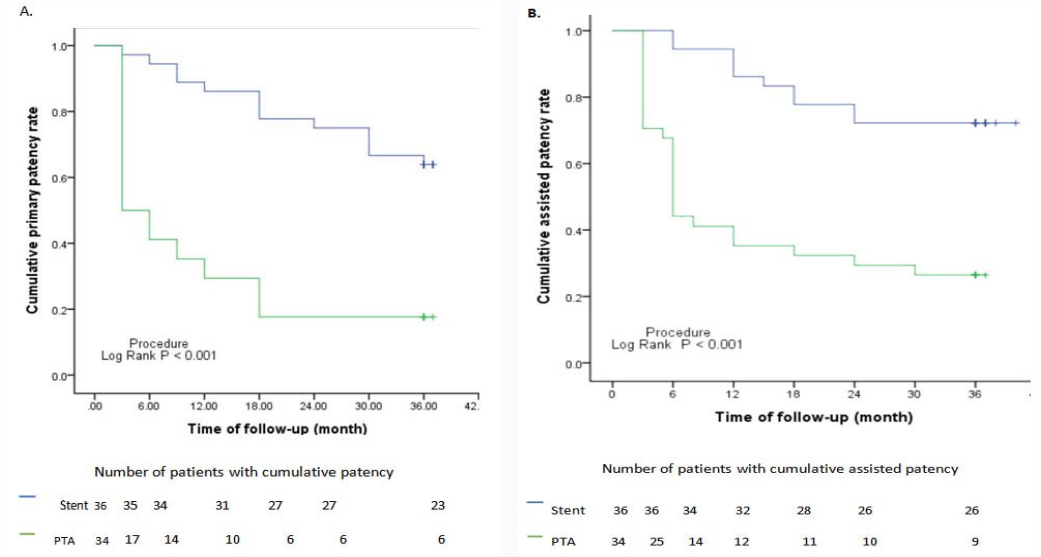

Figure 1: Kaplan-Meier curves for performance of time-to-patency analysis for patients treated with angioplasty alone and stent-angioplasty.
1A: Shows that patients with stent placement have better primary patency than those with simple angioplasty (Log Rank test: P<0.001).
1B: Indicates t that patients with stent placement have better assisted patency than those with simple angioplasty (Log Rank test: P=0.001).

post thrombotic syndrome, and stasis ulcer etc. In our center, almost all patients have been operated using these endovascular procedures since 2008. This study was to compare the safety and efficacy of endovascular interventions including angioplasty alone or angioplasty plus stenting in these patients with obstructive iliofemoral DVT and identify potential factors influencing venous patency.

Material and Methods

This study was approved by the institutional review board, and informed consent was waived off (IRB No: 2011-10-014IC and 2012-04-011AC). A retrospective review of data of 82 patients with obstructive iliofemoral DVT who had symptoms for >21 days was conducted. Of 82 patients, 72% (59) had DVT for approximately two month, and 28% (23) experienced DVT for more than two months. The primary symptoms of all patients were limb swelling, discoloration, pain, and venous claudication. The obstructive iliofemoral DVT was initially diagnosed using duplex sonography, venography, and/or Computed Tomography Venography (CTV).

In spite of the retrospective study, all patients were routinely followed and recorded according to the DVT protocol of our medical center before procedures. Thus, prospective medical data included blood pressure, pulse rate, body mass index (BMI), and blood profiles comprising Hemoglobin levels, platelet counts, PT & aPTT, fibrinogen levels, D-Dimer, protein C, S, antithrombin III, lupus anticoagulant and electrolytes etc. All patients were operated with endovascular interventions including angioplasty alone and stent placement according to CTV conditions, and vessel recoil or stenosis after initial angioplasty. In Taiwan, the cost of stent placement for iliofemoral veins needs to be paid by patients. Finally, 34 patients determined simple angioplasty without stent implantation. Thus, all patients were divided into two group including angioplasty alone (control group) and stent placement (stent group). All regularly followed-up over a more than 3 year period.

