NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg

A blood clot (thrombus) in a vein is usually treated with anticoagulant drugs, which stop further clotting but do not dissolve the clot. Clots can be dissolved using clot-busting drugs but these can cause serious bleeding. In this procedure, a clot in the leg is broken up and sucked out using a mechanical device introduced through a tube inserted into the vein. The aim is to prevent long-term problems such as swelling of the leg and ulceration.

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Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in July 2018.

Procedure name

- Percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg

Specialist societies

- British Society of Interventional Radiology
- Vascular Society of Great Britain and Ireland
- Royal College of Radiologists.

Description of the procedure

Indications and current treatment

Deep vein thrombosis (DVT) occurs most commonly in the deep veins of the legs. Signs and symptoms include pain, swelling, tenderness and colour change, but some DVTs cause no symptoms. Risk factors for DVT include surgery, immobility (caused by acute illness such as stroke), malignancy, acquired or inherited hypercoagulable states, pregnancy and dehydration.

DVT is associated with the risk of potentially life‑threatening pulmonary embolism and in the longer term with post‑thrombotic syndrome in the affected leg as a result of chronic venous insufficiency, which causes pain, swelling, and sometimes chronic ulceration. Massive oedema of the leg with cyanosis, blistering and ischaemia due to raised venous pressure (phlegmasia cerulean dolens) can occur rarely.

A DVT is normally treated with unfractionated or low molecular weight heparin, followed by oral anticoagulants (typically warfarin). The newer factor X inhibitors may be used without preliminary heparin. Extensive DVT is sometimes treated by systemic thrombolysis or by endovascular interventions such as catheter‑directed thrombolysis and percutaneous mechanical thrombectomy. Thrombolysis is associated with a risk of haemorrhagic complications including stroke. Surgical thrombectomy is an option in patients with DVT that is refractory to thrombolytic therapy, or for whom thrombolysis is contraindicated, but it is rarely used.

What the procedure involves

Percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg is usually done in conjunction with direct infusion of a thrombolytic drug into the thrombus but may also be used as a standalone therapy, if thrombolytic drugs are contraindicated. It can also be used following thrombolysis if residual thrombus persists.

Before the procedure, imaging is reviewed to determine appropriate access, usually the popliteal or femoral vein. Under local anaesthetic venous access is established and a catheter is advanced into the thrombus using fluoroscopic guidance. There are a range of mechanical thrombectomy devices which use different principles. The objective is mechanical disruption and aspiration of the thrombus. A temporary inferior vena cava filter may be used during the procedure to reduce the risk of pulmonary embolism from displaced clot.

Following the procedure treatment with anticoagulant drugs is usually given to prevent recurrence. Early ambulation and use of compression stockings is advised.

Adjuvant angioplasty or stenting of the vein may be needed if thrombus removal unmasks an anatomical lesion that contributed to the formation of the DVT.

Outcome measures

Villalta scale

The Villalta scale is used to diagnose and classify the severity of post-thrombotic syndrome. Points are given for 5 symptoms (pain, cramps, heaviness, paresthesia, pruritus) and 6 clinical signs (pretibial oedema, skin induration, hyperpigmentation, redness, venous ectasia, pain on calf compression), according to severity, ranging from 0 for not present to 3 for severe. Points are summed into a total score (range 0 to 33). Post-thrombotic syndrome is defined by a total score of 5 or above, or the presence of a venous ulcer. It is classified as mild if the score is 5 to 9, moderate if the score is 10 to 14, and severe if the score is 15 or above or a venous ulcer is present.

Efficacy summary

Post-thrombotic syndrome

In a randomised controlled trial (RCT) of 692 patients who had pharmacomechanical thrombolysis (PMT) plus anticoagulation, or anticoagulation alone, the proportion of patients with post-thrombotic syndrome between 6 and 24 months after treatment was similar in the 2 groups (47% [157/336] of patients compared with 48% [171/355], risk ratio [RR] 0.96, 95% confidence interval [CI] 0.82 to 1.11, p=0.56).[1] The proportion of patients with moderate to severe post-thrombotic syndrome was lower in the PMT group compared with the control group (18% [60/336] compared with 24% [84/355], RR 0.73, 95% CI 0.54 to 0.98, p=0.04). In an RCT of 183 patients who had percutaneous endovenous intervention (PEVI) plus anticoagulation or anticoagulation alone, 4.5% (4/88) of patients who had PEVI and 18.5% (15/81) of patients in the control group had mild post-thrombotic syndrome at 30-month follow-up (p=0.007). For moderate and severe post-thrombotic syndrome, the proportions were 1.1% (1/88) compared with 7.4% (6/81; p=0.06), and 1.1% (1/88) compared with 3.7% (3/81; p=0.35) respectively. The proportion of patients with any post-thrombotic syndrome was statistically significantly lower in the PEVI group than the control group (6.8% compared with 29.6%, p<0.001).[2]

Recurrent venous thromboembolism

In the RCT of 692 patients, recurrent venous thromboembolism was reported in the first 10 days for 2% (6/336) of patients who had PMT and 1% (4/355) of patients in the control group (RR 1.53, 95% CI 0.44 to 5.28, p=0.50). The total recurrence rate over 24 months was 12% (42/336) in the PMT group and 8% (30/355) in the control group (RR 1.47, 95% CI 0.94 to 2.29, p=0.09).[1] In the RCT of 183 patients, 4.5% (4/88) of patients who had PEVI had a venous thromboembolism after discharge compared with 16.0% (13/81) of patients in the control group (p=0.02) at 30-month follow-up.[2] In a registry of 329 patients, the proportion who had no rethrombosis was 94%, 87% and 83% at 3, 6 and 12-month follow-up respectively. Reintervention for recurrent thrombosis of the treated vessel was needed in 9% (30/329) of patients.[4]

Symptom scores

In the RCT of 692 patients, the Villalta score was statistically significantly lower in the PMT group compared with the control group at all follow-up periods. At 24-month follow-up the mean score was 3.43 in the PMT group and 4.50 in the control group (p=0.005). The venous clinical severity score was also lower in the PMT group at all follow-up periods; at 24 month follow-up, the mean score was 1.87 in the PMT group and 2.42 in the control group (p=0.03).[1]

Quality of life

In the RCT of 692 patients, the quality of life scores improved by a similar amount in the 2 groups from baseline to 24-month follow-up. There were no statistically significant differences between the groups.[1] In the registry of 329 patients, quality of life scores were statistically significantly better at 12-month follow-up compared with baseline. The mean Short Form 12 physical component score improved from 34.0 to 44.0, and the mean mental component score improved from 44.4 to 49.4 for patients with acute DVT ($p<0.0001$ for both).[4]

Pain

In the RCT of 692 patients leg-pain severity, measured on a 7-point Likert scale, improved by 1.62 points in patients who had PMT and 1.29 points in the control group ($p=0.02$) at day 10. At day 30 the improvement was 2.17 points in the PMT group and 1.83 in the control group ($p=0.03$).[1]

Patency

In a registry of 2,024 patients (2,203 limbs) grade II patency (50 to 94% thrombus removal) or grade III patency (>95% thrombus removal) was achieved in 97% of limbs with acute deep vein thrombosis (DVT).[3] In the registry of 329 patients, grade II clot removal (50 to 99% reduction) or grade III (100% reduction) was achieved in 41% and 56% of patients with acute DVT respectively.

Safety summary

Bleeding complications

Major bleeding within the first 10 days was reported in 1.7% (6/336) of patients who had PMT and 0.3% (1/355) of patients in the control group (risk ratio [RR] 6.18, 95% confidence interval [CI] 0.78 to 49.2, $p=0.049$) in a randomised controlled trial of 692 patients. Major bleeding during the 24-month follow-up was reported in 5.7% (19/336) and 3.7% (13/355) of patients respectively (RR 1.52, 95% CI 0.76 to 3.01, $p=0.23$). Any bleeding within the first 10 days was reported in 4% (15/336) of patients who had PMT and 2% (6/355) of patients in the control group (RR 2.64, 95% CI 1.04 to 6.68, $p=0.03$). Any bleeding during the 24-month follow-up was reported in 14% (46/336) and 11% (38/355) of patients respectively (RR 1.26, 95% CI 0.85 to 1.89, $p=0.25$).[1]

Major bleeding events were reported in 3.7% (12/329) of patients in a registry of 329 patients. These included intracranial bleeding (n=1), retroperitoneal bleeding (n=1), haemolytic anaemia needing transfusion (n=1), gastrointestinal bleeding secondary to gastritis and gastric cancer (n=2), and unspecified bleeding needing transfusion (n=6). The patient with intracranial haemorrhage died 7 days after the start of thrombolysis despite cessation of the urokinase infusion.[4] Gastrointestinal

bleeding was reported in 1 patient who had PMT with catheter-directed thrombolysis (CDT) in a non-randomised comparative study.[6]

Minor access-site haematomas were reported in 4% (2/49) of patients who had PMT and 5% (2/22) of patients who had CDT in a non-randomised comparative study of 93 patients.[5]

Vascular injury

Vascular injury was reported in less than 1% (3/2,024) of patients in a registry of 2,024 patients. In each event there was vascular injury from the initial guidewire traversal of the chronic total occlusion before the thrombectomy device was inserted. No further management or transfusion were needed.[3]

Renal failure

Acute renal failure, described as a serious event, was reported in 1 patient in the registry of 329 patients. The patient had bilateral lower extremity DVT with a medical history that included diabetes, previous DVT in the same area, and a current pulmonary embolism that was being treated medically. The patient was diagnosed with renal failure the day after the procedure and needed 6 weeks of dialysis, without further sequelae.[4]

Prolonged renal failure was described in 1 patient after PMT in a case report. Six days after the procedure the patient presented to the emergency department with generalised weakness and decreased urine output. He was diagnosed with an acute kidney injury with evidence of acute tubular necrosis. The underlying cause was considered to be haemoglobinuria, with marked hyperkalaemia. The patient was started on haemodialysis and continued to be dependent on haemodialysis 5 months later.[10]

Transient renal insufficiency

Transient renal insufficiency was reported in 1% (3/329) of patients in the registry of 329 patients. The events were described as non-serious.[4]

Acute pancreatitis

Acute pancreatitis in 1 patient after PMT was described in a case report. It was diagnosed the day after the procedure. The severity was judged to be mild. No causative factors were identified and the patient was diagnosed with haemolysis-induced pancreatitis. The patient was managed supportively with analgesia, intravenous fluids and bowel rest. He was discharged after 7 days when all symptoms had resolved.[9]

Bradycardia

Bradycardia was reported in 1% (3/329) of patients in the registry of 329 patients. The events were described as non-serious.[4]

Pulmonary embolism

Pulmonary embolism after PMT was described in 1 case report. The patient went on to develop a right hemiparesis, which was the result of a paradoxical embolism through a patent foramen ovale. During the procedure the patient had intense dyspnoea, hypoxaemia, bradycardia and central and peripheral cyanosis. Massive pulmonary embolism was suspected and treatment with systemic alteplase was started. On the third day after thrombectomy the patient had right-sided hemiparesis and loss of vision, somnolence and aphasia. MRI revealed multiple areas of ischaemia bilaterally, following the territory of the middle cerebral artery and left posterior cerebral artery, and bilateral cerebellar infarcts. Treatment with heparin was stopped and a filter fitted in the inferior vena cava. Transoesophageal echocardiogram showed a patent foramen ovale with flow diverted from the right to left atrium. The patient was discharged after 28 days with a prescription for warfarin and elastic compression stockings. Six months later the patient had returned to her usual employment and the only remaining deficit was bilateral, regressive hemianopsia.[7]

Pulmonary embolism, not needing treatment, was reported in 1 patient in the registry of 329 patients.[4] Symptomatic pulmonary embolism was reported in 1 patient who had PMT and 1 patient who had CDT in a non-randomised comparative study of 98 limbs.[6]

Device complications

Detachment of a catheter tip during PMT was described in a case report. During the procedure, the distal tip of the device became detached while the shaft of the device was being pulled back through the stenotic segment of the common iliac vein. The shaft was removed, while the guidewire was left in place with the detached metallic part remaining within the proximal region of the stenotic iliac segment. A self-expandable stent was placed to widen the stenotic segment and a snare catheter was used to catch the detached tip. The tip was withdrawn from the popliteal vein through a 2 cm percutaneous incision. A week later the remaining thrombus was removed with a manual aspiration thrombectomy.[8]

Mortality

One death was reported in the registry of 329 patients, which happened 6 months after the procedure. The paper states that there was no information available on the patient's status after discharge and it is therefore not possible to rule out the thrombectomy treatment as a contributory factor.[4]

In the RCT of 692 patients, mortality in the first 24 months after the procedure was 2% in both groups (RR 0.89, 95% CI 0.33 to 2.44, p=0.83).[1]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse events: pain during the procedure and arrhythmias. They considered that the following were theoretical adverse events: death, myocardial infarction, and venous perforation.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous mechanical thrombectomy for acute deep vein thrombosis of the lower limb. The following databases were searched, covering the period from their start to 4 April 2018: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with acute deep vein thrombosis of the lower limb
Intervention/test	Percutaneous mechanical thrombectomy
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 3,415 patients from 2 randomised controlled trials, 2 registries, 2 non-randomised comparative studies and 4 case reports.[1–10]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the appendix.

