Percutaneous mechanical thrombectomy in the treatment of acute iliofemoral deep vein thrombosis: a systematic review

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ABSTRACT

Background: Conventional treatment of deep vein thrombosis (DVT) of the lower extremities by anticoagulation alone has been proven to be insufficient to prevent recurrence and post-thrombotic syndrome (PTS). Early restoration of venous patency and preservation of valvular function by endovascular surgery has been advocated. The aim of this study was to review the efficacy and safety of percutaneous mechanical thrombectomy (PMT) against catheter-directed thrombolysis (CDT) in the treatment of acute iliofemoral DVT.

Methods: Three hundred sixty-nine articles were identified through screening of the PubMed, EMBASE, and Cochrane databases from January 2006 to December 2016.

Results: Fifteen retrospective studies and one prospective registry, totalling 1170 patients, were recruited for qualitative synthesis. The venous patency rate ranged from 75% to 100% with mean follow-up of 12.3 months. The rates of PTS and recurrent DVT were less than 17% and 15%, respectively. The overall mortality rate was 0.26%.

Compared with CDT, PMT was shown to reduce PTS at 1 year (Villalta score: 2.1 ± 3.0 in the PMT group and 5.1 ± 4.1 in the CDT group, P=0.03) and bleeding complications (packed cells transfused: 0.2 ± 0.3 units in the pharmacomechanical thrombectomy group and 1.2 ± 0.7 units in the CDT group, P<0.05).

Conclusion: Percutaneous mechanical thrombectomy is a safe and effective treatment for acute iliofemoral DVT in terms of restoration of venous patency, prevention of DVT recurrence, and PTS. Compared with CDT alone, PMT offers a lower risk of PTS and bleeding complications.

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Introduction

Deep vein thrombosis (DVT) is a major cause of morbidity and mortality, as it can lead to post-thrombotic syndrome (PTS) and pulmonary embolism. According to the American College of Chest Physicians treatment guidelines, DVT has conventionally been treated with low-molecular-weight heparin, unfractionated heparin, or fondaparinux followed by vitamin K antagonists for at least 3 months.[1] This recommended regimen is adequate for prevention of thrombus extension, but its effect on clot lysis is minimal. The reported 6-month venous patency rate in patients treated with anticoagulation alone was only 47.4%. Eventually, up to 55.6% of patients with iliofemoral DVT developed PTS as a result of valvular dysfunction.[2] Up to 5% to 10% of patients had severe PTS in the form of venous ulceration, which caused significant morbidity and socio-economic cost.[3]

In view of the suboptimal treatment outcomes of anticoagulation, aggressive means have been developed to achieve early restoration of venous patency and thus preservation of valvular function. A Cochrane review suggested that early thrombus removal by means of systemic thrombolysis can prevent venous dysfunction and PTS. However, its use was limited by its significantly increased risk of bleeding.[4]

Endovascular modalities including catheter-directed thrombolysis (CDT) and percutaneous mechanical thrombectomy (PMT) were developed to achieve accelerated thrombolysis with less bleeding risk. Catheter-directed thrombolysis was shown to be superior to anticoagulation alone in terms of higher thrombolysis rate and lower rates of recurrence and PTS.[2] It features loco-regional delivery of thrombolytic agent over the DVT site via a transluminal catheter. The dosage of the thrombolytic agent can be reduced compared with that of systemic thrombolysis, and thus, a reduction in bleeding complications can be achieved. Its benefits have been validated by a number of randomised controlled trials and meta-analyses, but its application rate remains low because of its substantial bleeding risk and cost.[5]

Percutaneous mechanical thrombectomy is another form of endovascular treatment, in which thrombectomy devices are passed to the site of DVT and blood clots are removed by different mechanical means. It can also be used as an adjunctive device to CDT or pharmacomechanical thrombectomy. When these two devices are used in combination, the dosage of thrombolytic agents can be lowered further and the duration of procedure can be shortened.[6] According to the American College of Chest Physicians guidelines, PMT provides the greatest benefits for young and functionally active patients with acute presentation (<14 days, or presence of phlegmasia cerulea dolens) of extensive proximal DVT.[1] Percutaneous mechanical thrombectomy has provided promising results in various studies, while high-level evidence to guide its implementation is still lacking. Against this background, this article aimed to review the evidence about PMT regarding its procedural outcomes and safety profile in the treatment of DVT.