Endpoints

The primary endpoints of this study were clinical symptoms, safety, and primary and assisted patency on 36-month follow-up. Patients were routinely restudied at intervals of 3 months to 6 months by Doppler ultrasound after endovascular interventions. Clinical symptoms were checked and recoded based on Villalta score and levels of valvular incompetence. If the Villalta score increases combined with abnormal Doppler findings including resistant flow and no compression of iliofemoral veins, further venography or CT venography will be arranged for assessment of patency. Primary patency of the iliofemoral vein was defined as compressible iliofemoral veins with flow, and no stenosis or a stenosis of less than 30% confirmed by last-imaging Doppler ultrasonography, and venography or CTV at 36 months.

Assisted patency was defined as compressible iliofemoral veins with flow, and no stenosis or a stenosis of less than 30% confirmed by last-imaging Doppler ultrasonography, and venography or CTV at 36 months, after patients received another percutaneous interventions to treat the previously involved veins, Safety was defined as the number of patients with major or minor bleeding, recurrent DVT and pulmonary embolism in 36-month follow-up. Recurrent DVT was defined as: (1). Non-compressibility at the new vein segment of the same leg (previously unaffected) (2). A proximal or distal extension with a change of thrombus length of more than 5 cm (3). Non-compressibility at the re-canalized vein that was thrombosed previously, or (4). A new non-compressible vein in the contralateral leg [4-6].

Technique

Before the procedure, antithrombotic drugs were discontinued to obtain an International Normalized Ratio (INR) of <1.5. At the beginning of the procedure, an Unfractionated Heparin (UFH) bolus of 3000U was intravenously administered to obtain an activated clotting time (ACT) of >200 s. In brief, percutaneous entry was obtained via the Lesser Saphenous Vein (LSV) or the popliteal and femoral veins with ultrasound guidance. After the vein was punctured, a 5- or 6-F introducer sheath was inserted into the thrombosed vessel over a guidewire. Initial venography was performed to evaluate the statue of the iliofemoral veins, including narrowing (small caliber), or obstruction of involved veins. The guidewire and catheter were

Table 1: Intervention characteristics and adverse effects.

Characteristic	Stent (n=36)	PTA* (n=34)	P value
Age, median (IQR), years	69.5(54.3 to 79.8)	64(49.8 to 78)	0.169
Gender (female)	18(50.0)	15(44.1)	0.622
BMI, median (IQR)	26.5(25.8 to 27.4)	26.5(25.2 to 28.3)	1
Duration of DVT			
≦ two months	24(66.7)	28(82.4)	0.133
➢Two months	12(334)	6(17.6)	
Site (Left)	26(72.2)	16(47.1)	0.032
Hypertension	6(16.7)	2(5.9)	0.298
DM	7(19.4)	5(14.7)	0.835
CAD	**4(11.1)**	**4(11.8)**	**1.000**
Hyperlipidaemia	4(11.1)	2(5.9)	0.723
CVA	3(8.3)	7(20.6)	0.262
Smoking	7(19.4)	8(23.5)	0.677
Recent trauma[1]	3(8.3)	6(17.6)	0.42
Recent operation[2]	8(22.2)	3(8.8)	0.226
Malignancy[3]	8(22.2)	2(5.9)	0.197
Thrombophilia[4]	9(25)	13(38.2)	0.233
Atrial fibrillation	2(5.6)	2	1
OCT	9(25)	4(11.8)	0.265

[1]Recent trauma is defined as trauma that occurred 14 to 30 days before the onset of DVT.
[2]Recent operation is defined as surgery experienced 30 to 90 days before the onset of DVT.
[3]Malignancy is defined as cancer diagnosed before the index VTE, and without recurrent or progressive event that required curative or palliative treatment.
[4]Thrombophilia is defined as documented biochemical hypercoagulable disorders, such as protein C or S deficiency, antithrombin III, and Lupus anticoagulant.
DVT: Denotes deep Vein Thrombosis; BMI: Body Mass Index; DM: Diabetes Mellitus; CAD: Coronary Artery Disease; CVA: Cerebral Vascular Accident; OCT: Oral Contraceptive Therapy
[6]Values in parentheses are percentages.
[7]IQR: Interquartile Range
*PTA: Percutaneous Transluminal Angioplasty