Table 2 Summary of key efficacy and safety findings on percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg

Study 1 Vedantham S (2017)

Details

Study type	**Randomised controlled trial (ATTRACT)**
Country	US (56 centres)
Recruitment period	2009 to 2014
Study population and number	**n=692 (337 pharmacomechanical thrombolysis plus anticoagulation, 355 control [anticoagulation alone])** Patients with symptomatic acute proximal deep vein thrombosis involving the femoral, common femoral or iliac vein.
Age and sex	Median 53 years (interquartile range 42 to 62 years); 62% (426/692) male
Patient selection criteria	Patients with symptomatic proximal deep vein thrombosis involving the femoral, common femoral, or iliac vein, with or without other involved ipsilateral veins. Exclusion criteria included age younger than 16 or older than 75 years, pregnancy, symptoms for more than 14 days, high bleeding risk, active cancer, established post-thrombotic syndrome or history of ipsilateral deep vein thrombosis in the previous 2 years.
Technique	Recombinant tissue plasminogen activator (rt-PA) was delivered into the thrombus by 1 of 3 methods. If the popliteal vein was occluded or the inferior vena cava was involved, rt-PA infusion was started through a multi-sidehole catheter for no longer than 30 hours. For the remaining patients, a first attempt single-session thrombus removal with rapid delivery of rt-PA through the AngioJet Rheolytic Thrombectomy System (Boston Scientific) or the Trellis Peripheral Infusion System (Covidien) was done, followed by rt-PA infusion for no longer than 24 hours if residual thrombus was present. After the initial delivery of rt-PA, physicians could use balloon maceration, catheter aspiration, thrombectomy with the AngioJet or Trellis system, percutaneous transluminal balloon venoplasty, stent placement, or a combination of procedures to clear residual thrombus and treat obstructive lesions. Patients in each treatment group had initial and long-term anticoagulant therapy, including the option of rivaroxaban when it became available, and were provided with elastic compression stockings at the 10-day follow-up visit and every 6 months.
Follow-up	**24 months**
Conflict of interest/source of funding	The trial was sponsored by the National, Heart, Lung and Blood Institute of the National Institutes of Health. Supplemental funding was provided by Boston Scientific and Covidien (now Medtronic). The trial drug and additional funding were provided by Genentech. Compression stockings were donated by BSN Medical. These companies played no role in the design or conduct of the trial or in the analysis or reporting of the data.

Analysis

Follow-up issues: 77% (257/336) of patients in the pharmacomechanical thrombolysis (PMT) group and 68% (243/355) of patients in the control group completed 24 months of follow-up. 21% (148/692) of patients were lost to follow-up (18% [62/336] in the PMT group and 24% [86/355] in the control group). In addition, 8% (28/336) of patients in the PMT group and 15% (52/355) of patients in the control group missed all 4 post-thrombotic syndrome assessments. One patient who was assigned to the PMT group was excluded from all analyses because they were found not to have a qualifying deep vein thrombosis. The fact that a high proportion of the patients who had no post-thrombotic syndrome assessments were in the control group may have resulted in an underestimate of the treatment effect.

Study design issues: Multicentre, randomised, open-label, assessor blinded, controlled trial. A Web-based central randomisation system was used to randomise patients to each group, stratified according to clinical centre and thrombus extent. The randomisation sequence, with varying block sizes, was computer-generated by an independent statistician. The sample size of 692 patients was based on 30% of patients in the control group having post-thrombotic syndrome, with

the hypothesis that PMT would reduce the proportion to 20% or lower (80% power, 2-sided α of 0.05, and assuming a 10% loss to follow-up).

The primary outcome was the development of post-thrombotic syndrome (defined as a Villalta score of 5 or higher or an ulcer in the leg with the index deep vein thrombosis), at any time between the 6-month and 24-month follow-up visits. Patients were also counted as having post-thrombotic syndrome if they had an unplanned endovascular procedure to treat severe venous symptoms beyond 6 months after randomisation, unless a Villalta score within the previous 4 weeks was lower than 5.

Patient-reported health-related quality of life was assessed with the 36-item Short Form Health Survey (SF-36) and the venous disease-specific Venous Insufficiency Epidemiological and Economic Study Quality of Life (VEINES-QOL) measure. A 7-point Likert scale (0 to 7) was used to assess leg pain, with higher scores indicating more severe pain. Thrombus removal was quantified by independent central readers who scored venograms obtained before and after the procedure (score range 0 to 24, with 0 representing no thrombus and 24 representing complete thrombosis).

The primary analysis was a modified intention-to-treat analysis.

Study population issues: The baseline characteristics of the patients were similar in the 2 treatment groups.

Other issues: 88% (297/336) of patients in the PMT group had 1 or more additional endovascular procedures (62% had balloon venoplasty, 62% had balloon maceration, 61% had rheolytic thrombectomy with AngioJet, 28% had stent placement, 21% had large-bore catheter aspiration and 5% had isolated thrombolysis with Trellis).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **691 (336 versus 355)**

Binary trial outcomes, number of patients (%)

Outcome	PMT n=336	Control n=355	Risk ratio (95% CI)	p value
Post-thrombotic syndrome between 6 and 24 months				
Ulcer at any follow-up	12 (4)	17 (5)		
Villalta score ≥5 without ulcer	144 (43)	154 (43)		
Late endovascular procedure only	1 (<1)	0		
Total	157 (47)	171 (48)	0.96 (0.82 to 1.11)*	0.56
Post-thrombotic syndrome according to follow-up visits				
At 6 months	78/291 (27)	113/285 (40)	0.68 (0.53 to 0.86)	
At 12 months	92/272 (34)	88/258 (34)	0.99 (0.78 to 1.26)	
At 18 months	85/245 (35)	76/222 (34)	1.01 (0.79 to 1.30)	
At 24 months	79/258 (31)	86/239 (36)	0.85 (0.66 to 1.09)	
Major non-post-thrombotic syndrome treatment failure	4 (1)	7 (2)	0.58 (0.17 to 1.98)#	0.38^
Any treatment failure	158 (47)	176 (50)	0.94 (0.80 to 1.09)*	0.39^
Moderate-to-severe post-thrombotic syndrome	60 (18)	84 (24)	0.73 (0.54 to 0.98)*	0.04^
Recurrent venous thromboembolism				
First 10 days	6 (2)	4 (1)	1.53 (0.44 to 5.28)#	0.50
Total over 24 months	42 (12)	30 (8)	1.47 (0.94 to 2.29)#	0.09
Mortality over 24 months	7 (2)	8 (2)	0.89 (0.33 to 2.44)	0.83

* adjusted for extent of deep vein thrombosis and clinical centre

adjusted for extent of deep vein thrombosis

^ For the secondary efficacy analyses, a p value of 0.01 or lower was considered to indicate statistical significance

Safety

Safety outcomes, number of patients (%)

Outcome	PMT n=336	Control n=355	Risk ratio (95% CI)	p value
Major bleeding				
First 10 days	6 (1.7)	1 (0.3)	6.18 (0.78 to 49.2)	0.049
Total over 24 months	19 (5.7)	13 (3.7)	1.52 (0.76 to 3.01)	0.23
Any bleeding				
First 10 days	15 (4)	6 (2)	2.64 (1.04 to 6.68)	0.03
Total over 24 months	46 (14)	38 (11)	1.26 (0.85 to 1.89)	0.25
Mortality in first 10 days	0	0		

Continuous trial outcomes

Outcome	PMT n=336		Control n=355		Between-group difference	
	n	Mean±SE	n	Mean±SE	Estimate± SE	p value*
Villalta score						
At 6 months	291	3.11±0.24	285	4.33±0.24	-1.22±0.31	<0.001
At 12 months	272	3.22±0.22	258	4.38±0.22	-1.17±0.28	<0.001
At 18 months	245	3.32±0.24	222	4.44±0.24	-1.12±0.31	<0.001
At 24 months	258	3.43±0.28	239	4.50±0.29	-1.06±0.38	0.005
VCSS score						
At 6 months	289	1.73±0.15	279	2.68±0.15	-0.95±0.21	<0.001
At 12 months	265	1.80±0.16	253	2.37±0.16	-0.56±0.23	0.01
At 18 months	240	1.74±0.17	215	2.80±0.18	-1.06±0.24	<0.001
At 24 months	235	1.87±0.18	214	2.42±0.19	-0.55±0.26	0.03
Change in SF-36 general quality of life, baseline to 24 months						
PCS	245	11.18±0.91	222	10.06±0.97	1.13±1.26	0.37
MCS	245	2.70±0.84	222	2.70±0.89	0.00±1.16	0.99
Change in VEINES disease-specific quality of life, baseline to 24 months						
Overall	249	27.67±1.71	226	23.47±1.83	4.20±2.39	0.08
Symptoms	248	20.58±1.70	226	17.31±1.81	3.27±2.37	0.17
Change in leg-pain severity, from baseline						
Day 10	317	-1.62±0.10	325	-1.29±0.10	-0.33±0.14	0.02
Day 30	314	-2.17±0.11	317	-1.83±0.11	-0.34±0.15	0.03
Change in index leg circumference (cm), from baseline						
Day 10	305	-0.26±0.17	323	0.27±0.16	-0.53±0.23	0.02
Day 30	304	-0.74±0.17	315	-0.28±0.16	-0.46±0.23	0.05

* For the secondary efficacy analyses, a p value of 0.01 or lower was considered to indicate statistical significance

Abbreviations used: CI, confidence interval; PMT, pharmacomechanical thrombolysis; SE, standard error; VCSS, venous clinical severity score; VEINES, Venous Insufficiency Epidemiological and Economic Study

Study 2 Sharifi M (2012)

Details

Study type	**Randomised controlled trial (TORPEDO)**
Country	US
Recruitment period	2007 to 2010
Study population and number	**n=183 (91 percutaneous endovenous intervention [PEVI] plus anticoagulation, 92 control [anticoagulation alone])** Patients with acute deep venous thrombosis (DVT) involving the femoropopliteal vein or more proximal venous segments.
Age and sex	Mean 61 years; 56% (103/183) male
Patient selection criteria	Adult patients with severe symptoms (leg oedema, erythema, induration, pain and tenderness) of DVT involving the femoropopliteal vein or more proximal venous segments. Patients were ineligible for the study if they had a contraindication to unfractionated or low-molecular-weight heparin, severe thrombocytopaenia, or major bleeding in the previous 4 weeks.
Technique	PEVI – patients were taken to the angiography suite within 24 hours of presentation and start of anticoagulation therapy. All patients had an inferior vena cava (IVC) filter placed before the intervention. Patients with acute DVT and otherwise preserved venous architecture had thrombectomy using the Trellis device (Covidien, US) or the AngioJet DVX catheter (MEDRAD Interventional/Possis, US). The Trellis device was preferred in patients with anaemia and renal insufficiency. For severely distorted venous anatomy with residual diameter stenosis ≥80%, and calcification, balloon venoplasty and stents were used. All patients had venography immediately after the procedure. If residual thrombus was >30% of the venographic luminal area after initial treatment, an infusion catheter was placed to administer low-dose thrombolytic therapy with tissue plasminogen activator for 20 to 24 hours. Patients in both groups were given compression stockings and advised to wear them for a minimum of 6 months and preferably 2 years. All patients in the PEVI group had aspirin for a minimum of 6 months in addition to warfarin.
Follow-up	**Mean 30 months (range 12 to 41)**
Conflict of interest/source of funding	The first author is a consultant to Covidien.

