



Original Article

# Catheter-directed thrombolysis and pharmacomechanical thrombectomy improve midterm outcome in acute iliofemoral deep vein thrombosis

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## Abstract

**Background:** Aggressive and early thrombus removal strategy has been widely used as a treatment for iliofemoral deep vein thrombosis (DVT). We compared the long-term venous outcome, including postthrombotic syndrome (PTS), in patients undergoing catheter-directed thrombolysis (CDT) and pharmacomechanical thrombectomy (PMT).

**Methods:** From January 2009 to December 2013, 61 patients with acute proximal DVT were enrolled in this prospective study. Thirty-one patients underwent CDT and 30 patients underwent PMT, and each patient was followed for at least 2 years after treatment. Observations included venous outflow resistance, venous insufficiency, thrombus score (TS), severity of PTS, and surgical complications.

**Results:** Venous outflow obstruction was similar in the CDT and PMT groups (32.3% vs. 30.0%,  $p = 0.695$ ), and venous insufficiency of each group was 38.7% and 30.0% ( $p = 0.774$ ), respectively. The TS at 24 months of each group showed no significant difference (0.90 vs. 0.70,  $p = 0.526$ ). The mean Villalta scale scores of the CDT and PMT groups were 3.13 and 1.87, respectively ( $p = 0.042$ ). Patients without PTS had significantly lower TS since 1 week postoperatively (1.59 vs. 4.60,  $p < 0.001$ ). The severity of PTS was highly correlated with the TS, rate of thrombolysis, and severity of obstruction, and was moderately correlated with the venous registry index and reflux severity.

**Conclusion:** CDT and PMT have similar venous outcomes in patients with acute iliofemoral DVT, although PTS is less severe following PMT than after CDT. We propose that early and thorough removal of thrombus, using either CDT or PMT, is beneficial to prevent PTS.

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**Keywords:** catheter-directed thrombolysis; deep vein thrombosis; pharmacomechanical thrombectomy; postthrombotic syndrome

## 1. Introduction

The importance of deep vein thrombosis (DVT) cannot be overemphasized, not only because DVT can have lethal consequences such as pulmonary embolism, but also because of

the potential for chronic postthrombotic sequelae. The incidence of postthrombotic syndrome (PTS) ranged from 20% to 50%, and is most frequently associated with iliofemoral venous thrombosis.<sup>1,2</sup> The traditional treatment of anticoagulant alone does not promote thrombus dissolution, preserve valve function, or reduce PTS. There is increasing evidence that early removal of thrombus results in less venous obstruction, less venous insufficiency, and therefore, a lower rate of occurrence of PTS.<sup>3,4</sup> The Society for Vascular Surgery and the American Venous Forum have suggested a strategy of early removal of thrombus in selected patients meeting the following criteria: (1) first episode of acute iliofemoral deep

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venous thrombosis, (2) symptoms <14 days in duration, (3) low risk of bleeding, and (4) ambulatory with good functional capacity and an acceptable life expectancy (Grade 2C).<sup>5</sup> With emerging surgical techniques, catheter-directed thrombolysis (CDT) and pharmacomechanical thrombectomy (PMT) are becoming the treatments of choice. In this study, we compared the efficacy, long-term outcome, and complications of these two therapies.

## 2. Methods

### 2.1. Patients

From January 2009 to December 2013, 61 patients with acute iliofemoral DVT for  $\leq 21$  days were enrolled in this prospective study. Duplex sonography was used to diagnose DVT and to confirm the extent of the thrombus. Patient characteristics and clinical characteristics are shown in Table 1. Patients in whom anticoagulants are contraindicated, and those with thrombolysis, severe anemia (hemoglobin <8 g/dL), severe renal failure (creatinine clearance rate <30 mL/min), thrombocytopenia (platelet count <150,000/cumm), or bilateral DVT were excluded. After having received a detailed, nondirective explanation of each procedure, as well as the cost of

PMT, 31 patients underwent CDT and 30 patients underwent PMT, pursuant to each patient's decision. Then, each patient was followed up for at least 2 years after the procedure.

This study was approved by the Institutional Review Board at Taipei Veterans General Hospital, and all patients provided their written consent.