gradually advanced through the area of obstruction into the inferior venae caca. If unsteady and unorganized thrombus burden is encountered, Catheter-Directed Thrombolysis (CDT) will be utilized for approximately 24-hour in these patients. On the second day, repeated venographies were arranged to check thrombuslysis of the iliofemoral veins, and following angioplasty was performed to correct the stenotic lesions. If intraoperative venography shows no recoil or a stenosis of less than 50% following of the involved iliofemoral vein, just simple angioplasty was applied. On the contrary, if the easy recoil or a stenosis of more than 50% is verified in the involved vein, stent deployment will be considered to prevent vessel recoil from external compression for these patients.

Post-Procedure Follow-up and Medications

In spite of the retrospective study, all patients were followed according to the DVT protocol at our medical center. Blood pressure, pulse rate, and puncture site were routinely checked four times daily. Hemoglobin levels, fibrinogen levels, D-Dimer, and platelet counts were monitored daily, and a PTT was evaluated twice daily.

After removal of the sheath, subcutaneous low-molecular weight heparin therapy was given and overlapped with warfarin based on levels of Prothrombin Time/International Normalized Ratio (PT/INR) in all patients for 5 days to 1 week. During follow-up, all patients were required to receive long-term coumadin and lifelong aspirin (75 mg/day) therapy and Pentoxifylline (400 mg twice daily). Elastic bandage or thigh-high-graduated elastic compression stockings were applied for all patients, and ambulation was initiated as soon as possible.

Statistical Analysis

Continuous and categorical variables were analyzed by paired nonparametric Wilcoxon signed rank test. The chi-square test was used for comparisons of frequencies and categorical variables. Kaplan-Meier curves were obtained for time-to-patency analysis for intervention procedures. The predictive factors of vein patency were analyzed using univariate and multivariate Cox regression methods. A P value of <0.05 was considered significant. All statistical analyses were performed using statistical analysis software (SPSS 22).

Results

This study included 82 patients with obstructive iliofemoral DVT who had symptoms for >21 days. Endovascular interventions were performed between January 2009 and October 2014. The study population was comprised of 37 women and 45 men, and the mean age was 67.8 ± 18.7 years (20 to 90 years). The average duration of clinical follow-up was 39.1 ± 5.8 months. During the follow-up, 12 of 82 patients were excluded from this study. Among 12 patients, Nine patients were lost to follow-up 6 months after treatment was initiated, and three patients died because of unrelated cancer and pneumonia at 5, 8, and 9 months. Finally, total 70 patients were enrolled and followed over at least 3 years. The mean age was 64.9 ± 15.6 years (20 to 90 years). Initially, 36 subjects underwent stent placement, and another 34 participants received simple angioplasty. The baseline demographics and clinical characteristics of these patients are presented in Table 1. In the study, the median (IQR) ages for the stent and control groups were 69.5 (54.3 to 79.8) years and 64 (49.8 to 78) years, respectively, which were insignificantly different between the two groups (P=0.169). Of total 70 patients, 74.3% (52) had DVT for approximately two months, and 25.7% (18) experienced DVT for more than two months. In DVT duration subgroups, there're no significant difference between the two groups (P=0.169). The involved leg was predominant at the left leg, and it appeared to be statistically significant in both the groups (P=0.032).

Table 2: Anatomic distribution and venographic findings of obstructed venous segments.

Characteristics	Stent(n=36)	PTA (n=34)
IVC+CIV+EIV	3	2
IVC+CIV+EIV+CFV	2	0
CIV+EIV	6	11
EIV	14	16
CIV+EIV+CFV	4	3
EIV+CFV	7	2
CTV findings		
Narrowing or irregular wall	12	23
Occluded veins	24	11
May-Thurner syndrome	5	0

IVC: Inferior Vena Cava; CIV: Common Iliac Vein; EIV: External Iliac Vein; CFV: Common Femoral Vein
Venographic findings, narrowing (small calibre) or occlusion of the iliofemoroal vein was defined based on the initial venography.