Analysis

Follow-up issues: Three patients were lost to follow-up and 11 died, leaving 97% (88/91) of patients in the PEVI group and 88% (81/92) of patients in the control group available for the final follow-up.

Study design issues: Randomised controlled trial. The primary endpoints were the development of post-thrombotic syndrome and recurrent venous thromboembolism at 6 months and at final follow-up. Post-thrombotic syndrome was defined as the presence of at least 2 new symptoms (leg burning, pain, aches, discomfort, restlessness or tingling) plus the following signs: oedema plus venous reflux; skin hyperpigmentation or lipodermatosclerosis; and healed or active ulcer. Post-thrombotic syndrome was classified as mild (oedema and reflux only), moderate (skin changes with or without oedema or reflux), or severe (healed or active ulcer with or without oedema or reflux or skin changes). A post-hoc analysis was done to investigate the effects of aspirin on the risk of post-thrombotic syndrome in the control group.

Study population issues: The baseline clinical characteristics of the 2 groups were comparable. On admission, 22% (20/91) of patients in the PEVI group and 21% (19/92) of patients in the control group had been diagnosed with pulmonary embolism. Over 50% of patients with no known history of DVT had venographic evidence of prior DVT.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 169 (88 versus 81)

Primary efficacy endpoints at 30 months
<table>
<tr><th></th><th>PEVI group n=88</th><th>Control group n=81</th><th>p value</th></tr>
<tr><td>DVT</td><td>4 (4.5%)</td><td>9 (11.1%)</td><td>0.15</td></tr>
<tr><td>Non-fatal PE</td><td>0</td><td>3 (3.7%)</td><td>0.11</td></tr>
<tr><td>Fatal PE*</td><td>1 (1.1%)</td><td>4 (4.9%)</td><td>0.15</td></tr>
<tr><td>Mild PTS</td><td>4 (4.5%)</td><td>15 (18.5%)</td><td>0.007</td></tr>
<tr><td>Moderate PTS</td><td>1 (1.1%)</td><td>6 (7.4%)</td><td>0.06</td></tr>
<tr><td>Severe PTS</td><td>1 (1.1%)</td><td>3 (3.7%)</td><td>0.35</td></tr>
<tr><td>Total PTS</td><td>6 (6.8%)</td><td>24 (29.6%)</td><td><0.001</td></tr>
<tr><td>VTE (after discharge)</td><td>4 (4.5%)</td><td>13 (16.0%)</td><td>0.02</td></tr>
</table>
* from initial randomisation (in the PEVI group, the patient died before PEVI)

In the PEVI group, 27 patients had 47 stents placed.

12 patients had the IVC filter removed at 35±4 days after implantation, but most patients chose to keep them

Post-hoc analysis of the 24 patients who developed PTS in the control group found that only 9 patients were taking aspirin, compared with 41 of the remaining 57 patients without PTS (relative risk 0.37, 95% CI 0.19 to 0.74, p=0.006).</td><td>There were no stent fractures.</td></tr>
<tr><td colspan="2">Abbreviations used: DVT, deep venous thrombosis; PE, pulmonary embolism; PEVI, percutaneous endovenous intervention; PTS, post-thrombotic syndrome; VTE, venous thromboembolism</td></tr>
</table>

Study 3 Dietzek A (2010)

Details

Study type	**Registry**
Country	US, Belgium and Ireland
Recruitment period	2005 to 2009
Study population and number	**n=2,024 patients (2,203 limbs)** Patients with venous thrombus who had isolated pharmacomechanical thrombolysis using a peripheral infusion system
Age and sex	Mean 53 years; 48% male
Patient selection criteria	Patient selection criteria were not described in detail. Deep venous thrombosis (DVT) was diagnosed by patient history, physical examination and duplex ultrasonography, and confirmed by intraprocedural venography.
Technique	Device: Trellis peripheral infusion system (Covidien, US). The type of lytic agent used during the procedure was determined by the treating physician and was most often alteplase. The dose varied depending on the device's infusion length. After isolated pharmacomechanical thrombolysis with the Trellis system, adjunctive procedures were used in 89% of patients. At least 40% of patients had no inferior vena cava filter placed.
Follow-up	**None**
Conflict of interest/source of funding	Not reported.

Analysis

Follow-up issues: There was no formal patient follow-up after the procedure.

Study design issues: Company-sponsored voluntary registry; retrospective review of prospectively collected data. The registry focused on collecting data on the technical aspects of using the device. Patency of the vessel was graded I to III, where grade III is >95% thrombus removal, grade II is 50 to 94% thrombus removal and grade I is <50% thrombus removal.

Study population issues: Some patients had a thrombus in a location other than the lower limb. Thrombus location was as follows: iliofemoral (25%), iliofemoral to popliteal (19%), inferior vena cava (IVC) and lower extremity (18%), subclavian only (10%), femoral to popliteal (12%), isolated femoral (6%), isolated iliac (6%), subclavian and upper extremity (1%), other (1%), IVC only (1%), isolated popliteal (1%). Thrombus age: 42% acute on chronic (≤14 days, previous DVT history, 35% acute (≤14 days), 10% subacute (>14 to 28 days), 10% subacute on chronic (>14 to 28 days, previous DVT history), 4% chronic (>28 days). 31% of patients already had IVC filters in situ, and an additional 25% received filters at the time of the procedure.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 2,024 patients, 2,203 limbs

Grade II or III patency was achieved in 96% of treated limbs at the end of the procedure.

Patency achieved by chronicity of venous thrombus per limb (n=2,203)
<table>
<tr><th>Final patency</th><th>Acute
n (%)</th><th>Acute on chronic
n (%)</th><th>Subacute
n (%)</th><th>Subacute on chronic
n (%)</th><th>Chronic
n (%)</th><th>All chronicities
n (%)</th></tr>
<tr><td>Grade I</td><td>21 (2.8)</td><td>51 (5.6)</td><td>9 (3.9)</td><td>12 (5.6)</td><td>6 (7.2)</td><td>99 (4.5)</td></tr>
<tr><td>Grade II</td><td>356 (46.8)</td><td>571 (62.5)</td><td>137 (59.6)</td><td>140 (64.8)</td><td>62 (74.7)</td><td>1,266 (57.5)</td></tr>
<tr><td>Grade III</td><td>383 (50.4)</td><td>292 (31.9)</td><td>84 (36.5)</td><td>64 (29.6)</td><td>15 (18.1)</td><td>838 (38)</td></tr>
<tr><td>Grade II/III</td><td>739 (97.2)</td><td>863 (94.4)</td><td>221 (96.1)</td><td>204 (94.4)</td><td>77 (92.8)</td><td>2,104 (95.5)</td></tr>
</table></td><td>Adverse events: <1% (3/2,024)
In each event, there was vascular injury from the initial guidewire traversal of the chronic total occlusion before the Trellis system was inserted. No further management or transfusion was needed.

There was no procedure-related pulmonary embolism.</td></tr>
</table>

Study 4 Garcia MJ (2015)

Details

Study type	**Registry (PEARL)**
Country	US and Europe (32 sites)
Recruitment period	2007 to 2013
Study population and number	**n=329** Patients with lower-extremity deep vein thrombosis (DVT)
Age and sex	Mean 52 years (range 17 to 87); 57% male
Patient selection criteria	Patients with imaging-confirmed diagnosis of lower-extremity DVT were included. There were no specific patient inclusion or exclusion criteria.
Technique	Device: AngioJet Thrombectomy Catheter Systems (Boston Scientific Corporation, US). In phase 1 of the registry, patients were treated with midlength AngioJet catheters and followed up for 3 months; in phase 2, patients were treated with any AngioJet catheter and completed 12 months of follow-up. Four treatment approaches were used: 4% (13/329) of patients had rheolytic thrombectomy only (without lytic delivery), 35% (115/329) had pharmacomechanical thrombolysis with delivery of lytic agent through the AngioJet catheter, 9% (29/329) had rheolytic thrombectomy before or after catheter-directed thrombolysis and 52% (172/329) of patients had rheolytic thrombectomy before or after pharmacomechanical catheter-directed thrombolysis and catheter-directed thrombolysis treatments. An ipsilateral popliteal vein access was used in 82% of patients. 35% (116/329) of patients had a stent placed and 74% (242/329) of patients had adjunctive balloon angioplasty.
Follow-up	**Up to 12 months**
Conflict of interest/source of funding	The authors are paid consultants for Boston Scientific Corporation (US) and received grant support during the conduct of the study.

Analysis

Follow-up issues: 88% (290/329) of patients completed the 3 month follow-up and 78% (143/184) of patients in phase 2 of the study completed the 12 month follow-up.

Study design issues: Prospective, multicentre voluntary registry. A thrombus score was assigned to each of the 7 venous segments (inferior vena cava and common iliac, external iliac, common femoral, central femoral, peripheral femoral, and popliteal veins) using venography, according to the following criteria: complete occlusion was given a score of 3, substantial occlusion (50% to 99%) was given a score of 2, partial occlusion (<50%) was given a score of 1 and a patent venous segment was given a score of 0. Thrombus scores were totalled for each patient, with a potential range of 0 to 42. The degree of thrombus removal was classified as follows: grade I (<50% reduction in thrombus score), grade II (50% to 99% reduction) and grade III (100% reduction). Patients enrolled in phase 2 completed a quality of life assessment (Short-Form 12) at baseline and follow-up.

S**tudy population issues**: 67% of the patients were considered to have acute DVT (≤14 days from onset of symptoms), 19% were treated within 15 to 30 days of the onset of symptoms and 14% had chronic lesions. The iliac vein was involved in 66% of patients, the femoral vein was involved in 89% and the popliteal vein was involved in 59% of patients. 40% (132/329) of patients had a previous DVT and 28% (92/329) of patients had a pre-existing caval filter.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 329
The procedure took less than 24 hours in 73% of patients.
Successful ‘complete’ thrombus removal was achieved in 39% of patients, such that there was no need for CDT.