### 2.2. CDT and PMT techniques

Prior to either procedure, each patient routinely received low-molecular-weight heparin (LMWH) daily after admission, but did not receive LMWH on the day of the procedure. At the beginning of the procedure, an intravenous bolus of 3000–5000 U of unfractionated heparin (UFH) was administered to obtain an activated clotting time exceeding 200 seconds. Percutaneous access was either through the lesser saphenous vein or through the popliteal vein under ultrasound guidance. After puncture, a 5F or 6F introducer sheath was inserted via the Seldinger technique. Venography was performed to examine the extent of thrombus.

The CDT protocol of this study was modified from the catheter-directed venous thrombolysis in acute iliofemoral vein thrombosis trial (The CaVenT Study).<sup>4</sup> The guide wire passed through the thrombosed lesion under the aid of a supporting catheter, followed by a multiple-sidehole infusion catheter. The catheter was placed within the thrombosed vessel and was secured in place. The urokinase solution was infused continuously at a dose of 600–1200 U/kg/h over 48–72 hours. Patient serum fibrinogen, hemoglobin level, and platelet count were checked daily, and the urokinase dose was adjusted accordingly to avoid hemorrhagic complications. During the CDT therapy, UFH was infused simultaneously via the access sheath at the dose of 5–10 U/kg/h to prevent thrombus formation. The activated partial thromboplastin time (aPTT) was maintained between 1.5 and 2.0 times the control level.

In the PMT group, an inferior vena cava (IVC) filter was deployed prior to the procedure. PMT was performed using one of two methods. The first method involved the balloon crush technique, which used a balloon catheter obstructing the proximal end of the thrombosed lesion. Urokinase at a dose of 3000–5000 U/kg was infused from the sheath, and retained for several minutes. The balloon was then withdrawn while aspirating thrombus fragments from the sheath using a large syringe. This sequence was repeated two to three times. Finally, percutaneous angioplasty (PTA) was performed over the thrombosed lesion progressively as the “crush and lyse” technique. The second PMT technique, the AngioJet device (Possis Medical, Inc., Minneapolis, MN, USA), was adapted in our hospital for rheolytic thrombectomy. The angiojet catheter was inserted to the thrombosed lesion, and the operation continued with a solution of urokinase (2000–3000 U/kg per 500 mL saline).

Repeat venography was performed after either procedure, and a multiple-sidehole infusion catheter was left in place for CDT for 1 additional day.

In each procedure, PTA was performed over a site with significant stenosis. Stenting was adapted if there was residual

Table 1  
Demographic and clinical characteristics of the study patients.

Characteristic	CDT (n = 31)	PMT (n = 30)	p
Age (y), mean $\pm$ SD	64.48 $\pm$ 15.7	66.97 $\pm$ 18.9	0.354
Female sex, n (%)	14 (45.2)	12 (40)	0.684
BMI, mean $\pm$ SD	26.3 $\pm$ 2.2	26.1 $\pm$ 2.6	0.577
Left side DVT, n (%)	15 (48.4)	17 (56.7)	0.517
Duration of symptoms, n (%)			
$\leq 2$ wk	27 (87.1)	20 (66.7)	
$\sim 3$ wk	4 (12.9)	10 (33.3)	
Predisposing factors, n (%)			
Malignancy	2 (6.5)	7 (23.3)	0.063
Smoking	9 (29.0)	8 (26.7)	0.837
CVA	3 (9.7)	3 (10)	0.966
Immobilization	3 (9.7)	3 (10)	0.966
Hypertension	2 (6.5)	10 (33.3)	0.008
SLE	2 (6.5)	3 (10)	0.614
CAD	2 (6.5)	4 (13.3)	0.367
Dyslipidemia	1 (3.2)	3 (10)	0.285
Atrial fibrillation	4 (12.9)	2 (6.7)	0.414
Diabetes mellitus	5 (16.1)	1 (3.3)	0.093
Thrombophilia	5 (16.1)	8 (26.7)	0.315
Orthopedics surgery	7 (22.6)	6 (20)	0.757
Recent trauma	5 (16.1)	5 (16.7)	0.955
Oral contraceptive pill	8 (25.8)	6 (20)	0.590

Recent trauma was defined as trauma that occurred 14–30 days prior to the onset of DVT. Previous orthopedic surgery was defined as surgery experienced 30–90 days prior to the onset of DVT.

The scope for a classification of immobilization was 4–30 days prior to the onset of DVT. Thrombophilia was defined as documented biochemical hypercoagulable disorders, such as protein C or S deficiency and Factor V Leiden.