Table 3: Venous outcomes function and safety associated with endovascular interventions at 24 months.

Outcomes	Stent(n=36)	PTA (n=34)	P value
Cumulative patency, n (%)			
24-month primary patency	27(75)	6(17.6)	<0.001
36-month	23(63.9)	6(17.6)	<0.001
24-month assisted patency	26(72.2)	10(29.4)	0.001
36-month assisted patency	26(72.2)	9(26.4)	<0.001
Venous function, n (%)			
Valvular incompetence at36 months, n (%)	21(58.3)	28(82.4)	0.028
36-month PTS, n (%)	18(50)	27(79.4)	0.01
36-month Villalta score, median (IQR), %	5.5(3.3 to 7.0)	7(5 to 8)	0.022
Wound healing at 36 months	3	0	
Adverse effects, n (%)			
Bleeding	10(27.8)	6(17.6)	0.313
Recurrent deep vein thrombosis	7(19.4)	18(52.9)	0.003
Pulmonary embolism	4(11.1)	6(17.7)	0.66

PTS: Post Thrombotic Syndrome; IQR: Interquartile Range

On the basis of initial venography or CTV, the anatomic distribution and venographic findings of obstructed veins was mentioned in Table 2. Venography or CTV before procedures revealed no statistical difference between Doppler US and CT instruments (McNemar Test, p=0.316; data not shown). Baseline CTV confirmed that all patient had obstructed veins including included left common iliac vein compression by the right common iliac artery and May-Thurner syndrome (n=5), occlusion of the iliofemoral segment from the neighboring inguinal area to bifurcation of inferior vena cava (n=35), IVC (n=3), and narrowing with irregular wall of iliofemoroal veins (n=35).

The survival analysis of the Kaplan–Meier curves and life table indicating significant difference of the 36-month cumulative primary patency and assisted patency in both groups are presented in Figure 1 (Figure 1A, Log Rank test; P<0.001; Figure 1B, Log Rank test; P<0.001). Venous outcomes and safety at 36 months after treatment were summarized in Table 3. The overall success rate of the endovascular technique was 88.9% (71 of 82 patients). The 36-month primary patency rate and 36-month assisted patency rate were 63.9% (23) and 72.2% (26), respectively, in the stent group and 17.6% (6) and 26.4% (9), respectively, in the control group (primary patency, P<0.001; assisted patency, P<0.001) (Table 3). Femoral valvular incompetence was observed in 72.2% and 82.4% of patients in the stent and control groups, respectively (P=0.313). The median (IQR) Villalta scores of patients in the stent and control groups (P=0.022) after 36 months were 5.5 (3.3 to 7.0) and 7.0 (5.0 to 8.0), respectively. PTS occurred in 66.7% and 79.4% of patients in the stent and control groups, respectively (P=0.231). Bleeding events during therapy were found in 27.8% and 17.6% of patients in the stent and control groups, respectively (P=0.313). At the 36-month follow-up, recurrent DVT was found in 19.4% and 52.9% of patients in the stent and control groups, respectively (P=0.003). There was no significant difference in the incidence of Pulmonary Embolism (PE) between the two groups. None of the patients died, but minimal complications, such as ecchymosis and hematoma at puncture sites, were noted. Three patients with active venous ulcers healed approximately 3 months after the procedure.

Using Cox regression analysis for the 36-month primary patency, we studied the potentially influencing factors including age, sex, Body Mass Index (BMI), Coronary Artery Disease (CAD), hyperlipidemia, diabetes mellitus, smoking, involved leg, recurrent DVT, duration of DVT, and treatment methods etc. (Table 4). The following three factors were significantly associated with outcomes of iliofemoral veins: body mass index (BMI) (HR=1.15, 95% CI: 1.02-1.3, P=0.023), duration

Table 4: Cox regression analysis of the assisted patency at 36 months.