Reduction in clot burden, n (%)
<table>
<tr><th rowspan="2">Group</th><th colspan="3">Clot removal grade</th></tr>
<tr><th>Grade I (<50% reduction)</th><th>Grade II (50% to 99% reduction)</th><th>Grade III (100% reduction)</th></tr>
<tr><td>All patients</td><td>13 (4.0)</td><td>123 (37.5)</td><td>192 (58.5)*</td></tr>
<tr><td colspan="4">By treatment group</td></tr>
<tr><td>Rheolytic</td><td>0</td><td>4 (30.8)</td><td>9 (69.2)</td></tr>
<tr><td>PCDT</td><td>6 (5.2)</td><td>42 (36.5)</td><td>67 (58.3)</td></tr>
<tr><td>CDT</td><td>2 (6.9)</td><td>9 (31.0)</td><td>18 (62.1)</td></tr>
<tr><td>PCDT plus CDT</td><td>5 (2.9)</td><td>68 (39.8)</td><td>98 (57.3)*</td></tr>
<tr><td colspan="4">By duration of symptoms</td></tr>
<tr><td>0 to 14 days</td><td>7 (3.2)</td><td>89 (40.8)</td><td>122 (56.0)</td></tr>
<tr><td>>14 days</td><td>6 (5.4)</td><td>34 (30.9)</td><td>70 (63.6)</td></tr>
</table>
* venography data was missing for 1 patient
Recurrence
9% (30/329) of patients needed reintervention for recurrent thrombosis of the treated vessel(s). An additional 7 patients (2%) reported recurrent thrombosis but did not have repeat intervention.

Freedom from rethrombosis by follow-up (determined by physician, based on patient reports of worsening symptoms, follow-up imaging or additional treatment after the initial procedure)
• 3 months=94% (95% CI 91% to 96%)
• 6 months=87% (95% CI 82% to 91%)
• 12 months=83% (95% CI 77% to 88%)

Recurrence of thrombosis was not related to the duration of symptoms, treatment approach, or clot removal grade.

Continued benefit from the thrombectomy procedure was reported by 93% of patients at 3 months (95% CI 90% to 96%), by 82% of patients at 6 months (95% CI 77% to 87%) and by 78% of patients at 12 months (95% CI 71% to 83%).
</td><td>
Adverse events reported as possibly related to the AngioJet device
• Bradycardia=0.9% (3/329)
• Pulmonary embolism without treatment=0.3% (1/329)
• Acute renal failure=0.3% (1/329) (described as a serious event)
• Transient renal insufficiency=0.3% (1/329)
• Elevated creatinine (1.0 to 1.7 mg/dl)=0.3% (1/329)
• Hyperbilirubinemia=0.3% (1/329)
• Leg pain=0.3% (1/329)

All but 1 of the adverse events were classified as nonserious, needing no or nominal treatment without additional hospitalisation.
The patient who had renal failure had bilateral lower extremity DVT with a medical history that included diabetes, previous DVT in the same area, and a current pulmonary embolism that was being treated medically. The patient received 240 ml of contrast medium during the 2-day procedure (total 21 hours) as well as a total AngioJet run time (18.5 minutes) that was beyond the manufacturer’s recommended run time. The patient was diagnosed with renal failure the day after the procedure and needed 6 weeks of dialysis, without further sequelae.

One death was reported in the registry, which occurred 6 months after the procedure. The paper states that there was no information available on the patient’s status after discharge and it is therefore not possible to rule out the thrombectomy treatment as a contributory factor.

Overall bleeding complication rate=4.5% (15/329); 12 major and 3 minor
Major bleeding events:
• Intracranial bleeding=0.3% (1/329)
• Retroperitoneal bleeding=0.3% (1/329)
• Haemolytic anaemia needing transfusion=0.3% (1/329)
• Anaemia needing transfusion=0.3% (1/329)
• Gastrointestinal bleeding secondary to gastritis and gastric cancer=0.6% (2/329)
• Unspecified bleeding needing transfusion=1.8% (6/329)
</td></tr>
</table>

Short Form 12 quality of life subscores over follow-up by chronicity of DVT

Model	Follow-up				p value	
	Baseline	3 months	6 months	12 months	Follow-up	Follow-up thrombus age
Mean physical component score ± standard error						
Acute	34.0±1.1 (n=108)	42.4±1.1 (n=104)	42.7±1.2 (n=87)	44.0±1.1 (n=88)	<0.0001	0.9342
Subacute	33.3±1.8 (n=37)	41.1±1.9 (n=33)	40.3±2.0 (n=31)	41.2±2.0 (n=24)		
Chronic	30.6±2.1 (n=29)	38.6±2.1 (n=27)	39.7±2.2 (n=25)	41.8±2.2 (n=24)		
Thrombus age p value=0.2056						
Mean mental component score ± standard error						
Acute	44.4±1.2 (n=108)	48.4±1.2 (n=104)	48.3±1.3 (n=87)	49.4±1.3 (n=88)	<0.0001	0.5556
Subacute	40.6±2.1 (n=37)	45.9±2.2 (n=33)	44.9±2.2 (n=31)	47.8±2.3 (n=28)		
Chronic	45.7±2.3 (n=29)	49.2±2.4 (n=27)	48.4±2.5 (n=25)	46.4±2.5 (n=24)		
Thrombus age p value=0.3682						

The paper states that the mean US population norm for Short Form 12 subscores is 50.

All bleeding events were determined to be related to catheter access, anticoagulation or thrombolytic drug; none were related to the AngioJet procedure.

Abbreviations used: CDT, catheter-directed thrombolysis; CI, confidence interval; DVT, deep vein thrombosis; PCDT, pharmacomechanical catheter-directed thrombolysis

Study 5 Lin PH (2006)

Details

Study type	**Non-randomised comparative study**
Country	US
Recruitment period	1997 to 2005
Study population and number	**n=93 (49 pharmacomechanical thrombectomy [PMT], 44 catheter-directed thrombolysis [CDT])** Patients with symptomatic lower extremity deep venous thrombosis (DVT)
Age and sex	• PMT: mean age 45 years; 45% (22/49) male • CDT: mean age 49 years; 43% (19/44) male
Patient selection criteria	Not described. All patients had symptomatic DVT in their lower extremities. No patient had a contraindication to thrombolysis or anticoagulation. No patients had isolated thrombus in the inferior vena cava. Patients chosen for intervention had overwhelming symptoms of lower extremity swelling, incapacitating pain, or phlegmasia dolen.
Technique	Device for PMT: AngioJet system (Possis Medical, US). All PMT procedures were done by vascular surgeons in the operating room. A removable or permanent vena caval filter was placed before PMT. The thrombolytic agent was based on the physician's choice. All CDT procedures were done by interventional radiologists in a standard radiology suite. After the procedure, all patients were continued on either subcutaneous low-molecular-weight heparin or intravenous unfractionated heparin, all with subsequent conversion to oral warfarin.
Follow-up	**Mean 13 months (range 1 to 49)**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: There were no losses to follow-up.

Study design issues: Retrospective, non-randomised comparative study. Patients who had PMT therapy using the AngioJet system were identified from hospital records and clinic charts, and compared with a cohort group who had CDT therapy. Patients in the CDT group were treated at an earlier phase in the study period than patients who had PMT. Thrombus removal was scored as complete if the dictated procedure report and an angiogram showed no clot remaining after the procedure.

Study population issues: The ascertained thrombus age from time of duplex ultrasound diagnosis to intervention was 15 days (range 0 to 34 days) in the PMT group and 13 days (range 0 to 31 days) in the CDT group.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **93 (49 versus 44)**

Treatment outcome

Variable	PMT therapy n=49 (52 limbs)	CDT therapy n=44 (46 limbs)	p value
Complete treatment success	39 (75%)	32 (70%)	Not significant
Partial treatment success	13 (25%)	14 (30%)	Not significant
Immediate clinical improvement	42 (81%)	33 (72%)	Not significant
No clinical improvement	4 (8%)	5 (11%)	Not significant
Adjuvant balloon angioplasty/iliac venous stenting	43 (82%)	36 (78%)	Not significant
Mean number of venograms	0.4±0.2	2.5±0.7	<0.001
Mean intensive care unit stay (days)	0.6±0.3	2.4±1.2	<0.04
Overall hospital length of stay (days)	4.6±1.3	8.4±2.3	<0.02

Primary patency rates at 1 year

- PMT=68%
- CDT=64%, p=not significant

Safety

Haemorrhagic complication

- PMT=4% (2/49) (2 minor access site haematomas)
- CDT=6% (3/44) (2 minor access site haematomas and 1 retroperitoneal haematoma)

p=not significant

Packed red blood cell transfusion (units)

- PMT=0.2±0.3
- CDT=1.2±0.7

P<0.05

There was no in-hospital mortality.

Abbreviations used: CDT, catheter-directed thrombolysis; PMT, pharmacomechanical thrombectomy

Study 6 Park KM (2014)

Details

Study type	**Non-randomised comparative study**
Country	Korea
Recruitment period	2005 to 2011
Study population and number	**n=90 patients (98 limbs); 23 percutaneous mechanical thrombectomy [PMT] only, 30 PMT plus catheter-directed thrombolysis [CDT], 45 CDT only.** Patients with acute iliofemoral deep vein thrombosis (DVT)
Age and sex	• PMT only: mean age 64 years; 56% male • PMT plus CDT: mean age 51 years; 50% male • CDT only: mean age 63 years; 27% male p=0.008 for age and p=0.101 for sex
Patient selection criteria	Patients with acute iliofemoral DVT, with symptoms of leg swelling, pain or redness for less than 3 weeks. All patients had extensive thrombus involving the iliac vein extending peripherally to the entire lower extremity. The study population was limited to patients who had been treated only with urokinase as the thrombolytic agent and with Trerotola as the mechanical thrombectomy device. Contraindications to CDT included recent stroke, surgery, serious gastrointestinal bleeding, primary or metastatic central nervous system malignancy, and coagulopathy. No patients had symptomatic pulmonary embolism.
Technique	Device for PMT: Arrow-Trerotola (Arrow International). An inferior vena cava filter was inserted before PMT or thrombolysis in 95% of patients. In the PMT group, patients also had CDT if there was residual thrombus after 3 passes of the thrombectomy device. Urokinase was used for CDT. Patients with underlying stenosis or occlusion of the iliac vein (such as those with May-Thurner syndrome) were treated with reconstruction using a stent. Patients in all groups were initially offered anticoagulation with intravenous unfractionated heparin. Systemic heparin was switched to warfarin after MT or CDT. Anticoagulation was continued for 6 months.
Follow-up	**Mean 28 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: No losses to follow-up were described.

Study design issues: Retrospective non-randomised comparative study. Data were collected from a chart review. The primary endpoint was clinical and technical result after CDT or PMT. The secondary endpoint was iliac vein patency.

Study population issues: In 23 patients, there were contraindications to thrombolysis (recent surgery and trauma within 3 weeks [n=15], recent gastrointestinal bleeding or haemoptysis [n=5], haemorrhagic stroke or intracranial haemorrhage [n=3]). Onset between symptom development and start of interventional procedure ranged from 3 to 13 days (mean 7 days). There were no differences in demographic and clinical features among the 3 groups, except age. More patients in the CDT only group had an iliac stent inserted than in the PMT only group (93% versus 49% respectively, p<0.001). CT venography was used to evaluate venous patency rather than duplex scanning because duplex scanning was not covered by Korean insurance.

In 1 patient, cyanotic discolouration with severe swelling and pain raised suspicion for phlegmasia cerulean dolens, but gangrenous change did not definitively occur. 52% of patients had pulmonary embolism, confirmed by initial CT angiography.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **98 limbs (23 PMT only, 30 PMT and CDT, 45 CDT only)**

Comparison of procedure details and results

Characteristics	PMT n=23	PMT + CDT n=30	CDT n=45	p value
Procedure details				
Thrombolysis	0 (0%)	31 (100%)	45 (100%)	<0.001
Stent	11 (49%)	11 (37%)	42 (93%)	<0.001
Inferior vena cava filter	22 (99%)	30 (100%)	41 (91%)	0.174
Procedural time (hours)	2.7±2.0	18.2±8.2	29.3±9.4	<0.001
Urokinase dose (million units)	0	5.13±3.72	7.51±4.54	<0.001
Technical results				
Complete removal (Grade 3)	12 (53%)	20 (66%)	22 (48%)	0.099
Partial removal (Grade 2)	7 (30%)	5 (17%)	10 (22%)	
Failure (Grade 1)	4 (17%)	5 (17%)	13 (28%)	
Clinical results				
Improvement	18 (78%)	24 (80%)	32 (71%)	0.498
No change	5 (22%)	6 (20%)	13 (29%)	
Villalta Score				
Initial	9.19±4.93	7.85±3.12	8.62±5.87	0.567
7 days	2.53±4.18	2.08±3.76	2.12±4.23	0.518
1 month	3.98±3.21	3.15±3.11	3.21±3.76	0.298
1 year	4.99±4.65	4.89±4.19	4.23±3.42	0.683

Primary patency rate of the iliac vein at 1 year (using CT venography) = 82%

Primary patency rate of the iliac vein at 3 years = 64%

(There was no statistically significant difference in primary patency rate between the 3 groups, logrank=0.857).