BMI = body mass index; CAD = coronary artery disease; CDT = catheter-directed thrombolysis; CVA = cerebral vascular accident; DVT = deep vein thrombosis; PMT = pharmacomechanical thrombectomy; SD = standard deviation; SLE = systemic lupus erythematosus.

stenosis of more than 70% despite repeat PTA (Table 2). Blood pressure, pulsation, and the puncture site were checked four times daily, and hemoglobin, fibrinogen levels, and platelet count were measured daily. aPTT was examined twice daily, and venography was performed via the sheath on the 2<sup>nd</sup> postoperative day and then every other day, or daily, as needed. After completion of CDT, systemic UFH was administered to maintain aPTT between 1.5 and 2.5 times control, overlapping enteral warfarin until the international normalized ratio reached 2–3.

### 2.3. Follow-up

The safety outcome was evaluated by the occurrence of bleeding and serious adverse events, including pulmonary embolism and death. Major bleeding was defined as obvious bleeding, including intracranial hemorrhage, gastrointestinal bleeding, and retroperitoneal hematoma, resulting in hemodynamic instability, blood transfusion >2 U, surgical intervention, or death. All other bleeding events were considered minor episodes.

The efficacy outcome included early and immediate ilio-femoral venous patency, valvular competence, recanalization of the occluded vein, evolution of thrombus burden, and the occurrence of PTS. Different modalities adapted for evaluation were as follows. (1) Venous outflow (VO) resistance was assessed using air plethysmography to evaluate venous obstruction. The outflow fraction at 1 second (OF1) was the amount of venous volume emptied in 1 second divided by the total venous volume. An OF1 >38% was considered to represent absence of functional obstruction, 30–38% represented moderate obstruction, and <30% represented severe obstruction. We used an OF1 of <38% as the presence of VO obstruction. (2) Venous insufficiency was evaluated with Doppler ultrasound. A valvular reflux >0.5 second was set to designate valve incompetence, and the severity was directly proportional to reflux time. (3) Color Doppler ultrasound was performed by vascular specialist physicians and experienced technicians. The evolution of DVT was analyzed according to

the thrombus score (TS) classification modified by Porter and Moneta<sup>6</sup> and Haenen et al,<sup>7</sup> and the thrombolysis rate was calculated by the TS. Vein segments were classified using the standard definition (external iliac, common femoral, proximal and distal femoral, popliteal, and great saphenous veins), and scores for the degree of venous obstruction were determined as follows: 0 = open vein free of thrombus; 1 = partially occluded vein with a flow Doppler signal; 2 = completely occluded vein with no flow signal. TS was calculated by summing the TS of six venous segments. (4) Twenty-four months after each procedure, PTS was assessed using the Villalta scale, which included five symptoms (pain, cramps, heaviness, pruritus, and paresthesia) and six signs (pretibial edema, skin induration, hyperpigmentation, venous ectasia, redness, and compression pain). A total score of 5–9 was considered mild PTS, 10–14 was moderate PTS, and >15 was severe PTS. In our statistical analysis, we used a total score >10 to indicate presence of PTS. (5) The venous registry index (VRI) was used to classify the degree of thrombolysis prior to and within 48 hours after each procedure using venography. Complete thrombolysis (grade III) was when clot lysis of 90–100% was achieved, partial thrombolysis (grade II) was when clot lysis of 50–90% was achieved, and minimal or no thrombolysis (grade I) was when clot lysis of < 50% was achieved.

### 2.4. Statistical analysis

The differences of continuous variables were compared by Mann–Whitney *U* test, and the differences of categorical variables were compared by Chi-square test between two groups. Additionally, the Kruskal–Wallis test was used to test the Villalta score between different severity categories in venous obstruction and valvular incompetence. The Spearman's rank correlation coefficient was applied to depict the correlation between Villalta score and the TS. A *p* value <0.05 was considered statistically significant.

## 3. Results

Thirty-one patients underwent CDT, and 30 patients underwent PMT with subsequent CDT. Among patients receiving PMT, eight received the balloon crush technique and 22 received AngioJet. No major complication or major bleeding event was noted in either group. The total urokinase dosage was significantly lower in the PMT group (1,797,300 U vs. 2,763,500 U, *p* = 0.001). A greater number of patients in the PMT group had gross hemoglobinuria (*p* = 0.048), but there was no significant difference in the number of patients receiving blood transfusion (Table 2).