Variable	Univariate	P Value	Multivariate	P Value
	Or *(95% CI†)		Or *(95% CI†)	
Age	0.99(0.97 to 1.01)	0.395		
Gender(F/M)	0.68(0.38 to 1.21)	0.19		
BMI	1.15(1.02 to 1.3)	0.023		
Duration of DVT				
≦ Two months / > two months	7.26(2.58 to 20.5)	<0.001	5.13(1.68 to 15.7)	0.004
Smoke (No/Yes)	0.68(0.35 to 1.32)	0.259		
Malignancy (No/Yes)	1.32(0.56 to 3.1)	0.532		
DM(No/Yes)	0.86(0.43 to 1.73)	0.664		
CAD(No/Yes)	1.06(0.42 to 2.67)	0.91		
Hyperlipidaemia (No/Yes)	0.75(0.29 to 1.9)	0.539		
Immobilization (No/Yes)	0.37(0.18 to 0.77)	0.008	0.49(0.21 to 1.1)	0.084
Recurrent DVT (No/Yes)	0.2(0.11 to 0.37)	<0.001	0.35(0.17 to 0.72)	0.004
Thrombophilia (No/Yes)	0.5(0.28 to 0.9)	0.021	0.59(0.3 to 1.15)	0.121
Involved leg (L/R)	0.71(0.4 to 1.27)	0.248		
Thrombosed CFV (No/Yes)	3.84(1.19 to 12.38)	0.024		
Treatment method (PCI/angioplasty)	0.39(0.22 to 0.7)	0.002	0.5(0.26 to 0.96)	0.036

*Or: Hazard ratio; †CI: Confidence Interval; BMI: Body Mass Index; DVT: Deep Vein Thrombosis; CFV: Common Femoral Vein
Venographic patterns, narrowing (small calibre) or occlusion of the iliofemoroal vein was defined based on the initial venography.
Treatment method, PCI (angioplasty plus stenting) and angioplasty Multivariable analysis, additionally adjusted for age, gender, and BMI.

of DVT (HR=7.26, 95% CI: 2.58 to 20.5, P<0.001), Immobilization (HR=0.37, 95% CI: 0.18 to 0.77, P=0.008), recurrent DVT (HR=0.2, 95% CI: 0.11 to 0.37, P<0.001), thrombophilia (HR=0.5, 95% CI: 0.28-0.9, P=0.021), and treatment method (HR=0.39, 95% CI: 0.22-0.7, P=0.002). Furthermore, these significant factors were incorporated, and analyzed in the multivariate Cox regression after adjusting age, BMI and sex using the stepwise regression method. Finally, three main factors were independently associated with the 36-month primary patency: duration of DVT (HR=5.13, 95% CI: 1.68 to 15.7, P=0.004), recurrent DVT (HR= 0.35, 95% CI: 0.17 to 0.72, P=0.004), and treatment method (HR=0.5, 95% CI: 0.26 to 0.96, P=0.036) (Table 4).

Discussion

This study assessed the efficacy and safety of endovascular treatment in patients with chronic and iliofemoral obstructive DVT. This study showed the 36-month primary patency was independently correlated with DVT duration, recurrent DVT and treatment method. The results of this study can provide physicians with evidence to manage obstructive iliofemoral DVT, and prevent intervention failure and preserve venous function early using stent placement. Patients with chronic obstructive iliofemoral DVTs have been traditionally treated with anticoagulants and conservative treatments such as application of thigh-high-graduated elastic compression stockings, use of intermittent compression devices, and long-term use of anticoagulants to prevent thrombus progression, recurrence and sequelae. Despite such managements, majority of patients experience intractable pain, swelling, and venous claudication, especially in the extensive iliofemoral venous thrombosis. Until the 1990s, endovascular re-canalization of obstructed iliofemoral venous lesions or establishments of surgical bypass (Palma bypass) were considered to reconstruct the antegrade flow via the iliac venous system and to improve patients' symptoms. Several papers on the crossover bypass technique claimed to achieve durable symptomatic relief [7,8], and the majority of studies lack reliable follow-up results. Since the introduction of endovascular techniques, this endovascular treatment provides a lot of the advantages including the small magnitude of intervention, minimal complications, reliable diagnostic venography, and effective management of thrombus burden and stenotic lesions. Besides of the technical success rate reaching 88% in this study, this endovascular procedure had certain technical limitations. For example, in patients with extensive thrombosis from the popliteal vein to iliofemoral veins and severe edema of the involved leg, venous puncture following by manipulation of wires passing through the thrombosed lesions may be difficult. Besides, chronic iliofemoral DVT of approximately two-month duration has usually a more insecure and unorganized thrombus, and consequently has potential thrombus embolization and recoil while angioplasty balloon working. Thus, for each patient treatment planning, vascular surgeons required maximum information concerning about the severity, extent, and cause of venous obstruction, as well as thrombus burden through MRI, CTV or venography examinations. With this information, it was possible to select patient candidates for endovascular intervention and determine the most suitable venous access route for the procedure.