Methods

Literature search

A systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis) statement (http://www.prisma-statement.org/). An electronic search was performed using the PubMed, EMBASE, and Cochrane Databases from January 2006 to December 2016. The medical subject heading (MeSH) terms used were "mechanical thrombectomy" and "venous thrombosis" or "deep vein thrombosis".

Study selection

The inclusion criteria were as follows: DVT of the lower extremities; human study; study population aged ≥18 years; and articles published in English. Reviews and case reports were excluded. All studies of interest were obtained as full-text articles and assessed by two authors independently. Final decisions on inclusion in the study were made by the entire research team.

Data extraction and outcome measurement

Relevant data were extracted with the following items recorded: author, title, year of publication, number and age of patients, co-morbidities, duration of follow-up, onset of symptoms, location of DVT, type of thrombectomy device, and adjunctive modalities. Efficacy was measured in terms of rates of venous patency, recurrence, and PTS. Complications including bleeding, pulmonary embolism, and mortality were recorded. Secondary outcomes included dosage of thrombolytic agents, cost, and duration of procedure.

經皮機械血栓切除術治療急性髂股深靜脈血栓：系統綜述

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背景：單獨使用抗凝治療下肢深靜脈血栓（DVT）已被證實不足以預防復發和血栓後綜合徵（PTS），故提倡以血管內手術及早恢復靜脈通暢和保持瓣膜功能。本研究旨在回顧經皮機械血栓切除術（PMT）對比導管溶栓（CDT）於治療急性髂股深靜脈血栓的療效和安全性。

方法：2006年1月至2016年12月期間於PubMed、EMBASE和Cochrane數據庫篩選369篇文獻。

結果：選定15項回溯性研究和一項前瞻性登記研究項目，合共1170名患者進行定量研究分析。靜脈通暢率界乎75%至100%，平均隨訪期為12.3個月。血栓後綜合徵和深靜脈血栓復發率分別低於17%和15%。整體死亡率為0.26%。與導管溶栓相比，經皮機械血栓切除術後1年內較少出現血栓後綜合徵（Villalta量表評分：5.1±4.1比2.1±3.0，P=0.03）和出血併發症（輸血需求：藥物機械血栓切除術0.2±0.3單位比導管溶栓1.2±0.7單位，P<0.05）。

結論：經皮機械血栓切除術治療急性髂股深靜脈血栓是安全有效的治療，可恢復靜脈通暢、預防深靜脈血栓復發和血栓後綜合徵。與單獨使用導管溶栓相比，經皮機械血栓切除術可降低血栓後綜合徵和出血併發症的風險。

Data analysis

Statistical meta-analysis was not performed because of the heterogeneity of the original data. Therefore, descriptive data were summarised and presented in tables to provide a comprehensive overview of different clinical aspects of the studies.

Results

Our initial search yielded a total of 369 articles, including 260 articles from PubMed, 98 articles from EMBASE, and 11 studies from the Cochrane Library. Thirty-one duplicated records and 283 irrelevant studies were excluded upon screening of titles and abstracts, leaving 55 potentially eligible studies. A further 39 articles were excluded after full-text articles were assessed: 28 review articles; one study on the patients with inferior vena cava (IVC) filter; one study on the effect of clot age; seven studies without full text; and two non-English studies. Fifteen retrospective studies and one prospective registry were included into our analysis, in which seven articles reported comparative evidence of PMT versus CDT. There were no published randomised trials available.

Baseline patient demographics and characteristics of the studies are summarised in Table 1.[6-21] A total of 1170 patients were included (range, 16-329 patients) with a mean age of 53.5 years (range, 16 to 88 years). The mean follow-up time was 12.3 months (range, 1-82 months).