VO outflow obstruction was found in 10 patients in the CDT group (32.3%) and in nine patients in the PMT group (30%) (*p* = 0.849). Valvular incompetence was found in 12 patients in the CDT group (38.7%) and in nine patients in the PMT group (30%) (*p* = 0.474). The venous outcome is shown in Table 3. The VRI was not significantly different in the two groups. The PMT group had a greater initial thrombus burden

Table 2  
Intervention characteristics and adverse effects.

	CDT ( <i>n</i> = 31)	PMT ( <i>n</i> = 30)	<i>p</i>
UK dose (×10,000 IU), mean ± SD	276.35 ± 67.8	179.73 ± 23.1	<0.001
IVC filter, <i>n</i> (%)	0 (0)	30 (100)	<0.001
PTA, <i>n</i> (%)	18 (58.0)	30 (100)	<0.001
+ stent, <i>n</i> (%)	2 (6.5)	7 (23.3)	
Hospital stay (d), mean ± SD	10.9 ± 7.5	9.9 ± 5.0	0.579
Adverse effects, <i>n</i> (%)	7 (22.6)	14 (46.7)	0.048
Gross hemoglobinuria	1 (3.2)	13 (43.3)	
Micro hemoglobinuria	2 (6.5)	0 (0)	
Ecchymosis	2 (6.5)	0 (0)	
Mucosal bleeding	2 (6.5)	1 (3.3)	
Blood transfusion	9 (29.0)	11 (36.7)	0.704
pRBC	3 (9.7)	5 (16.7)	

IVC = inferior vena cava; PTA = percutaneous transluminal angioplasty; pRBC = packed red blood cells; SD = standard deviation; UK = urokinase.

Table 3  
Venous outcomes and presence of postthrombotic syndrome (PTS) at 24 months after treatment.

	CDT (n = 31)	PMT (n = 30)	p
Venous registry index (VRI), n (%)			0.150
VRI < 50%	6 (19.4)	3 (10)	
90% > VRI ≥ 50%	10 (32.3)	14 (46.7)	
VRI ≥ 90%	15 (48.4)	13 (43.3)	
Functional venous obstruction, n (%)	10 (32.3)	9 (30)	0.849
Valvular incompetence, n (%)	12 (38.7)	9 (30)	0.474
Villalta score, mean ± SD	3.13 ± 3.0	1.87 ± 2.7	0.042
Postthrombotic syndrome, n (%)	6 (19.4)	6 (20)	1.000
Thrombus score, mean ± SD			
Preoperative	8.45 ± 1.4	9.27 ± 1.5	0.033
1 wk	2.19 ± 2.3	2.23 ± 1.9	0.876
1 mo	1.77 ± 2.1	1.37 ± 1.8	0.463
3 mo	1.19 ± 1.7	0.87 ± 1.5	0.468
6 mo	1.03 ± 1.6	0.73 ± 1.2	0.561
12 mo	1.10 ± 1.8	0.83 ± 1.4	0.646
24 mo	0.90 ± 1.3	0.70 ± 1.3	0.526
Thrombolysis rate, mean% ± SD			
1 wk	-75.6 ± 25.5	-76.96 ± 18.3	0.911
1 mo	-79.9 ± 24.5	-86.70 ± 17.4	0.383
3 mo	-86.35 ± 19.9	-91.48 ± 13.8	0.371
6 mo	-88.03 ± 18.7	-92.91 ± 11.6	0.436
12 mo	-87.14 ± 21.4	-91.56 ± 14.4	0.586
24 mo	-89.46 ± 15.9	-93.25 ± 11.7	0.378

Functional venous obstruction definition: venous outflow fraction at 1 second <38%.

CDT = catheter-directed thrombolysis; PMT = pharmacomechanical thrombectomy; SD = standard deviation.

compared with the CDT group assessed by TS (9.27 vs. 8.45,  $p = 0.033$ ). During follow-up at 1 week, 1 month, 3 months, 6 months, 12 months, and 24 months, the TS of each group showed no significant difference (Fig. 1). In each group, six patients developed PTS 24 months after the procedure ( $p = 1.000$ ), but the mean Villalta scale of the CDT group was higher than that in the PMT group (3.13 vs. 1.87,  $p = 0.042$ ).

All the patients who developed PTS had significantly venous obstruction, compared to only 14.3% in PTS-free

patients. Higher VRI within 48 hours after the procedure ( $p < 0.0001$ ) and lower thrombolysis rate 1 week after the procedure were observed in patients with PTS (Table 4, Fig. 2). However, no statistical difference was seen in valvular incompetence ( $p = 0.309$ ).