Hence, all patients of our study were examined through CT plus venography before procedures. 35 developed vein obstruction; 28 patients were documented with vein obstruction by Doppler ultrasonography plus D-dimer testing. Therefore, Doppler ultrasonography is also sensitive (89% to 100%) and specific (94% to 99%) for symptomatic DVT of the proximal veins. Because of insignificant statistical difference between these two instruments (p=0.313), Doppler US can be conveniently used to accurately evaluate the thrombosed veins and vein patency and during follow-up [9-12]. 74.3% (52) of all patients had DVT of approximately two-month duration, and 25.7% (18) had DVT of more than two-month duration. Chronic iliofemoral DVT of duration of less than two months has usually a more unstable and unorganized thrombus, and thus develops potential thrombus embolization and recoil while manipulating, and poor prognosis. Our treatment strategies for these unsteady and unorganized DVT of approximately two month duration included thrombus removal with CDT, and sometimes pharmacomechanical thrombectomy plus IVC filter before percutaneous interventions. Subsequent balloon angioplasty and stent placement wan be performed safely and easily. Endovascular intervention was successfully performed in 71 patients with iliofemoral venous obstruction, and 70 patients had an at least 34-month follow-up. Approximately 34 of 70 patients with diseased iliofemoral veins underwent balloon angioplasty alone, and 36 patients underwent angioplasty plus stent implantation. The 36-month primary patency rate and 36-month assisted patency rate were 63.9% (23) and 72.2% (26), respectively, in the stent group and 17.6% (6) and 26.4% (9) for the control group (primary patency, P<0.001; assisted patency, P<0.001). These results are consistent with those of published series, which reported a 3-year primary patency rate and a secondary patency rate of 50% to 85% and 90% for stent placement, respectively [13-15]. Additionally, those patients with successful interventions receiving angioplasty plus stent placement showed significant improvements in swelling, venous claudication, and Villalta score (Table 3). Consequently, our results show that angioplasty plus stent implantation can be safely performed and can effectively relieve symptoms of obstruction. These results are compatible with those reported by Raju et al. [13]. And Hartung et al. [19] [13,16,17].

The predictive factors for vein patency were also evaluated in this study. Both univariate and multivariate Cox regression analyses were used to assess potential factors influencing venous outcomes. Interestingly, recurrent DVT, DVT duration and treatment methods were identified as principal predictive factors of the 36-month primary patency after adjustment for sex, age and BMI. In the subgroup analysis, approximately one-month DVT had much more insecure and unorganized thrombus, which needed more hard-working procedures for thrombus removal, and thus resulted in thrombus progression and poor prognosis.

There is one major concern regarding recurrent DVT and PE. Our findings demonstrated that there is a significant difference in the incidence of recurrent DVT and PE between the stent and control groups (recurrent DVT, 19.4% *vs.* 52.9%, P=0.003; PE, 11.1% *vs.* 17.7%, P=0.66) at the 36-month follow-up. However, the subgroup analysis showed that most of patients developed recurrent DVT was associated with risk factors related to lupus anticoagulant, protein C or S, malignancy and surgery. These results are compatible with those reports of published literature [3,14-16,19,20]. Additionally, these patients with recurrent DVTs routinely underwent CDT treatment or pharmacomechanical thrombolysis and subsequently simple angioplasty or angioplasty plus stent placement in this study. With respect to recurrent DVT induced by an Inferior Vena Cava (IVC) filter [13,14], the subgroup analysis of this study indicated no evidence of recurrent DVT was related to an IVC filter. Besides, a