Safety

Complications

	PMT n=23	PMT + CDT n=30	CDT n=45
Major complications			
Symptomatic pulmonary embolism	1	0	1
Gastrointestinal bleeding	0	1	0
Intracranial haemorrhage	0	0	1
Minor complications			
Ecchymosis	2	2	4
Haematoma	0	1	2

The patient with gastrointestinal bleeding had an endoscopic gastroduodenoscopy, which showed a duodenal ulcer that was coagulated.

The patient with intracranial haemorrhage died at 7 days after start of thrombolysis despite cessation of the urokinase infusion.

The symptomatic pulmonary embolisms happened in patients without an inferior vena cava filter. The patients had dyspnoea without hypotension. They recovered without further treatment other than inferior vena cava filter insertion and anticoagulation.

Abbreviations used: CDT, catheter-directed thrombolysis; PMT, percutaneous mechanical thrombectomy

Study 7 Bastianetto P (2014)

Details

Study type	**Case report**
Country	Brazil
Recruitment period	Not reported
Study population and number	**n=1** Patient with pulmonary embolism and stroke after percutaneous mechanical thrombectomy for acute deep vein thrombosis (DVT)
Age and sex	29 year old female
Patient selection criteria	Not applicable
Technique	Initial treated with continuous unfractionated heparin for 2 days was followed by percutaneous mechanical thrombectomy with an AngioJet device.
Follow-up	**6 months**
Conflict of interest/source of funding	Not reported

Key efficacy and safety findings

Case report – pulmonary embolism and stroke

The patient presented with pain and swelling of the left lower limb. Doppler ultrasonography showed acute venous thrombosis in the superficial femoral, common femoral and external iliac veins. Initial treatment was heparin, but the symptoms remained and 2 days later the thrombosis had progressed to the popliteal and great saphenous veins. Worsening oedema, continual pain, increased muscle tension and cyanosis indicated a case of *Phlegmasia cerulean dolens*. The patient was then treated by percutaneous mechanical thrombectomy.

During the procedure, the patient had intense dyspnoea, hypoxaemia, bradycardia and central and peripheral cyanosis. Massive pulmonary embolism was suspected and treatment with systemic alteplase was started.

On the third day after thrombectomy, the patient had right-sided hemiparesis and loss of vision, somnolence and aphasia. MRI revealed multiple areas of ischaemia bilaterally, following the territory of the middle cerebral artery and left posterior cerebral artery, and bilateral cerebellar infarcts. Treatment with heparin was stopped and a filter fitted in the inferior vena cava.

Transoesophageal echocardiogram showed a patent foramen ovale with flow diverted from the right to left atrium.

The patient was discharged after 28 days with a prescription for warfarin and elastic compression stockings.

Six months later, the patient had returned to her usual employment and the only remaining deficit was bilateral, regressive, hemianopsia.

Study 8 Yavuz A (2016)

Details

Study type	**Case report**
Country	Turkey
Recruitment period	Not reported
Study population and number	**n=1** Patient with May-Thurner syndrome treated by percutaneous mechanical thrombectomy
Age and sex	72 year old male
Patient selection criteria	Not applicable
Technique	The patient was initially started on heparin and a retrievable inferior vena cava filter was fitted. Percutaneous mechanical thrombectomy was done using an Aspirex device.
Follow-up	**1 week**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Case report – detachment of catheter tip during thrombectomy

The patient presented with swelling of the left leg for about 2 months, which had become more severe over the last 2 weeks. Doppler ultrasound revealed an extensive iliofemoral deep vein thrombosis. May-Thurner syndrome was diagnosed.

During the thrombectomy procedure, the distal tip of the device became detached while the shaft of the device was being pulled back through the stenotic segment of the common iliac vein. The shaft was removed, while the guidewire was left in place with the detached metallic part remaining within the proximal region of the stenotic iliac segment. A self-expandable stent was placed to widen the stenotic segment and a snare catheter was used to catch the detached tip. The tip was withdrawn from the popliteal vein through a 2 cm percutaneous incision.

A week later, the remaining thrombus was removed with a manual aspiration thrombectomy.

Study 9 Dass P (2015)

Details

Study type	**Case report**
Country	Australia
Recruitment period	Not reported
Study population and number	**n=1** Patient with left iliocaval deep vein thrombosis
Age and sex	40 year old male
Patient selection criteria	Not applicable
Technique	Initial treatment included anticoagulation with heparin. Percutaneous mechanical thrombectomy was done using the AngioJet system (Bayer Healthcare, US). An inferior vena cava filter was not used.
Follow-up	**7 days**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Case report – acute pancreatitis

The patient presented with a 5 day history of left lower quadrant abdominal pain and lower back pain, and clinical examination revealed a swollen left thigh. CT revealed an extensive left iliocaval deep vein thrombosis. The upper superficial femoral vein as well as the common femoral and iliac veins were occluded.

After percutaneous mechanical thrombectomy with an AngioJet system, stents were placed in the left common and external iliac veins and the right common iliac vein.

The day after the procedure, the patient had severe epigastric abdominal pain and he was diagnosed with acute pancreatitis. The severity was judged to be mild. No causative factors were identified and the patient was diagnosed with haemolysis-induced pancreatitis. The patient was managed supportively with analgesia, intravenous fluids and bowel rest. He was discharged after 7 days when all symptoms had resolved.

Study 10 Mathews JC (2011)

Details

Study type	**Case report**
Country	US
Recruitment period	Not reported
Study population and number	**n=1** Patient with deep vein thrombosis of the lower extremity
Age and sex	48 year old male
Patient selection criteria	Not applicable
Technique	Percutaneous mechanical thrombectomy (localised thrombolysis combined with mechanical thrombectomy; device not named).
Follow-up	**5 months**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Case report – Prolonged renal failure

The patient presented with a 1-week history of painful swelling of the left leg. Doppler examination revealed an extensive deep vein thrombosis and the patient had percutaneous mechanical thrombectomy. He was discharged on subcutaneous low-molecular weight heparin and warfarin.

Six days later, the patient presented to the emergency department with generalised weakness and decreased urine output. He was diagnosed with an acute kidney injury with evidence of acute tubular necrosis. The underlying cause was considered to be haemoglobulinuria.

In view of marked hyperkalaemia, the patient was started on haemodialysis. He continues to be dependent on haemodialysis 5 months later.

Validity and generalisability of the studies

- The authors of the large RCT noted that a high proportion of patients were ineligible for the trial, which largely reflected the exclusion of patients who would not have pharmacomechanical thrombolysis in clinical practice, but it could reduce the generalisability of the trial.[1]
- There are different devices available for this procedure, with different mechanisms of action, and there are variations in how the procedure is done.
- Definitions of 'percutaneous mechanical thrombectomy' differ between studies.
- The proportion of patients who had inferior vena cava filters inserted varied between studies.
- The proportion of patients who had a stent inserted after the procedure varied.
- A high proportion of patients across the studies had adjunctive procedures at the same time as the percutaneous mechanical thrombectomy.
- Patients had deep vein thromboses at different locations of their lower limb; outcomes from this procedure may differ according to the clot location.
- Most of the studies defined acute deep vein thrombosis as within 14 days, but some of the included studies also treated subacute and chronic deep vein thromboses.
- The imaging used to diagnose the degree of thrombus varied between the studies.

Existing assessments of this procedure

Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum on 'Early thrombus removal strategies for acute deep venous thrombosis' were published in 2012.[11] The guidelines include the following recommendations:

'1.1 We recommend use of precise anatomic terminology to characterize the most proximal extent of venous thrombosis as involving the iliofemoral veins, with or without extension into the inferior vena cava; the femoropopliteal veins; or isolated to the calf veins in preference to simple characterization of a thrombus as proximal or distal. (1A)

2.1. We suggest a strategy of early thrombus removal in selected patients meeting the following criteria (a) a first episode of acute iliofemoral deep venous thrombosis, (b) symptoms <14 days in duration, (c) a low risk of bleeding, and (d) ambulatory with good functional capacity and an acceptable life expectancy. (2C)

2.2 We recommend early thrombus removal strategies as the treatment of choice in patients with limb-threatening venous ischemia due to iliofemoral deep venous thrombosis with or without associated femoropopliteal venous thrombosis (phlegmasia cerulea dolens). (1A)

2.3. We recommend that patients with isolated femoropopliteal deep venous thrombosis be managed with conventional anticoagulation therapy because there is currently insufficient evidence to support early thrombus removal strategies in this patient population. (1C)

3.1. We suggest percutaneous catheter-based techniques (pharmacologic or pharmacomechanical) as first-line therapy for early thrombus removal in patients meeting the criteria in 1.1. (2C)

3.2. We suggest a strategy of pharmacomechanical thrombolysis be considered over catheter-directed pharmacologic thrombolysis alone if expertise and resources are available. (2C)'

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Ultrasound‑enhanced, catheter‑directed thrombolysis for deep vein thrombosis. NICE interventional procedures guidance 523 (2015). Available from http://www.nice.org.uk/guidance/IPG523

Technology appraisals

- Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism. NICE technology appraisal 354 (2015). Available from http://www.nice.org.uk/guidance/TA354

- Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism. NICE technology appraisal 341 (2015). Available from http://www.nice.org.uk/guidance/TA341
- Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism. NICE technology appraisal 327 (2014). Available from http://www.nice.org.uk/guidance/TA327
- Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism. NICE technology appraisal 261 (2012). Available from http://www.nice.org.uk/guidance/TA261

NICE guidelines

- Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. NICE guideline 89 (2018). Available from http://www.nice.org.uk/guidance/NG89
- Venous thromboembolic diseases: diagnosis, management and thrombophilia testing. NICE clinical guideline 144 (2012; last updated: November 2015). Available from http://www.nice.org.uk/guidance/CG144

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Adviser Questionnaires for percutaneous mechanical thrombectomy for peripheral venous occlusion were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 8 companies who manufacture a potentially relevant device for use in this procedure. NICE received 3 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Evidence on portal vein thrombosis has been excluded.
- Evidence on percutaneous aspiration thrombectomy alone has been excluded.
- Evidence on ultrasound‑enhanced, catheter‑directed thrombolysis for deep vein thrombosis has been excluded; there is existing Interventional Procedures guidance for this procedure.
- Ongoing trials
  - Outcome of Percutaneous Mechanical Thrombectomy to Treat Acute Deep Venous Thrombosis (NCT02959801); China; single group assignment; n=50; estimated study completion date December 2017.
  - Post-Market Clinical Follow-up Study With ASPIREX®S to Assess the Safety and Effectiveness in the Treatment of DVT (P-MAX) (NCT03116750); France, Germany, Ireland; prospective cohort; n=80; estimated study completion date October 2022.