The severity of PTS, using the Villalta scale, was highly correlated with postoperative TS and severity of venous obstruction, and was moderately correlated with severity of valvular incompetence (Figs. 3 and 4). The postoperative TS also strongly correlated with severity of venous obstruction.

Table 4  
Venous outcome in patients with/without postthrombotic syndrome (PTS) at 24 months after treatment.

	No PTS (n = 49)	PTS (n = 12)	p
Procedure, n (%)			1.000
CDT	25 (51.0%)	6 (50)	
PMT	24 (49.0%)	6 (50)	
Venous registry index (VRI), n (%)			<0.0001
VRI < 50%	2 (4.7)	7 (58.3)	
90% > VRI ≥ 50%	22 (44.9)	5 (41.7)	
VRI ≥ 90%	25 (51.0)	0 (0)	
Functional venous obstruction, n (%)	7 (14.3)	12 (100)	<0.0001
Valvular incompetence, n (%)	15 (30.6)	6 (50)	0.309
Thrombus score, mean ± SD			
Preoperative	8.6 ± 1.4	10.1 ± 1.6	0.032
1 wk	1.6 ± 1.8	4.6 ± 1.2	<0.0001
1 mo	0.9 ± 1.5	3.9 ± 1.2	<0.0001
3 mo	0.4 ± 1.0	3.3 ± 1.0	<0.0001
6 mo	0.3 ± 0.7	3.0 ± 1.1	<0.0001
12 mo	0.3 ± 0.7	3.2 ± 1.3	<0.0001
24 mo	0.3 ± 0.7	2.8 ± 1.1	<0.0001
Thrombolysis rate, mean% ± SD			
1 wk	82.5 ± 19.2	50.9 ± 13.6	<0.0001
1 mo	89.7 ± 16.9	56.1 ± 16.2	<0.0001
3 mo	95.2 ± 11.0	63.1 ± 13.7	<0.0001
6 mo	96.5 ± 8.2	65.7 ± 14.5	<0.0001
12 mo	96.4 ± 8.6	60.5 ± 19.5	<0.0001
24 mo	96.7 ± 7.9	69.6 ± 12.1	<0.0001

CDT = catheter-directed thrombolysis; PMT = pharmacomechanical thrombectomy; VRI = venous registry index.

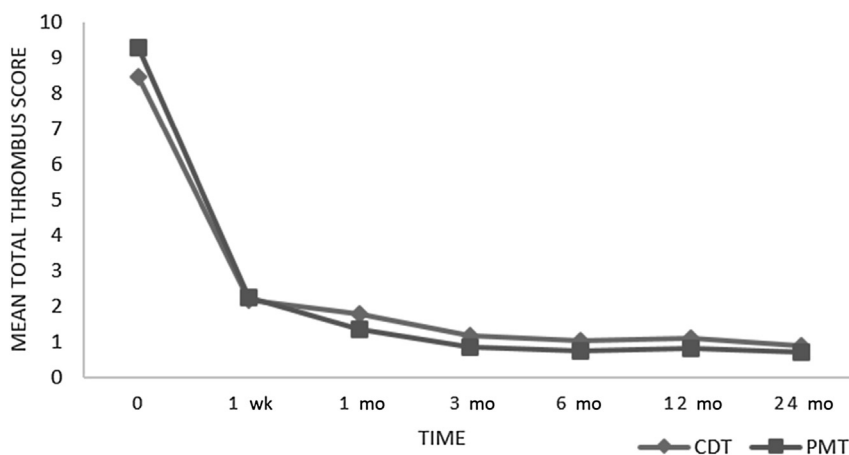


Fig. 1. Recanalization of thrombosed veins of patients in both the CDT and the PMT groups according to the mean total thrombus score. CDT = catheter-directed thrombolysis; PMT = pharmacomechanical thrombectomy.