retrievable IVC filter was not routinely used, and in only 8 patients. After approximately 3 to 6 months, majority of the patients underwent removal of these filters. Hence, a prospective study should be conducted with a larger population to study if the IVC filter is a factor of recurrent DVT, although stent implantation is used worldwide for peripheral arterial disease, the efficacy of stent implantation in venous obstruction remains unclear.

A recent study showed that the primary patency rate of Wallstent implantation for chronic iliofemoral venous obstruction was 87% at 72 months, which is greater than that of our 36-month result. However, that study enrolled patients with chronic DVT, of which 97% comprised the non thrombotic subset and 75% comprised the post thrombotic subset [21]. Conversely, 52 of 70 patients of our study had DVT with duration of approximately two- month, and a lot of thrombus presented unsteady and unorganized on manipulation. Our preliminary finding indicated DVT duration was a potential risk factor of primary patency at 36 months. Wallstent offers strength and flexibility but has a significant foreshortening. It makes precise placement difficult and requires overlapping of multiple stents to prevent incomplete treatment of obstructive lesions. The biggest drawback of Wallstent is that the tip is weak, which causes partial expansion or unexpected shortening or elongation during post-dilatation. Nitinol stents allow precise placement, but it has weak strength. Another short-term study for venous nitinol stent showed cumulative patency rates of 99%, 96%, and 92% at 3, 6 and 12 months, respectivel [21]. Post-thrombotic veins are often scarred and have firm intraluminal fibrotic bands. The iliac vein compression syndromes are caused by extrinsic compression of the artery and bone. Therefore, stents need a high resistive force. A covered stent might cause a contained leak, and a low-pressure venous system tends to thromboses [22]. The long-term outcome following repeat dilation of venous stents is currently unknown. A Larger-scale study with venous stents with a large size, high resistant force, precise placement, and good flexibility for chronic obstructive iliofemoral veins need to be designed.

This study had several limitations, including the small number of patients, its retrospective nature, and the relatively mid-term follow-up period. Therefore, future prospective control studies must be conducted with a large sample size. In conclusion, our mid-term results suggest that endovascular intervention with balloon dilation plus stent placement is a minimally invasive and effective treatment for chronic DVT with obstructive iliofemoral veins. Moreover, this study enables us to conclude that angioplasty plus stenting appears to have better treatment results than angioplasty alone and thus should be warranted for patients with subacute and chronic obstructive iliofemoral DVT. Hence, a larger and randomized trial must be conducted in the future.