TABLE 1. Patient demographics and study characteristics[6-21]

First author, year	No. of patients	Age (years)*	Follow-up period (mo)*	Time since onset (days)*	Location of DVT
Garcia, 2015[6]	RT = 13 PCDT = 115 PCDT+CDT = 172 RT+CDT = 29 (n=329)	52.2 ± 16	12	≤14, 67% 15-30, 19% >30, 14%	Iliac, 66% Femoral, 89% Popliteal, 59%
Huang, 2015[7]	PMT = 16 CDT = 18 (n=34)	PMT = 62.7 ± 10.1 CDT = 62.1 ± 15	12	-	-
Arko, 2007[8]	30	50.9 ± 18	6.2 (3-24)	5.7 (3-14)	Iliofemoral = 14 Iliofemoropopliteal = 6 Femoropopliteal = 5 Subclavian = 5
Lin, 2006[9]	PMT = 52 CDT = 46	PMT = 45 ± 12 CDT = 49 ± 10	13 (1-49)	PMT = 15 (0-34) CDT = 13 (0-31)	-
Kim, 2006[10]	PMT+CDT = 19 CDT = 26	PMT+CDT = 53 ± 20.7 CDT = 42.9 ± 13.2	32.1 ± 38.7	≤14	-
Kim, 2006[11]	PMT+CDT = 27 CDT = 40	PMT+CDT = 43.1 ± 13.8 CDT = 45 ± 16.3	-	-	-
Ozpak, 2016[12]	21	48.7 ± 10.7 (27-69)	6	≤14	Iliofemoral, 71.4% Popliteal, 28.6% Femoral, 38.1%
Jia, 2016[13]	68	61.7 ± 7.8	21.9 ± 6.3	≤14	Popliteal-iliofemoral = 29 Iliofemoral = 31 Iliac = 8
Gagne, 2015[14]	139 (151 Limbs)	59.7 (16-88)	12	8.5 ± 10.8	Iliofemoral, 45% Iliofemoropopliteal, 29.8% Femoral, 2.7% Femoropopliteal, 7.9% Iliac, 6.6% IVC/iliac, 6.6%
Lee, 2013[15]	AT+CDT = 71 CDT = 29 (n=100)	60.5 ± 14.6	12 (1-82)	-	-
Karahan, 2016[16]	67	42.5 ± 21.3	-	-	Iliofemoral
Bozkurt, 2015[17]	16	58.5 (21-79)	6	≤14	Femoropopliteal = 5 Iliofemoral = 9 Iliac = 1 IVC = 1

Park, 2014[18]	MT = 23
	MT+CDT = 30
	CDT = 45
	(n=90, 98 limbs)
		58 ± 16	16 (0-78)	7 (3-13)	Iliac:
					  CDT, 80%
					  MT+CDT, 83%
					  MT, 83%
					Femoral:
					  CDT, 96%
					  MT+CDT, 97%
					  MT, 96%
					Popliteal:
					  CDT, 69%
					  MT+CDT, 80%
					  MT, 78%
					Calf:
					  CDT, 56%
					  MT+CDT, 67%
					  MT, 63%

Shi, 2011[19]	25	54.2 ± 15.7	12.3 ± 2.5	6.3 ± 2.5	IVC = 5 Iliofemoral = 16 Femoropopliteal = 9
Shi, 2009[20]	16	53.3 ± 15.6	13 (6-35)	4.9 (1-15)	Iliofemoropopliteal = 14 Iliofemoropopliteal+IVC = 2
Lee, 2006[21]	25	56 (28-64)	16 (12-33)	7 (3-13)	Extensive iliofemoral

Abbreviations: AT = aspiration thrombectomy; CDT = catheter-directed thrombolysis; DVT = deep vein thrombosis; IVC = inferior vena cava; MT = mechanical thrombectomy; MTS = May-Thurner syndrome; PCDT = pharmacomechanical catheter-directed thrombolysis; PMT = percutaneous mechanical thrombectomy; PTA = percutaneous transluminal angioplasty; RT = rheolytic thrombectomy; rtPA = recombinant tissue plasminogen activator; SD = standard deviation
* Data are shown as mean ± SD and/or range, unless otherwise specified