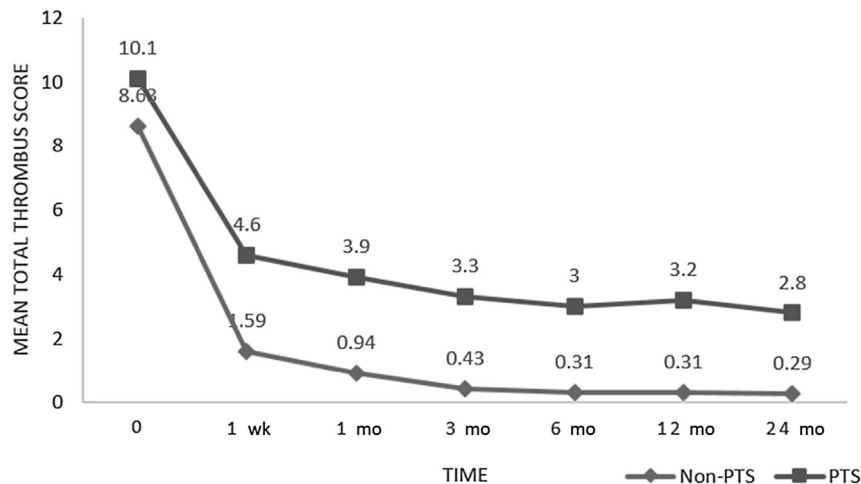


Fig. 2. Recanalization of thrombosed veins of patients in both the non-PTS and the PTS groups according to the mean total thrombus score. PTS = postthrombotic syndrome.

#### 4. Discussion

PTS is the consequence of venous valvular incompetence, VO obstruction, and calf muscle pump dysfunction following an acute episode of DVT.<sup>8</sup> PTS refers to symptoms of chronic lower extremity pain, edema, hyperpigmentation, and stasis ulceration, and is the most devastating sequela of DVT influencing quality of life. The efficacy of DVT treatment was evaluated not only by the acute phase, but also by the occurrence of PTS. Resolution of symptoms depends on the recovery of venous obstruction and the development of collateral bypass veins. Although collateral veins were often observed in those patients undergoing LMWH treatment, the rationale of early thrombus removal is that it restores venous patency, reduces venous hypertension, and furthermore prevents not only proximal but also distal venous insufficiency.

Although the American College of Chest Physicians still regards anticoagulants as the first-line therapy in acute proximal DVT, in selected patients—those with iliofemoral DVT, symptoms for <14 days, good functional status, life expectancy of >1 year, and low risk of bleeding—CDT could be chosen over anticoagulant alone.<sup>9</sup> The Egypt trial and CaVenT trial both showed better venous patency and less PTS in the CDT group compared with traditional anticoagulant treatment.<sup>3,4</sup> The efficacy of CDT has been proven, although PMT also emerges as a potentially faster, less invasive, and safe alternative.<sup>10–12</sup>

In our study, both treatment groups were similar with regard to VO obstruction, valvular incompetence, and the occurrence of PTS, showing similar efficacy in preservation of venous function. Most retrospective studies demonstrated that PMT was associated with shorter treatment time, lower urokinase dose, and shorter hospital stay, but with no difference in thrombus clearance.<sup>11–15</sup> Using Clinical, Etiologic, Anatomic, and Pathologic (CEAP) classification and Villalta scores, Hager et al<sup>10</sup> also found similar results in both groups. The clinical benefit of reduction of absolute thrombus burden using PMT needs further investigation. Lin et al<sup>13</sup> showed that 81%

of patients undergoing PMT exhibited immediate clinical improvement within 24 hours, as did 72% of the patients undergoing CDT (the difference was not statistically significant). We repeated venography within 48 hours after each procedure and used VRI to quantify thrombolysis rate, which showed no significant difference between the two groups. The TS during follow-up differed between the CDT and the PMT groups, although it did not reach statistical significance. However, after a 2-year follow-up, we used a total Villalta score for comparison, and the severity of PTS was lower in the PMT group. This may imply the advantage of PMT in midterm results, and we are looking forward to its long-term result.

When we pooled results from all patients and compared factors associated with PTS, the TS after 3 months and the severity of obstruction were highly correlated with the Villalta score, the severity of valvular incompetence and the VRI were moderately correlated with the Villalta score. The post-operative TS was also highly correlated with VO resistance but poorly correlated with valvular incompetence. All patients with PTS ( $n = 12$ ) had venous obstruction, but only half of them had valvular incompetence. We supposed that valvular incompetence is mainly the consequence of VO obstruction, an associated comorbidity, rather than the most attributing cause of PTS. In the study by Comerota et al,<sup>16</sup> with a minimum follow-up of 2 years, CEAP and Villalta scores had a direct and significant correlation with the extent of residual thrombus. It seems reasonable that more complete removal of thrombus is associated with decreased severity of venous obstruction, and consequently reduced PTS.