References

1. Palma EC, Esperon R. Treatment of the post-thrombophlebitic syndrome by means of internal saphenous transplants. Bol Soc Cir Urug. 1959;30:115-25.
2. Gruss JD. Venous bypass for chronic venous insufficiency. In: Bergan JJ, Yao JST, editors. Venous disorders. Philadelphia: WB Saunders; 1991:316-30.
3. Halliday P, Harris J, May J. Femoro-femoral crossover grafts (Palma operation): along-term follow-up study. In: Bergan JJ, Yao JST, editors. Surgery of the veins. Orlando: Grune & Stratton; 1985:241-54.
4. Kyrle PA, Kammer M, Eischer L, Weltermann A, Minar E, Hirschl M, et al. The long-term recurrence risk of patients with unprovoked venous thromboembolism: an observational cohort study. J Thromb Haemost. 2016;14(12):2402-9.
5. Carrier M, Rodger MA, Wells PS, Righini M, Le Gal G. Residual vein obstruction to predict the risk of recurrent venous thromboembolism in patients with deep vein thrombosis: a systematic review and meta-analysis. J Thromb Haemost. 2011;9(6):1119-25.
6. Nagler M, Ten Cate H, Prins MH, Ten Cate-Hoek AJ. Risk factors for recurrence in deep vein thrombosis patients following a tailored anticoagulant treatment incorporating residual vein obstruction. Res Pract Thromb Haemost. 2018;2(2):299-309.
7. Halliday P, Harris J, May J. Femoro-femoral crossover grafts (Palma operation): along-term follow-up study. In: Bergan JJ, Yao JST, editors. Surgery of the veins. Orlando: Grune & Stratton; 1985:241-54.
8. Gruss JD. Venous bypass for chronic venous insufficiency. In: Bergan JJ, Yao JST, editors. Venous disorders. Philadelphia: WB Saunders; 1991:316-30.
9. Haenen JH, Wollersheim H, Janssen MC, Van't Hof MA, Steijlen PM, van Langen H, et al. Evolution of deep venous thrombosis: a 2-year follow-up using duplex ultrasound scan and strain-gauge plethysmography. J Vasc Surg. 2001;34(4):649-55.
10. Lee CY, Lai ST, Shih CC, Wu TC. Short-term results of catheter-directed intrathrombus thrombolysis versus anticoagulation in acute proximal deep vein thrombosis. J Chin Med Assoc. 2013;76(5):265-70.
11. González-Fajardo JA, Martin-Pedrosa M, Castrodeza J, Tamames S, Vaquero-Puerta C. Effect of the anticoagulant therapy in the incidence of post-thrombotic syndrome and recurrent thromboembolism: comparative study of enoxaparin versus coumarin. J Vasc Surg. 2008;48(4):953-59.
12. Hull RD, Liang J, Townshend G. Long-term low-molecular-weight heparin and the post-thrombotic syndrome: a systematic review. Am J Med. 2011;124(8):756-65.
13. Raju S, McAllister S, Neglen P. Recanalization of totally occluded iliac and adjacent venous segments. J Vasc Surg. 2002;36(5):903-11.
14. Nazarian GK, Bjarnson H, Dietz CA, Bernadas CA, Hunter DW. Iliofemoral venous stenoses: effictiveness of treatment with metallic endovascular stents. Radiology. 1996;200(1):193-9.
15. O'Sullivan GJ, Semba CP, Bittner CP. Endovascualr management of iliac vein compression (May- Thurner) synderome. J Vasc Interv Radiol. 2000;11(7):823-36.
16. Decousus H, Leizorovicz A, Parent F, Page Y, Tardy B, Girard P, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. N Engl J Med 1998;338(7):409-15.
17. Rosenthal D, Wellons ED, Lai KM, Bikk A, Henderson VJ. Retrievable inferior vena cava filters: initial clinical results. Ann Vasc Surg. 2006;20(1):157-65.
18. Kalva SP, Wicky S, Waltman AC, Athanasoulis CA. Trap Ease vena cava filter: experience in 751 patients. J Endovasc Ther. 2006;13(3):365-72.
19. Hartung O, Loundou AD, Barthelemy P, Arnoux D, Boufi M, Alimi YS. Endovascular management of chronic disabling ilio-caval obstructive lesions: long-term results. Eur J Vasc Endovasc Surg. 2009;38(1):118-24.
20. Galioto NJ, Danley DL, Van Maanen RJ. Recurrent venous thromboembolism. Am Fam Physician. 2011;83(3):293-300.
21. Gagne PJ, Taras Kucher NG, Thompson M, Stewart T, Bentley D. A 7-Year Single-Center Experience with the Wallstent as Treatment for Chronic Iliofemoral Venous Obstruction: Long-Term Clinical and Technical Outcomes. J Vasc Surg Venous Lymphat Disord. 2018;6(2):285-6.

22. de Wolf MA, de Graaf R, Kurstjens RL, Penninx S, Jalaie H, Wittens CH. Short-Term Clinical Experience with a Dedicated Venous Nitinol Stent: Initial Results with the Sinus-Venous Stent. Eur J Vasc Endovasc Surg. 2015;50(4):518-26.

23. Seshandri Raju, Razavi MK, Brooke Spencer, David M. Williams. Endovascular Today - Venous Stenting: Expectations and Reservations. Endovascular Today. 2013.