Type of device	Thrombolysis	IVC filter	Angioplasty ± stenting (indication)
AngioJet	CDT, 61%	-	PTA, 74% Stenting, 35%
AngioJet	Urokinase	-	PTA (stenosis <70%); wall stent (stenosis recoiled)
Trellis = 18 AngioJet = 12	Tenecteplase for partial thrombus removal	Temporary, 21/25	PTA+stenting = 17 PTA = 11
AngioJet	Urokinase, reteplase, rtPA	Temporary = 28 Permanent = 15	PMT, 82% CDT, 78%
AngioJet	Urokinase	-	PMT+CDT, 15.8% CDT, 23.1%
AngioJet	Urokinase	-	PMT+CDT, 15% CDT, 18%
Aspirex	-	All	1 PTA (femoral vein stenosis) 2 PTA+stenting (iliac vein stenosis, MTS)
Aspiration	21/68	All	Luminexx nitinol stent, 47% (MTS/malignancy)
Trellis	CDT, 30.1% AngioJet, 5.3% EKOS, 6.8%	Temporary = 29 Permanent = 57	PTA, 74% Stenting, 54%
Aspiration	Urokinase	46%	32% (MTS/>50% residual thrombus)
Cleaner	Reteplase	-	-
Cleaner	Alteplase	All except 1 with IVC chronic obstruction	PTA = 12 Wall stent = 9
Trerotola	Urokinase	Temporary = 68 Permanent = 25	Wall stent, 65% (MTS)
Amplatz	-	All	PTA, 13/25 Stenting, 11/25 (MTS)
Amplatz = 10 Rotarex = 6	Urokinase	All	PTA = 3 Stenting = 1 (MTS)
Trerotola, Aspiration	Urokinase	5/25 (Contra-indicated to CDT)	80%

Four different categories of thrombectomy devices were used among the included studies: rheolytic devices,[6-11] aspiration devices,[12-16] rotational devices,[16-21] and ultrasound-enhanced thrombolysis devices.[14] They aimed to achieve transcatheter removal of thrombi via different mechanical means.

The AngioJet system (Possis Medical, Minneapolis [MN], US) is a rheolytic device that generates high-velocity saline jets at the side of catheter, which create a localised low-pressure zone and thus result in maceration and aspiration of the thrombus.

During aspiration thrombectomy, the thrombus was aspirated out through the percutaneous catheter as the catheter was gradually pulled out. The process was repeated until complete removal of the thrombus or at least 90% disappearance of thrombi. Two of the aspiration systems were Aspirex (Straub Medical, Wangs, Switzerland) and the Trellis infusion system (Covidien, Mansfield [MA], US), which is a sophisticated system that contains an oscillation drive unit that mixes the thrombus with thrombolytic agents between two occlusion balloons.

Rotational devices feature high-frequency revolution of a helix that is controlled by a foot pedal. At least four different types of rotational devices were included, including the Amplatz thrombectomy device (Microvena, White Bear Lake [MN], US), Rotarex (Straub Medical, Wangs, Switzerland), Trerotola (Arrow International, Redding [PA], US), and Cleaner (Rex Medical, Fort Worth [TX], US and Argon Medical Devices, Inc, Plano [TX], US). They all consisted of a motor-driven fragmentation helix or basket that was rotated in the thrombosed vein. The thrombus was then aspirated out via the catheter.

An ultrasound-enhanced thrombolysis device (EKOS Corporation, Bothell [WA], US) was selectively used in one study[14] for patients with inadequate thrombus removal despite the use of a rotational device. A high-frequency ultrasound wave was emitted through transducers inside the catheter to achieve maceration of the thrombus and mix it with thrombolytic agents.

Efficacy

Nine non-comparative and seven comparative studies were included in our analysis. Efficacy in terms of rates of venous patency, PTS, and recurrent thrombosis is shown in Table 2.[6-21] Venous patency was measured most frequently by Duplex ultrasound (n=9) followed by computed tomographic (CT) venography (n=4) and contrast venography (n=2). Imaging modalities were not mentioned in three studies. Venous patency was further quantified according to a 3-tier system in five studies: Grade I (<50% clot lysis), Grade II (50%-99% clot lysis), and Grade III (100% clot lysis).[22] Venous patency was measured at 6 months in four studies and at 1 year in the other 12 studies. Venous patency rates ranged from 75% to 100%.

Rates of PTS were reported in terms of Villalta score (n=2)[23] or Venous Clinical Severity Score (VCSS) [n=2].[14] Four studies reported the rates of valvular incompetence from 8% to 24%. The rates of DVT recurrence, reported in eight studies, ranged from 0% to 17%.