Interestingly, the TS had continuously decreased after the initial treatment in the study. It reached a nadir at 3 months and subsequently remained stable. In the clinical and echogenic findings, the lower the TS, the more complete is the recovery of the involved venous wall. In those patients with remarkable reduction of TS, valve function may be better preserved at the follow-up. However, this definitive mechanism of related inflammation change and wall remodeling needs further investigation. As a result, the reduction of TS

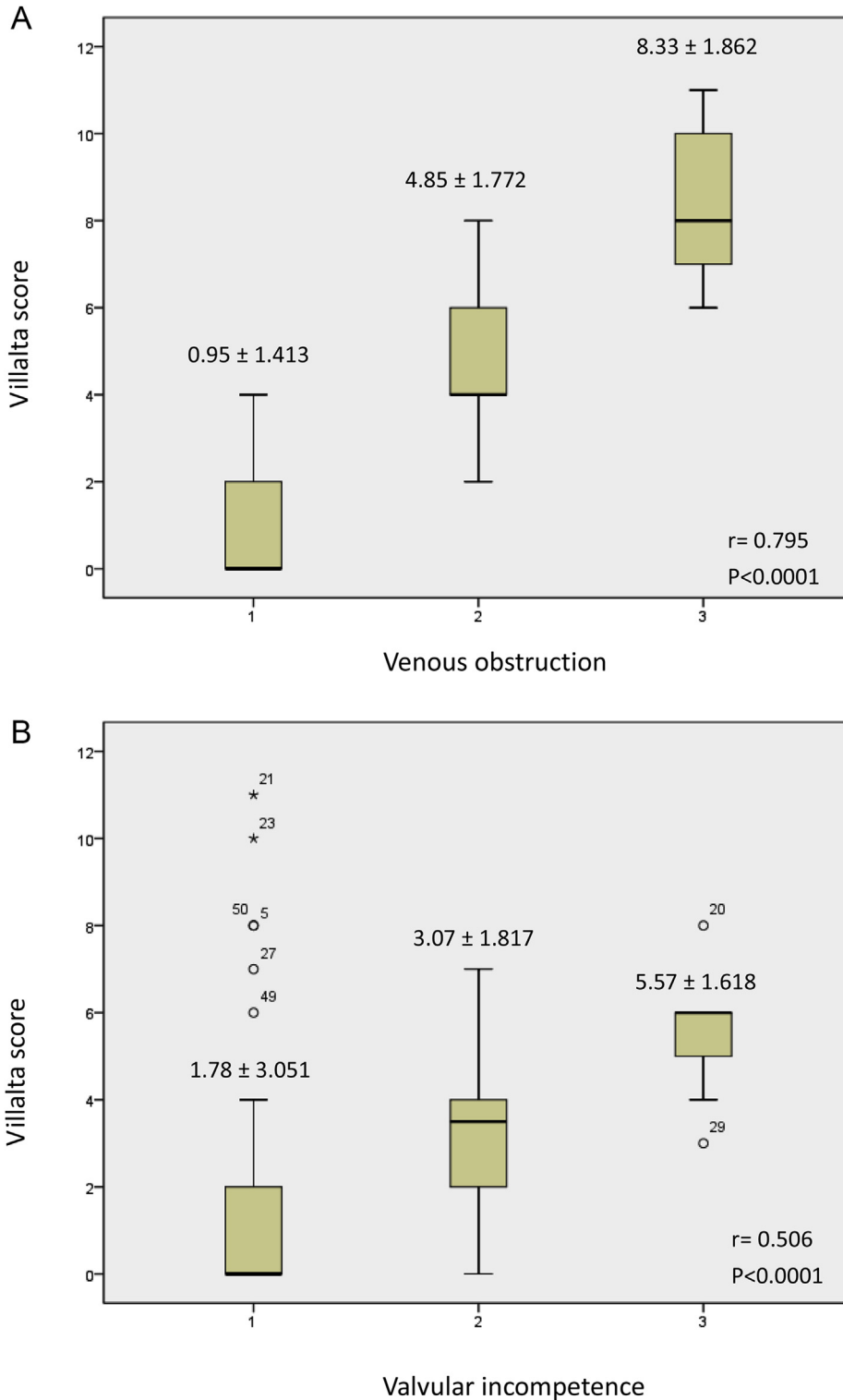


Fig. 3. Correlation between Villalta score at 24 months with (A) venous obstruction (1 = mild; 2 = moderate; 3 = severe) and (B) valvular incompetence (1 = mild; 2 = moderate; 3 = severe). Kruskal–Wallis test was applied to measure *p* value. Spearman's rank correlation coefficient was applied to measure the correlation (*r*).