References

1. Vedantham S, Goldhaber SZ, Julian JA et al. (2017) Pharmacomechanical Catheter-Directed Thrombolysis for Deep-Vein Thrombosis. New England Journal of Medicine 377: 2240–52
2. Sharifi M, Bay C, Mehdipour M et al. (2012) Thrombus obliteration by rapid percutaneous endovenous intervention in deep venous occlusion (TORPEDO) trial: midterm results. Journal of endovascular therapy 19: 273–80
3. Dietzek AM (2010) Isolated pharmacomechanical thrombolysis of deep venous thrombosis utilizing a peripheral infusion system: Manufacturer's Voluntary Registry Report 2005-2009. International Angiology 29: 308-316
4. Garcia MJ, Lookstein R, Malhotra R et al. (2015) Endovascular Management of Deep Vein Thrombosis with Rheolytic Thrombectomy: Final Report of the Prospective Multicenter PEARL (Peripheral Use of AngioJet Rheolytic Thrombectomy with a Variety of Catheter Lengths) Registry. Journal of Vascular & Interventional Radiology 26: 777–85
5. Lin PH, Zhou W, Dardik A et al. (2006) Catheter-direct thrombolysis versus pharmacomechanical thrombectomy for treatment of symptomatic lower extremity deep venous thrombosis. American Journal of Surgery 192: 782–8
6. Park KM, Moon IS, Kim JI et al. (2014) Mechanical thrombectomy with Trerotola compared with catheter-directed thrombolysis for treatment of acute iliofemoral deep vein thrombosis. Annals of Vascular Surgery 28: 1853–61
7. Bastianetto P, Pinto DM (2014) Pulmonary embolism and stroke associated with mechanical thrombectomy. Jornal Vascular Brasileiro 13: 137–41
8. Yavuz A, Andic C, Gur AK et al. (2016) Successful Retrieval of the Detached Porous Metallic Tip of a Mechanical Aspiration Catheter during Thrombectomy in a Case with May-Thurner Syndrome: A Case Report. International Journal of Angiology 25: e32–e36
9. Dass P, Robertson J, Muthu C et al. (2015) A rare cause of acute pancreatitis: Percutaneous mechanical rheolytic thrombectomy of deep venous thrombosis. Vascular 23: 545–49
10. Mathews JC, Pillai U, Lacasse A (2011) Prolonged renal failure post-percutaneous mechanical thrombectomy. NDT Plus 4: 241–3
11. Meissner MH, Gloviczki P, Comerota AJ et al. (2012) Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. Journal of Vascular Surgery 55: 1449–62

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	04/04/2018	Issue 4 of 12, April 2018
HTA database (Cochrane)	04/04/2018	Issue 4 of 4, October 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane)	04/04/2018	Issue 3 of 12, March 2018
MEDLINE (Ovid)	04/04/2018	1946 to Present with Daily Update
MEDLINE In-Process & MEDLINE Epubs ahead of print (Ovid)	04/04/2018	April 03, 2018
EMBASE (Ovid)	04/04/2018	1974 to 2018 Week 14
BLIC (British Library)	04/04/2018	n/a

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Venous thromboembolism/
2	Venous thrombosis/
3	((Venous or vein* or vascular*) adj4 (thromboembolism* or thrombosis* or thromboses or thrombus or thrombo embolism or "thrombo embolism" or occlus* or clot*)).tw.
4	(VTE or DVT).tw.
5	Postthrombotic syndrome/
6	((Postthrombotic or post-thrombotic or "post thromobotic") adj4 syndrome*).tw.

7	("paget schroetter" or paget-schroetter).tw.
8	(may-thurner or "may thurner").tw.
9	or/1-8
10	Mechanical Thrombolysis/
11	((mechanic* or pharmacomechanical or catheter-direct* or "catheter direct*" or catheter-mediat* or "catheter mediat*" or "catheter peripheral" or "catheter-peripheral") adj4 (thrombolys* or thrombectom* or thrombus or thrombi or clot* or remov* or disrupt* or retriev* or aspirat* or macerat*)).tw.
12	Catheterization, Peripheral/ and (Embolectomy/ or Thrombectomy/)
13	or/10-12
14	(indigo or angiojet or aspirex or cleaner or arrow or trellis or angiovac).tw.
15	13 or 14
16	9 and 15
17	animals/ not humans/
18	16 not 17

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Case series with fewer than 30 patients and case reports were excluded, unless they reported a unique safety event.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Arko FR, Arko MZ, Murphy EH (2011) Endovascular intervention for lower-extremity deep venous thrombosis. Vascular Disease Management 8: 71-79	Review	PMT offers the benefit of early thrombus removal, while limiting thrombolytic dosages and bleeding complications. PMT additionally offers a treatment option for patients with absolute contraindications for lytic therapy.	Not a systematic review; no meta-analysis.
Arko FR, Davis CM 3rd, Murphy EH et al. (2007) Aggressive percutaneous mechanical thrombectomy of deep venous thrombosis: early clinical results. Archives of Surgery 142: 513-8	Case series n=30 FU=mean 6 months	Venous patency was maintained in 27 patients (90%) and lower extremity valvular function was maintained in 22 (88%) of 25 treated lower limbs.	Larger or more recent studies are included.
Avgerinos ED, El-Shazly O, Jeyabalan G et al. (2016) Impact of inferior vena cava thrombus extension on thrombolysis for acute iliofemoral thrombosis. Journal of Vascular Surgery 4: 385-91	Case series n=102	Inferior vena cava (IVC) thrombosis does not have an impact on the technical success of thrombolysis in patients with iliofemoral DVT; the presence of a thrombosed IVC filter, though, may make failure more likely. Caval thrombosis may not affect primary patency but is associated with a lower incidence of PTS after successful lysis.	Study focuses on the impact of inferior vena cava thrombus extension on thrombolysis outcomes.
Avgerinos ED, Hager ES, Naddaf A. et al. (2015) Outcomes and predictors of failure of thrombolysis for iliofemoral deep venous thrombosis. Journal of Vascular Surgery 3: 35-41	Case series n=93 FU=mean 20 months	Overall rate of post-thrombotic syndrome (PTS) at 1, 2 and 3 years was 9%, 20% and 28%. 1 major complication: access site haematoma that needed surgical evacuation.	Results were reported together for CDT and PMT.
Avgerinos ED, Hager ES, Jeyabalan G et al. (2014) Inferior vena cava filter placement during thrombolysis for acute iliofemoral deep venous thrombosis. Journal of Vascular Surgery 2: 274-81	Case series n=80	IVC filters during thrombolysis should be used selectively in patients with preoperative clinical PE, in women and potentially in patients with multiple risk factors for DVT, or when stand-alone PMT is planned.	Study focuses on the use of IVC filters.

Bjarnason H, Kruse JR, Asinger DA et al. (1997) Iliofemoral deep venous thrombosis: safety and efficacy outcome during 5 years of catheter-directed thrombolytic therapy. Journal of Vascular & Interventional Radiology 8: 405-18	Case series n=77 FU=1 year	Current data suggest that catheter-directed thrombolytic therapy is safe and effective in achieving intermediate-term venous patency. The long-term clinical benefits of this procedure remain, however, to be established.	More recent studies are included.
Blackwood S, Dietzek AM (2016) Pharmacomechanical thrombectomy: 2015 update. Expert Review of Cardiovascular Therapy 14: 463-75	Review	PMT offers rapid recanalisation, avoids local wound complications associated with open venous thrombectomy and bleeding associated with intravenous systemic thrombolysis. Multiple devices are available.	Not a systematic review; no meta-analysis.
Comerota AJ, Grewal N, Martinez JT et al. (2012) Postthrombotic morbidity correlates with residual thrombus following catheter-directed thrombolysis for iliofemoral deep vein thrombosis. Journal of Vascular Surgery 55: 768-73	Case series n=71 FU=mean 19 months	In patients with iliofemoral DVT treated with catheter-based techniques of thrombus removal, postthrombotic morbidity is related to residual thrombus. When thrombus clearance was complete, the postthrombotic syndrome was avoided. Residual thrombus is associated with an increasing risk of postthrombotic syndrome.	Larger or more recent studies are included.
Culleton S, O'Sullivan G (2015) Novel methods of pharmacomechanical thrombolysis and thrombectomy for acute venous occlusions. Italian Journal of Vascular and Endovascular Surgery 22: 131-140	Review	There are a number of new devices available for pharmacomechanical thrombectomy and thrombolysis. Long term prospective randomised controlled trials to assess the long-term efficacy and safety of these devices are warranted.	Not a systematic review; no meta-analysis.
Dasari TW, Pappy R, Hennebry TA. (2012) Pharmacomechanical thrombolysis of acute and chronic symptomatic deep vein thrombosis: a systematic review of literature. Angiology 63: 138–45	Systematic review 8 case series (n=2,528)	Pharmacomechanical thrombolysis leads to the immediate resolution of clinical symptoms of DVT in the majority of patients. Pharmacomechanical thrombolysis may be a safe and novel method, when appropriate expertise and resources are available, for the treatment of symptomatic acute and chronic DVT.	No meta-analysis, more recent studies are included.
Dopheide JF, Sebastian T, Engelberger RP et al. (2018) Early clinical outcomes of a novel rheolytic directional thrombectomy technique for patients with iliofemoral deep vein thrombosis. Vasa 47: 56-62	Case series n=40 FU=6 months	In patients with iliofemoral DVT of native or stented vessels, rheolytic thrombectomy followed by stent placement appears to be effective and safe. The novel technique enables single-session DVT treatment in the majority of patients without the need for prolonged CDT.	Larger studies are included.
Dumantepe M, Uyar I (2018) The effect of	Case series	Rheolytic thrombectomy with or without stenting is superior to	Larger studies are included.

Angiojet rheolytic thrombectomy in the endovascular treatment of lower extremity deep venous thrombosis. Phlebology 33: 388–96	n=68 FU=12 months	anticoagulant therapy alone in terms of both ensuring venous patency and improving clinical symptoms. This technique is a safe, effective and easily performed method of endovascular treatment with a low rate of major treatment complications and shows promising clinical mid-term results.	
Escobar GA, Burks D, Abate MR et al. (2017) Risk of Acute Kidney Injury after Percutaneous Pharmacomechanical Thrombectomy Using AngioJet in Venous and Arterial Thrombosis. Annals of Vascular Surgery 42: 238–45	Non-randomised comparative study n=102	In this observational study, AngioJet is an independent risk factor for acute kidney injury. Concomitant open surgery and drop in hematocrit also raise the odds of acute kidney injury. Renal injury after AngioJet is under-reported in the literature, and may be related to haemolysis from the device.	Study focuses on the risk of acute kidney injury, which is already described as a safety outcome.
Ezelsoy M, Turunc G, Bayram M (2015) Early Outcomes of Pharmacomechanical Thrombectomy in Acute Deep Vein Thrombosis Patients. Heart Surgery Forum 18: E222-5	Case series n=50 FU=median 14 months	PMT with adjunctive thrombolytic therapy is an effective treatment modality in patients with significant DVT. Also, early thrombus removal in patients with acute DVT prevents development of postthrombotic morbidity.	Larger studies are included.
Fleck D, Albadawi H, Shamoun F et al. (2017) Catheter-directed thrombolysis of deep vein thrombosis: literature review and practice considerations. Cardiovascular Diagnosis & Therapy 7: S228-S237	review	Pharmacomechanical CDT (PCDT) techniques have the potential to reduce treatment time and associated healthcare costs. Numerous observational and retrospective studies have consistently shown a benefit of CDT plus anticoagulation over anticoagulation alone for prevention of PTS.	No meta-analysis, more recent studies are included.
Gaballah M, Shi J, Kukreja K et al. (2016) Endovascular Thrombolysis in the Management of Iliofemoral Thrombosis in Children: A Multi-Institutional Experience. Journal of Vascular & Interventional Radiology 27: 524-30	Case series n=57 FU=median 1.5 years	Techniques included CDT with PCDT (33%) or PMT (36%), CDT alone (27%), PCDT alone (5%) or with adjunctive angioplasty (55%), and stent placement (6%). There was 1 major complication of bleeding needing transfusion. Minor complications (bleeding) occurred in 7 patients (12%). 7 patients had repeat thrombolysis for recurrent thrombosis. The PTS rate was 59% per modified Villalta scale but only 2% per Villalta scale.	A variety of techniques were used.
Gagne P, Khoury T, Zadeh BJ et al. (2015) A Multicenter, Retrospective Study of the Effectiveness of the Trellis-8 System in the Treatment of Proximal Lower-Extremity Deep Vein Thrombosis. Annals	Case series n=139 FU=12 months	Patients with acute lower-extremity DVT involving the proximal veins can be safely and successfully treated with an isolated pharmacomechanical thrombolysis device (IPMTD). Major procedural bleeding was absent. The occurrence of severe PTS after	Larger or more recent studies are included.