Complications

The major complications of thrombectomy are shown in Table 3.[6-21] Six studies reported rates of pulmonary embolism ranging from 0.3% to 17%, but none of them was clinically significant. No patient had pulmonary embolism in the remaining 11 studies. Garcia et al[6] reported major bleeding complications in 3.6% of patients, including intracranial bleeding, gastrointestinal bleeding secondary to gastritis or gastric cancer, retroperitoneal bleeding, and haemolytic anaemia requiring transfusion. Minor bleeding complications were reported at frequencies of up to 28%, most of which were access site bleeding. Blood transfusion and surgical intervention were seldom required. No operative mortality was reported in 12 studies, while only two cases of fatal intracranial haemorrhage were noted in two separate studies. Another mortality was reported by Garcia et al,[6] with an unknown cause of death. The overall mortality in this series was 0.26%.

Secondary outcomes

Seven studies reported comparative evidence about PMT versus CDT (Table 4[6,9,10,11,15,18]). Huang et al[7] showed that PMT significantly reduced PTS at 1 year, with lower Villalta scores in the PMT group (2.1±3.0) than in the CDT group (5.1±4.1; Wilcoxon rank-sum test, P=0.03). However, no statistical difference was shown in Villalta scores in another retrospective study conducted by Park et al.[18]

Lin et al[9] compared bleeding complications between the two groups in terms of the number of units of packed red blood cells transfused. There was a significant reduction of blood transfusion from 1.2±0.7 units in the CDT group to 0.2±0.3 units in the PMT group (Pearson Chi squared, P≤0.05).[9]

The dosage of thrombolytic infusion and average procedural time were significantly reduced in the CDT with adjunctive PMT group compared with the CDT alone group, as reported in at least four different retrospective studies.[10,11,15,18]

From the economic perspective, two retrospective studies performed cost analysis, and PMT was found to be associated with 44% to 49% reduction in total hospital costs.[9,10] It was also consistent with shorter hospital and intensive care unit (ICU) stays in the PMT group (4.6±1.3 days

TABLE 2. Efficacy of percutaneous mechanical thrombectomy[6-21]

First author, year	Patency rate	Post-thrombotic syndrome	DVT recurrence

Garcia, 2015[6]	1 Year by venography
	Grade III:
	  RT, 69.2%
	  PCDT, 58.3%
	  PCDT+CDT, 62.1%
	  RT+CDT, 57.3%
	Grade II:
	  RT, 30.8%
	  PCDT, 36.5%
	  PCDT+CDT, 31%
	  RT+CDT, 69.8%
	Grade I:
	  RT, 0%
	  PCDT, 5.2%
	  PCDT+CDT, 6.9%
	  RT+CDT, 2.9%
		NR	17%

Huang, 2015[7]	1 Year by Duplex
	PMT, 93.8%
	CDT, 88.9%
		Villalta scores (P=0.03)
		  PMT, 2.06 ± 2.95
		  CDT, 5.06 ± 4.07
			NR

Arko, 2007[8]	6.2 Months by Duplex, 90%	Valvular incompetence, 12%	NR
Lin, 2006[9]	1 Year by venography PMT, 68% CDT, 64%	NR	6.5%

Kim, 2006[10]	Grade III:
	  PMT+CDT, 84.2%
	  CDT, 80.7%
	Grade II:
	  PMT+CDT, 15.8%
	  CDT, 11.5%
	Grade I:
	  PMT+CDT, 0%
	  CDT, 7.7%
		NR	PMT+CDT, 15.4%
			CDT, 25%

Kim, 2006[11]	Grade III:
	  PMT+CDT, 82%
	  CDT, 73%
	Grade II:
	  PMT+CDT, 19%
	  CDT, 15%
	Grade I:
	  PMT+CDT, 0%
	  CDT, 13%
		NR	NR

Ozpak, 2016[12]	6 Months by Duplex, 85%	VCSS at 6 months
		  Oedema, 50%
		  Skin pigmentation, 3%
		  Pain, 3%
		  Varicose veins, 3%
		Valvular incompetence, 24%
			NR