can probably be attributed to an intrinsic thrombolytic effect with the assistance of anticoagulation. The mean thrombolysis rate at 1 week was 76%, including 23 patients who had complete thrombolysis (TS 0). Other patients with partial thrombolysis had an additional 10% thrombolysis noted at

follow-up at 1 month and 3 months. This thrombolysis rate resembled that of our (previous) 2009 study, which compared traditional anticoagulation therapy and CDT.<sup>17</sup> In the previous study, a gradual reduction of TS was also noted in the anti-coagulation group. In spite of slow thrombus regression,

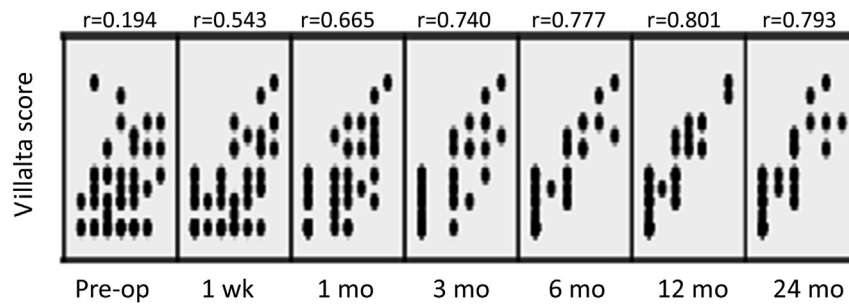


Fig. 4. Correlation between Villalta score at 24 months and thrombus score at different periods. Spearman's rank correlation coefficient was applied to measure the correlation ( $r$ ).

anticoagulant treatment may potentially induce endogenous thrombolysis. However, without an initial aggressive thrombus removal strategy to reduce the absolute thrombus burden, the venous outcome was inferior to that of the CDT group. Furthermore, in this study, no patient with complete thrombolysis (VRI >90%) within 48 hours after treatment developed PTS, nor did any patient without venous obstruction (VOI >38%). The definite thrombus removal at early stage and the amount of residual thrombus are an important prognostic factor in developing PTS. We believe that a thorough, early intervention to remove thrombus, either CDT or PMT, was beneficial to prevent PTS.

One major concern regarding these thrombolysis and thrombectomy techniques is their potential complications. Our previous study comparing anticoagulants and CDT showed no significant difference regarding bleeding events.<sup>17</sup> As patient experience with urokinase increased, we followed the patients' hemoglobin, platelet, and fibrinogen closely, and set a strict safety end point for each treatment course. The dose of urokinase would also be adjusted according to the patients' age, underlying disease, and clinical status. However, although PMT required a significantly lower dose of urokinase than did CDT, this treatment can be associated with additional embolic and hemolytic complications. Pulmonary embolism is rarely reported in the literature describing PMT, but no studies recommend against the use of IVC filter simultaneously with PMT.<sup>11,18</sup> One of our PMT techniques is balloon crush technique, which causes fragmentation of the thrombus. Therefore, we routinely deployed an IVC filter prior to starting PMT to prevent centrally drifting emboli, and used urokinase as a pulse-spray solution to reduce embolic particle size. Additional study is necessary to establish whether deployment of an IVC filter is beneficial in patients undergoing PMT. As for hemolytic complications, half of the patients in our study experienced hemoglobinuria after PMT. Nevertheless, hemoglobinuria after PMT rarely causes severe anemia or renal dysfunction if the medical team is aware of this complication, and implements early management when appropriate.

Several limitations were noted in this study. The first limitation of this study is its nonrandomized nature, in spite of prospectively recording patient's clinical data. The second limitation is the heterogeneity of treatment among patients receiving PMT. Also, the follow-up venography was performed on the 2<sup>nd</sup> postoperative day, but the exact timing was diverse.

The third limitation is that under the National Health Insurance of Taiwan, there were various factors other than medical issues lengthening the duration of hospital stay. We could not use hospital stay or cost-effectiveness analysis as one treatment outcome. Further randomized studies and a more precise follow-up schedule should be conducted to compare the effects of PMT and CDT on safety and efficacy outcome.

In conclusion, in patients with acute iliofemoral DVT, both CDT and PMT have similar venous outcomes except that PMT has the advantage of greater reduction in the severity of PTS when compared with CDT. The amount of residual thrombus correlated with the severity of VO obstruction and PTS. We conclude that an early and thorough removal of thrombus, using either CDT or PMT, is beneficial to prevent PTS.

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