of Vascular Surgery 29: 1633-41		primary treatment with Trellis-8 system IPMTD is low.	
Goktay AY, Senturk C (2017) Endovascular Treatment of Thrombosis and Embolism. Advances in Experimental Medicine & Biology 906: 195-213	review	Endovascular methods include intrasinus infusion of thrombolytics or heparin, balloon angioplasty, mechanical thrombectomy or a combination of different techniques. There is a higher rate or recanalisation with endovascular methods compared with other medical therapies.	Not a systematic review; no meta-analysis.
Grewal NK, Martinez JT, Andrews L et al. (2010) Quantity of clot lysed after catheter-directed thrombolysis for iliofemoral deep venous thrombosis correlates with postthrombotic morbidity. Journal of Vascular Surgery 51: 1209-14	Case series n=42 FU=mean 14 months	Patients with extensive DVT treated with catheter-based interventions to eliminate thrombus suffer relatively little postthrombotic morbidity. The degree of clot lysis directly correlates with long-term outcome. Improved QOL, the Villalta scale, and clinical class of CEAP are linearly correlated with the amount of clot resolution.	Larger or more recent studies are included.
Hager E, Yuo T, Avgerinos E et al. (2014) Anatomic and functional outcomes of pharmacomechanical and catheter-directed thrombolysis of iliofemoral deep venous thrombosis. Journal of Vascular Surgery 2: 246–52	Non-randomised comparative study n=79 FU=median 32 months	This study suggests that PMT as a stand-alone therapy is as effective as CDT with or without PMT in preserving valve function and preventing postthrombotic syndrome. Long-term physiologic and functional outcomes are comparable between the modalities, with preserved venous valve function in the majority of patients.	Larger or more recent studies are included.
Hager ES, Yuo T, Tahara R et al. (2013) Outcomes of endovascular intervention for May-Thurner syndrome. Journal of Vascular Surgery 1: 270-5	Case series n=70 FU=mean 30 months	Stenting of May-Thurner syndrome has proven to be safe, efficacious, and durable for up to 36 months in both the postthrombotic patient as well as those treated for oedema alone.	Larger or more recent studies are included.
Hilleman DE, Razavi MK (2008) Clinical and economic evaluation of the Trellis-8 infusion catheter for deep vein thrombosis. Journal of Vascular & Interventional Radiology 19: 377–83	Registry n=147	Thrombolysis in DVT with the Trellis-8 infusion catheter (TIC) is associated with a greater technical success rate, a lower rate of bleeding, and a lower cost than that reported for CDT. These preliminary results indicate that further evaluation of the TIC in the treatment of DVT is warranted.	Larger or more recent studies are included.
Huang CY, Hsu HL, Kuo TT et al. (2015) Percutaneous pharmacomechanical thrombectomy offers lower risk of post-thrombotic syndrome than catheter-directed thrombolysis in patients with acute deep vein thrombosis of the	Non-randomised comparative study n=39 FU=1 year	Both PMT and CDT are effective treatment modalities in patients with acute proximal DVT. Compared with CDT, PMT provides similar treatment success, but with lower risk of PTS at 1-year follow-up.	Larger or more recent studies are included.

lower limb. Annals of Vascular Surgery 29: 995-1002			
Janssen MC, Wollersheim H, Schultze-Kool LJ et al. (2005) Local and systemic thrombolytic therapy for acute deep venous thrombosis. Netherlands Journal of Medicine 63: 81-90	Review	No adequate randomised controlled trials have been done comparing CDT or PMT with conventional therapy. Given the current data, thrombolytic treatment, CDT or PMT should not be applied except in extraordinary cases. First, the long-term effectiveness in terms of reducing PTS, remains uncertain. Second, the risks of thrombolytic therapy and PMT are higher. Third, current conventional therapy is relatively inexpensive, convenient and safe.	More recent studies are included.
Jeyabalan G, Saba S, Baril DT et al. (2010) Bradyarrhythmias during rheolytic pharmacomechanical thrombectomy for deep vein thrombosis. Journal of Endovascular Therapy 17: 416-22	Case series n=57	The occurrence of bradyarrhythmias during peripheral venous use of the AngioJet device is poorly described in the literature. Routine pre-treatment with various agents is not recommended during use of the device in peripheral venous beds as the incidence of bradyarrhythmias appears to be very low, with no defined mechanism of onset.	Bradycardia is already described as a safety outcome.
Karageorgiou J, Fowler K, Vedantham S et al. (2016) Endovascular intervention for deep venous thrombosis in patients with inferior vena cava filters. Vascular Medicine 21: 459–66	Case series n=82 FU=mean 18 months	Interventions were technically successful in restoring flow in 87% of patients, and clinically successful in improving symptoms in 79% of patients. 24% of patients had complications (10% minor and 14% major). There were 2 deaths from intracranial haemorrhage. The probability of thrombosis-free survival at 1, 3, 6, 9 and 12 months was 0.85 (CI 0.74-0.93), 0.81 (CI 0.69-0.89), 0.74 (CI 0.62-0.83), 0.70 (CI 0.57-0.8) and 0.70 (CI 0.57-0.8), respectively.	The report focuses on patients with inferior vena cava filter-associated DVT. Outcomes were not reported separately for PMT.
Karahan O, Kutas HB, Gurbuz O et al. (2016) Pharmacomechanical thrombolysis with a rotator thrombolysis device in iliofemoral deep venous thrombosis. Vascular 24: 481-6	Case series n=67	New thrombolytic devices seem to reduce in-hospital mortality risks and may potentially decrease post-thrombotic morbidity.	Larger studies are included.
Karthikesalingam A, Young EL, Hinchliffe RJ et al. (2011) A systematic review of percutaneous mechanical thrombectomy in the treatment of deep venous thrombosis. European Journal of	Systematic review n=16 studies (481 patients)	Technical success of 82-100% was reported with Grade II or III lysis in 83-100% of patients. The different devices all appeared to be safe, with no reported procedure-related deaths or strokes and <1% incidence of symptomatic pulmonary embolism. Bleeding complications were reported in 6/16	No meta-analysis, more recent studies are included.

Vascular & Endovascular Surgery 41: 554–65		studies, in which 4-14% of patients required transfusion (global incidence 11/146 patients, 7.5%).	
Kiernan TJ, Cepeda B, Kiernan GD et al. (2009) Current status of pharmacological thrombolytic therapy and mechanical thrombectomy for the treatment of acute deep venous thrombosis. Cardiovascular & Hematological Agents in Medicinal Chemistry 7: 12-8	review	CDT with or without mechanical thrombectomy has been shown to be more effective and appears to be safer than systemic infusion. Although current guidelines do not advocate the routine use of thrombolysis or thrombectomy for acute DVT, the use of strict eligibility criteria in selecting high-risk patients such as those with massive ileofemoral DVT at risk of gangrene, has improved the safety and acceptability of this treatment.	No meta-analysis, more recent studies are included.
Kim HS, Patra A, Paxton BE et al. (2006) Catheter-directed thrombolysis with percutaneous rheolytic thrombectomy versus thrombolysis alone in upper and lower extremity deep vein thrombosis. Cardiovascular & Interventional Radiology 29: 1003-7	Non-randomised comparative study n=57	The mean urokinase dose required for CDT alone was 5.6 +/- 5.3 million units compared with 2.7 +/- 1.8 million units for urokinase CDT with rheolytic PMT (p=0.008). Complete clot lysis was achieved in 73% (29/40) of DVT treated with urokinase CDT alone compared with 82% (22/27) treated with urokinase CDT with rheolytic PMT.	Larger or more recent studies are included.
Kim HS, Patra A, Paxton BE et al. (2006) Adjunctive percutaneous mechanical thrombectomy for lower-extremity deep vein thrombosis: clinical and economic outcomes. Journal of Vascular & Interventional Radiology 17: 1099-104	Non-randomised comparative study n=45	Percutaneous CDT with rheolytic PMT is as effective as CDT alone for acute iliofemoral DVT but requires significantly shorter treatment and lower lytic agent dose, resulting in lower costs. Randomized studies to confirm the benefits of pharmacomechanical thrombolysis in the treatment of DVT are warranted.	Larger or more recent studies are included.
Kim IS, Jo WM, Chung HH et al. (2018) Comparison of clinical outcomes of pharmaco-mechanical thrombectomy in iliac vein thrombosis with and without May-Thurner syndrome. International Angiology 37: 12-18	Case series n=47 FU=median 48 months	Although May-Thurner syndrome (MTS) and DVT have different aetiologies, clinical results for both diseases using PMT were not significantly different. Therefore, PMT can be offered as an acceptable initial therapy in DVT patients with and without MTS.	Study focuses on the treatment of patients with May-Thurner syndrome. Larger studies are included.
Koksoy C, Yilmaz MF, Basbug HS et al. (2014) Pharmacomechanical thrombolysis of symptomatic acute and subacute deep vein thrombosis with a rotational thrombectomy device. Journal of Vascular & Interventional Radiology 25: 1895-900	Case series n=41 FU=3 months	At the end of the PMT procedure, 29 patients (71%) had complete (grade III) thrombus resolution. Grade I and II lysis were noted in 1 (2%) and 11 (27%) patients, respectively.	Larger or more recent studies are included.

Kuo TT, Huang CY, Hsu C P et al. (2017) Catheter-directed thrombolysis and pharmacomechanical thrombectomy improve midterm outcome in acute iliofemoral deep vein thrombosis. Journal of the Chinese Medical Association: JCMA 80: 72–9	Non-randomised comparative study n=61 FU=2 years	CDT and PMT have similar venous outcomes in patients with acute iliofemoral DVT, although post-thrombotic syndrome is less severe following PMT than after CDT.	Larger studies are included.
Lee KA, Ramaswamy RS (2017) Interventional approaches to deep venous thrombosis. Current Opinion in Cardiology 32: 679-686	Review	Short-term results from pharmacomechanical catheter-directed thrombolysis are promising; however, the long-term efficacy has yet to be established. The recently completed Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis trial will be a pivotal study in defining the future role of pharmacomechanical catheter-directed thrombolysis in prevention of PTS.	Not a systematic review; no meta-analysis. The ATTRACT trial is included in table 2 (study 1).
Li Q, Yu Z, Wang J et al. (2016) Long-term prognostic analysis of early interventional therapy for lower extremity deep venous thrombosis. Experimental & Therapeutic Medicine 12: 3545-3548	Non-randomised comparative study n=85 FU=median 19 months	Early catheter-directed invention of thrombolysis with thrombectomy for lower extremity DVT has good clinical effect in the short-term and long-term.	It is unclear how many patients were treated with PMT.
Lichtenberg M, Stahlhoff FW, Boese D. (2013) Endovascular treatment of acute limb ischemia and proximal deep vein thrombosis using rotational thrombectomy: A review of published literature. Cardiovascular Revascularization Medicine 14: 343-8	Review	Rotational thrombectomy is an effective and reliable means of doing thrombectomy in the arteries as well as veins.	More recent studies are included.
Lin PH, Ochoa LN, Duffy P (2010) Catheter-directed thrombectomy and thrombolysis for symptomatic lower-extremity deep vein thrombosis: review of current interventional treatment strategies. Perspectives in Vascular Surgery & Endovascular Therapy 22: 152–63	Review and case series n=178 (116 acute DVT) FU=mean 35 months	Based on the literature currently available, thrombolysis or percutaneous mechanical thrombectomy with treatment of underlying lesions for acute iliofemoral venous thrombosis should be considered for symptomatic patients with a reasonable life expectancy.	Larger or more recent studies are included.
Lindsey P, Echeverria A, Poi MJ et al. (2018)	Case series n=172	Iliac vein thrombotic occlusion is associated with an increased	Study focuses on the risk of