Jia, 2016[13]	1 Year, 96.9%	Villalta scores: <5, 88%; 5-9, 5.9%	10.9%

Gagne, 2015[14]	Duplex or CT venography, 94%	VCSS at 1 year
		  Oedema, 14%
		  Skin changes, 6%
		  Pain, 4%
		  Varicose veins, 2%
			NR

Lee, 2013[15]	1 Year by Duplex or CT venography AT+CDT, 90.4% CDT, 75.9%	AT+CDT, 17.24% CDT, 12.68%	AT+CDT, 15.5% CDT, 24%
Karahan, 2016[16]	6 Months by Duplex, 100%	Valvular incompetence, 12%	0
Bozkurt, 2015[17]	6 Months by Duplex, 75%	NR	7.1%, due to irregular anticoagulant drug use
Park, 2014[18]	1 Year by CT venography MT, 78% MT+CDT, 80% CDT, 71%	No difference between MT/CDT	NR
Shi, 2011[19]	1 Year by Duplex Grade III, 96% Grade II, 4%	4%	NR
Shi, 2009[20]	13 Months by Duplex Grade III, 50% Grade II, 25%	6.2%	0.97%
Lee, 2006[21]	1 Year by CT venography, 85%	Valvular incompetence, 8%	NR

Abbreviations: AT = aspiration thrombectomy; CDT = catheter-directed thrombolysis; CT = computed tomography; DVT = deep vein thrombosis; MT = mechanical thrombectomy; NR = not reported; PCDT = pharmacomechanical catheter-directed thrombolysis; PMT = percutaneous mechanical thrombectomy; RT = rheolytic thrombectomy; VCSS = Venous Clinical Severity Score

TABLE 3. Complications of percutaneous mechanical thrombectomy[6-21]

First author, year	Pulmonary embolism	Bleeding	Mortality
Garcia, 2015[6]	0.3%	Major, 3.6% (ICH, GIB secondary to gastritis or gastric cancer, retroperitoneal bleeding, haemolytic anaemia and unspecified bleeding requiring transfusion); minor, 0.9%	0.3% (Unknown cause)
Huang, 2015[7]	No	1 Minor epistaxis in CDT	No
Arko, 2007[8]	17% (5/30) on CT (asymptomatic; all without IVC filter)	No	No
Lin, 2006[9]	No	PMT, 4%, 0.2 ± 0.3 unit transfusion CDT, 6%, 1.2 ± 0.7 unit transfusion P<0.05	No
Kim, 2006[10]	PMT, 5.3%; CDT, 3.8%	PMT, 5.3% (1 intra-abdominal haematoma required transfusion) CDT, 7.7% (1 popliteal haematoma required surgical decompression)	No
Kim, 2006[11]	PMT, 4%; CDT, 3%	PMT, 4%; CDT, 5%	No
Ozpak, 2016[12]	NR	NR	NR
Jia, 2016[13]	No	No	No
Gagne, 2015[14]	No	No	No
Lee, 2013[15]	CDT+AT, 6/37 CDT, 0/9	3 Haematoma in CDT	No
Karahan, 2016[16]	No	No	No
Bozkurt, 2015[17]	No	Minor subcutaneous bleeding at access site, 28.6% (4/14)	Unrelated to thromboemboli, 1/14
Park, 2014[18]	2.2%	Major MT = 0 MT+CDT = 1 GIB CDT = 1 ICH Minor MT = 2 MT+CDT = 3 CDT = 6	2.2% in CDT
Shi, 2011[19]	No	Minor bleeding at access site, 8% (2/25)	No
Shi, 2009[20]	No	1 Massive GIB Subcutaneous bleeding, 18.8% (3/16)	0.97% (1/103 ICH)
Lee, 2006[21]	No	No	No

Abbreviations: AT = aspiration thrombectomy; CDT = catheter-directed thrombolysis; CT = computed tomography; GIB = gastrointestinal bleeding; ICH = intracranial bleeding; IVC = inferior vena cava; MT = mechanical thrombectomy; NR = not reported; PMT = percutaneous mechanical thrombectomy

of hospital stay and 0.6±0.3 days of ICU stay in the PMT group vs 8.4±2.3 days of hospital stay and 2.4±1.2 days of ICU stay in the CDT group; Pearson Chi squared, P<0.02 to 0.04).

No statistically significant differences in venous patency or symptom improvement between the two groups were reported in this series of comparative studies.

Comparison between types of thrombectomy devices

Three studies compared outcomes of different thrombectomy devices. Garcia et al[6] created the first prospective multi-centre (PEARL) registry to document the use of the AngioJet rheolytic device. A total of 329 patients were stratified into four treatment subgroups: (1) rheolytic thrombectomy (RT) alone; (2) RT plus CDT; (3) pharmacomechanical CDT (PCDT), and (4) PCDT combined with CDT. Each of these subgroups differed in terms of the presence, timing, and delivery means of thrombolytic agents. Rheolytic thrombectomy was given before or after CDT in subgroup 2, and PCDT was defined as delivery of lytic agent through an AngioJet catheter. This registry demonstrated no statistical difference in venous patency rate between the subgroups, while a significant reduction in procedural time in non-CDT group was observed (Table 4). The investigators concluded that RT was effective and safe, and therefore, the needs for concomitant CDT and intensive care could potentially be reduced.

Shi et al[20] and Arko et al[8] compared the outcomes of Amplatz versus Rotarex and Trellis versus AngioJet devices, which again showed no significant differences in clinical outcomes between the two groups.

TABLE 4. Secondary outcomes of percutaneous mechanical thrombectomy* [6,9-11,15,18]

First author, year	Subgroup	Procedural time (hours)	Dosage of thrombolytic (million units)	Hospital stay (days)	Cost (US$)
Garcia, 2015[6]	RT PCDT PCDT+CDT RT+CDT	1.4 2 22 41 P<0.0001			
Lin, 2006[9]	PMT			Overall hospital stay: 4.6 ± 1.3 ICU stay: 0.6 ± 0.3	Total hospital cost: $47 742 ± 19 247 Hospital room cost: $18 392 ± 8321
	CDT			Overall hospital stay: 8.4 ± 2.3 ICU stay: 2.4 ± 1.2 P <0.02 to 0.04	Total hospital cost: $85 301 ± 24 832 Hospital room cost: $53 632 ± 1743 P <0.01 to 0.02
Kim, 2006[10]	PMT+CDT CDT	30.3 ± 17.8 56.5 ± 27.4 P=0.001	2.95 ± 1.82 6.70 ± 5.9 P=0.011		$5128 ± 2744 $10 127 ± 8836 P=0.026
Kim, 2006[11]	PMT+CDT CDT	26.3 ± 16.6 48.0 ± 27.1 P=0.0004	2.7 ± 1.8 5.6 ± 5.6 P=0.008		
Lee, 2013[15]	AT+CDT CDT	22.0 ± 7.1 40.9 ± 15.6 P<0.001	1.61 ± 0.44 22.01 ± 7.10 P<0.001		
Park, 2014[18]	MT MT+CDT CDT	2.7 ± 2/1 18.2 ± 8.2 29.3 ± 9.4 P<0.001	0 5.13 ± 3.72 7.51 ± 4.54 P<0.001		

Abbreviations: AT = aspiration thrombectomy; CDT = catheter-directed thrombolysis; ICU = intensive care unit; MT = mechanical thrombectomy; PCDT = pharmacomechanical catheter-directed thrombolysis; PMT = percutaneous mechanical thrombectomy; RT = rheolytic thrombectomy

* Data are shown as mean ± standard deviation, unless otherwise specified

Use of adjunctive treatments

Inferior vena cava filter placement, angioplasty, and stenting were the most commonly performed adjunctive treatments in addition to thrombectomy. Inferior vena cava filters were used in 46% to 100% of patients among 11 studies. The majority of the filters were removed shortly after the procedure without major complications. Lee et al[15] reported that 6 of 37 patients had thrombus entrapment in prophylactic IVC filters in the thrombectomy group compared with 0 of 9 patients in the CDT alone group. Arko et al[8] reported that 17% of patients showed asymptomatic pulmonary embolism on CT after thrombectomy, in which all patients did not receive IVC filters. This showed that prophylactic IVC filtration could be a useful measure for prevention of pulmonary embolism, especially in patients who undergo aggressive thrombectomy.