Thromboembolic Risk of Endovascular Intervention for Lower Extremity Deep Venous Thrombosis. Annals of Vascular Surgery 49: 247–54	FU=mean 28 months	thromboembolic risk in DVT intervention. Retrievable inferior vena cava filter should be considered when doing percutaneous thrombectomy in patients with iliac venous occlusion to prevent pulmonary embolism.	procedure-related thromboembolism.
Liu G, Li W, Lu X et al. (2017) Comparison of direct iliofemoral stenting with staged stenting after AngioJet rheolytic thrombectomy in patients with acute deep vein thrombosis. Journal of Vascular Surgery 25: 133–39	Case series n=91 FU=1 year	Both direct and staged stenting are effective treatment modalities in patients with acute proximal DVT. Compared with staged, direct provides similar treatment success and significant reductions in hospital lengths of stay but with more risk of PTS at 1-year follow-up.	Study focuses on direct versus staged stenting after thrombectomy.
Liu F, Lu P, Jin B (2011) Catheter-directed thrombolysis for acute iliofemoral deep venous thrombosis. Annals of Vascular Surgery 25: 707-15	Review	The development of CDT, the adjunctive techniques of PMT, and pharmacomechanical thrombolysis has improved the effectiveness of thrombolysis and also reduced bleeding complications.	More recent studies are included.
Malgor RD, Gasparis AP (2012) Pharmaco-mechanical thrombectomy for early thrombus removal. Phlebology (27 Suppl 1) 155-62	review	PMT is a feasible, safe and faster alternative to expedite the thrombolysis process in patients with venous thromboembolism.	More recent studies are included.
Martinez Trabal JL, Comerota AJ, LaPorte FB et al. (2008) The quantitative benefit of isolated, segmental, pharmacomechanical thrombolysis (ISPMT) for iliofemoral venous thrombosis. Journal of Vascular Surgery 48: 1532-7	Non-randomised comparative study n=43	Treatment time (55 vs 23 hours; p<0.0001) and dose of rt-PA (59.3 vs 33.4 mg; p=0.0009) were decreased and overall lytic success (60% vs 80%; p=0.0016) increased with ISPMT. Adjunctive venoplasty and stenting, complications, hospital length-of-stay (LOS), and intensive care unit LOS were similar between groups.	Larger or more recent studies are included.
Morrow KL, Kim AH, Plato SA 2nd et al. (2017) Increased risk of renal dysfunction with percutaneous mechanical thrombectomy compared with catheter-directed thrombolysis. Journal of Vascular Surgery 65: 1460-1466	Case series n=145 (92 venous thrombosis)	The use of PMT as a treatment for vascular thrombosis is associated with renal dysfunction. Patients treated with PMT require postoperative vigilance and renal protective measures.	Outcomes were not stratified by indication and intervention. Renal dysfunction is already included as a safety outcome.
Ng TT, Sigman M, Weaver FA (2014) Basic data related to thrombolytic therapy for acute venous thrombosis. Annals of	Review	PMT potentially reduces thrombolytic dose and infusion time while minimising bleeding complications. Current guidelines recommend the use of PMT for	More recent studies are included.

Vascular Surgery 28: 1039–44		venous thrombosis if expertise and resources are available.	
Protack CD, Bakken AM, Patel N et al. (2007) Long-term outcomes of catheter-directed thrombolysis for lower extremity deep venous thrombosis without prophylactic inferior vena cava filter placement. Journal of Vascular Surgery 45: 992-7	Case series n=69 FU=mean 2 years	Catheter-directed thrombolysis without universal prophylactic IVC filter placement is safe and effective in treating acute DVT. Pulmonary embolization did not occur during CDT. Selective rather than routine IVC filter placement is a safe and appropriate approach.	Results were presented for all patients, even though some were treated with CDT alone.
Raju S, Davis M, Martin A (2014) Assessment of residual thrombus after venous thrombolytic regimens. Journal of Vascular Surgery 2: 148-54	Case series n=67	Venographic patency can be established in most limbs with DVT or stent thrombosis by PMT alone. Venographic patency was a poor guide to the presence and extent of residual thrombus. Follow-up CDT was useful in significantly increasing complete clot clearance, but residual thrombus remained in over two-thirds of treated limbs overall.	Larger studies are included.
Rao AS, Konig G, Leers SA et al. (2009) Pharmacomechanical thrombectomy for iliofemoral deep vein thrombosis: an alternative in patients with contraindications to thrombolysis. Journal of Vascular Surgery 50: 1092-8	Case series n=43 FU=mean 5 months	PMT can be safely and effectively used for subacute iliocaval and iliofemoral DVT and in patients with contraindications for lytic therapy, resulting in improved functional outcomes relative to their debilitated state before the procedure.	Larger studies are included.
Rodriguez LE, Aboukheir-Aboukheir A, Figueroa-Vicente R et al. (2017) Hybrid operative thrombectomy is noninferior to percutaneous techniques for the treatment of acute iliofemoral deep venous thrombosis. Journal of Vascular Surgery 5: 177-184	Non-randomised comparative study n=71 FU=2 years	Percutaneous techniques (PT) and hybrid operative thrombectomy (HOT) have demonstrated good outcomes in the perioperative and intermediate periods. HOT is noninferior to PT as a technique for early thrombus removal and has the advantages that thrombus resolution is established in one operation and length of stay is significantly decreased. HOT avoids thrombolytic therapy, which may reduce major bleeding events.	Larger studies are included.
Sharifi M, Bay C, Skrocki L et al. (2012) Role of IVC filters in endovenous therapy for deep venous thrombosis: The FILTER-PEVI (filter implantation to lower thromboembolic risk in percutaneous endovenous intervention) trial. CardioVascular and Interventional Radiology 35: 1408-1413	RCT (filter versus no filter) n=141	Inferior vena cava filter implantation during percutaneous endovenous intervention (PEVI) reduces the risk of iatrogenic pulmonary embolism by eightfold without a mortality benefit. A selective approach may be exercised in filter implantation during PEVI.	Study focuses on the use of inferior vena cava filters. Another RCT by the same author is included (study 2).

Stanley GA, Murphy EH, Plummer MM et al. (2013) Midterm results of percutaneous treatment for acute and chronic deep venous thrombosis. Journal of Vascular Surgery 1: 52–8	Case series n=80 (52 acute DVT) FU=mean 3.8 years	Ultrasound-accelerated thrombolysis or percutaneous mechanical thrombectomy used alone or in tandem for treatment of acute and chronic deep venous thrombosis improves symptoms in the involved limb and maintains venous patency at midterm follow-up. Valvular function in the lower extremity is better preserved when sufficient treatment is provided acutely after the onset of symptoms.	The main results were not reported separately according to which intervention was used.
Strijkers RHW, Arnoldussen CWKP, Wittens CHA (2014) Thrombectomy without lysis: The future? Phlebology 29: 125-134	Review	Clot removal therapy will most likely become standard treatment in iliofemoral DVT, to prevent PTS.	Not a systematic review; no meta-analysis.
Sudheendra D, Vedantham S. (2018) Catheter-Directed Therapy Options for Iliofemoral Venous Thrombosis. Surgical Clinics of North America 98: 255-265	Review	CDT combined with mechanical thrombectomy allows for greater thrombus removal and decreased use of thrombolytics. The risk of acute kidney injury from haemoglobulinuria during PMT can be reduced with periprocedural hydration, alkalinisation of urine and diuresis.	Not a systematic review; no meta-analysis.
Vedantham S (2018) Catheter-directed thrombolysis to avoid late consequences of acute deep vein thrombosis. Thrombosis Research 164: 125–8	Review	CDT and pharmacomechanical CDT offer rapid thrombus removal, and likely faster relief of initial acute DVT symptoms compared with anticoagulation alone, at the price of an increase in major bleeding and the rate risk of devastating bleeding.	Not a systematic review; no meta-analysis.
Vedantham S, Sista AK, Klein SJ et al. (2014) Quality improvement guidelines for the treatment of lower-extremity deep vein thrombosis with use of endovascular thrombus removal. Journal of Vascular and Interventional Radiology 25: 1317-1325	Review	Successful endovascular thrombus dissolution is most likely for patients whose DVT symptoms began within the preceeding 2 weeks. It is important and feasible to do longitudinal follow-up in DVT thrombolysis populations.	More recent studies are included.
Vogel D, Walsh ME, Chen JT et al. (2012) Comparison of vein valve function following pharmacomechanical thrombolysis versus simple catheter-directed thrombolysis for iliofemoral deep vein thrombosis. Journal of Vascular Surgery 56: 1351-4	Case series n=69	In patients undergoing catheter-based intervention for iliofemoral DVT, PMT does not adversely affect valve function compared with CDT alone. A higher than expected number of patients had reflux in their uninvolved limb.	Larger or more recent studies are included.
Wang W, Wu Y, Fang T et al. (2017) Thrombectomy Combined with Indwelling-	Non-randomised	Thrombectomy plus CDT yields a higher venous patency rate and lower recurrence rate than pure	Larger studies are included.

catheter Thrombolysis is more Effective than Pure Thrombectomy for the Treatment of Lower Extremity Deep Venous Thrombosis. Open Medicine 12: 177-183	comparative study n=40 FU=3 to 6 months	thrombectomy for the treatment of lower extremity DVT.	
Wang CN, Deng HR (2018) Percutaneous endovenous intervention plus anticoagulation versus anticoagulation alone for treating patients with proximal deep vein thrombosis: a meta-analysis and systematic review. Annals of Vascular Surgery 14: 39–48	Systematic review and meta-analysis 4 RCTs	Percutaneous endovenous intervention plus anticoagulation reduced the occurrence of PTS, recurrent DVT, and venous obstruction. Another advantage is an increased patency rate at 6 and 12 months. The disadvantage is an increased occurrence of major bleeding events.	Only 1 of the RCTs included PMT. The other 3 RCTs used CDT or percutaneous aspiration thrombectomy.
Ye K, Qin J, Yin M et al. (2017) Outcomes of Pharmacomechanical Catheter-directed Thrombolysis for Acute and Subacute Inferior Vena Cava Thrombosis: A Retrospective Evaluation in a Single Institution. European Journal of Vascular & Endovascular Surgery 54: 504–12	Case series n=54 FU=mean 26 months	The primary technical success and the stent-assisted technical success were 63% (34/54) and 100% (54/54) respectively. There were 11 patients (20%) with immediate recurrent thrombosis. Minor bleeding complications occurred in 7 patients, and 1 patient with major bleeding needed a blood transfusion. The occurrence of PTS was 13% (7/54). The 3-year primary and secondary iliocaval patency was 63% and 81%, respectively.	Larger studies are included.
Yuksel A, Tuydes O (2017) Midterm Outcomes of Pharmacomechanical Thrombectomy in the Treatment of Lower Extremity Deep Vein Thrombosis With a Rotational Thrombectomy Device. Vascular & Endovascular Surgery 51: 301–306	Case series n=46 FU=mean 16 months	No serious adverse event related to procedure and mortality was observed. Reocclusion=17.5% Venous patency rates of patients at 1-, 3-, 6-, and 12-month follow-up visits were 95%, 92.5%, 89.7%, and 79.5%, respectively. Postthrombotic syndrome-free survival rate was 67.5%.	Larger studies are included.