Angioplasty with or without stenting was performed in 15 studies, ranging from 14% to 80% of patients. The two main indications were iliac vein compression syndrome (May-Thurner syndrome) and residual thrombus after thrombectomy. One study reported a significantly improved iliac vein patency rate in the group with stents (28.95%) than without stents (11.29%; log rank test, P=0.026).[15]

Discussion

Catheter-directed thrombolysis and PMT are both emerging techniques for treatment of acute DVT of the lower extremities that have the advantage of early restoration of venous patency and thus reduction of post-thrombotic complications. A 2015 meta-analysis compared the efficacy of CDT plus anticoagulation versus that of anticoagulation alone in the treatment of proximal DVT. It showed that additional CDT was associated with significantly improved 6-month venous patency and PTS rates. However, there was a two-fold increase in bleeding complications in the CDT group, and concomitant close monitoring under intensive care setting has had a substantial economic burden.[5] These two main reasons have precluded the incorporation of CDT into the standard treatment recommendation despite encouraging procedural outcomes.

As compared with CDT, PMT is another

endovascular option that has provided promising clinical outcomes with better controlled bleeding risk. This review has served as a comprehensive overview of clinical and safety outcomes across different categories of thrombectomy devices. It demonstrated well that the procedural outcomes of both PMT alone and that with pharmacomechanical devices were non-inferior to that of CDT in treatment of acute DVT in the lower extremities. The rates of PTS, bleeding complications, and hospital costs of PMT were all shown to be favourable to those of CDT alone. In addition, the mortality risk of PMT was minimal and comparable to that of patients treated with anticoagulation alone: 0.4% recurrent fatal venous thromboembolism and 0.2% fatal major bleeding events.[24] As illustrated in this review, the balanced risks and benefits of PMT provide a basis for the future initiation of randomised controlled trials on its use.

In addition, PMT is potentially superior to CDT especially in patients in whom thrombolysis therapy is contra-indicated. According to the Society of Interventional Radiology recommendations, CDT is absolutely contra-indicated in patients with recent cerebrovascular events, neurosurgery or intracranial trauma, active internal bleeding, and those with absolute contra-indications to anticoagulation. Other strong relative contra-indications are listed in the Standard of Practice[25]: recent major surgery, obstetrical delivery or major trauma within 10 days, etc. These patients are prone to the development of DVT, and they have been conventionally treated with anticoagulation or IVC filters. Percutaneous mechanical thrombectomy is another option in this clinically challenging situation. Further studies on this particular group of high-risk patients are necessary to investigate the efficacy and safety of this novel technique.

Nevertheless, this review has several limitations. The studies were heterogeneous in terms of outcome measurements and the use of thrombectomy devices. Post-thrombotic syndrome was measured in terms of Villalta score, VCSS, or valvular incompetence rate. Although these systems were well-defined objective scales for monitoring and documentation of PTS, it was difficult to compare efficacy across studies. Similarly, the important index of venous patency rate was variously measured by Duplex ultrasound, CT venogram, or venography. Inaccuracies during direct comparison between studies were unavoidable.

Other adjunctive modalities in addition to the principal thrombectomy devices including iliac vein angioplasty, stenting, and prophylactic IVC filter were used in a major proportion of the studies. No standardised criteria were outlined for the usage of these devices, and they created a confounding factor during data analysis. With inadequate information on sub-categorisation of the study populations, analysis specific to each type of adjunctive devices was not feasible. Most of the studies were retrospective, and no randomised trials were available for quantitative analysis.

Conclusion

Percutaneous mechanical thrombectomy is a safe and effective treatment for acute iliofemoral DVT in terms of restoration of venous patency, prevention of DVT recurrence, PTS, and pulmonary embolism. The overall clinical outcomes of PMT are superior to those with anticoagulation alone. Compared with CDT alone, adjunctive PMT has a lower risk of PTS and bleeding complications. Randomised studies to demonstrate the efficacy of PMT versus anticoagulation and CDT and compare the efficacy of different types of PMT devices would be most beneficial to guide future strategies for treatment of acute proximal DVT.

Author contributions

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Concept or design: All authors.
Acquisition of data: All authors.
Analysis or interpretation of data: PC Wong, YC Chan, Y Law.
Drafting of the manuscript: PC Wong, YC Chan, Y Law.
Critical revision: All authors.

Conflicts of interest

The authors declare no conflicts of interest.

Declaration

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