A Systematic Review of Percutaneous Mechanical Thrombectomy in the Treatment of Deep Venous Thrombosis

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Abstract  Background: In selected cases of deep vein thrombosis (DVT), catheter-directed thrombolysis (CDT) may be superior to conventional treatment with anticoagulation alone, as it can prevent DVT recurrence and the development of post-thrombotic syndrome (PTS). Percutaneous mechanical thrombectomy (PMT) devices offer a minimally invasive adjunctive strategy and the data on these emerging technologies require review.

Objectives: To review the evidence for PMT devices in DVT in terms of case selection, technical feasibility and procedural outcomes.

Methods: Medline, trial registries, conference proceedings and article reference lists were searched to identify case series reporting PMT device use. Data were extracted for review.

Results: 16 retrospective case series have reported the use of rheolytic, rotational, or ultrasound-assisted PMT in a total of 481 patients. No randomised trials were available. 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 PE. Bleeding complications were reported in 6/16 studies, in which 4–14% of patients required transfusion (global incidence 11/146 patients, 7.5%).

Conclusion: PMT appears feasible and safe, though the level of evidence available is poor. Major RCTs and registry data are required to determine the economic and clinical benefit of various devices used alone or in combination, for differing thrombus characteristics and...
Introduction

Deep venous thrombosis (DVT) is a major public health challenge, representing a significant clinical and economic disease burden on healthcare systems. In the UK alone, approximately 59,000 new cases of DVT arise per year and venous thromboembolism (VTE) accounts for more deaths than the composite mortality of breast cancer, AIDS and road traffic accidents. Up to 21% of DVT may lead to pulmonary embolism (PE), a potentially life-threatening complication. Furthermore, DVT may cause severe morbidity in the short-term from phlegmasia caerulea dolens (PCD) and in the longer-term from chronic venous hypertension leading to the post-thrombotic syndrome (PTS). Up to 10% of patients with DVT develop venous ulceration. The resulting economic burden of patients with previous DVT is significant, costing the UK approximately £640 million per annum.

The conventional treatment of acute DVT is immediate anticoagulation with low molecular-weight heparin or unfractionated heparin, followed by a period (3–6 months) of oral anticoagulation with warfarin. This aims to prevent thrombus propagation and to reduce the risks of PE and DVT recurrence. However, anticoagulation does not have significant fibrinolytic activity and patients with severe, extensive, proximal DVTs remain at high risk of developing subsequent PTS and potentially ulceration as demonstrated in natural history studies. In cases of DVT treated with anticoagulation alone, natural history studies have shown that early spontaneous clot lysis frequently resulted in preservation of valvular function (which intuitively might reduce post-thrombotic morbidity). Evidence supporting the benefit of early clot removal has largely been acquired after open thrombectomy; a Scandinavian randomized controlled trial reported improved patency, lower venous pressures, less oedema and fewer post thrombotic symptoms at 10 years’ follow-up in patients randomised to open thrombectomy compared to anticoagulation alone. Early lysis or thrombectomy has been proposed as an attractive option in the treatment of DVT as this might prevent venous obstruction, valvular incompetence and venous hypertension from developing. This in turn might reduce the incidence or severity of PTS and reduce the incidence of subsequent venous ulceration.

However, this hypothesis of early clot removal in acute DVT has not been conclusively proven. A number of multicentre randomised controlled trials are currently underway to investigate the effectiveness of catheter-directed thrombolysis (CDT) in the management of DVT. Other techniques to reduce the clot burden are surgical thrombectomy that exposes patients to anaesthetic, procedural and infective risks, or percutaneous mechanical thrombectomy (PMT). PMT devices offer an appealing, endovascular solution for aggressive thrombus removal and may be used as an adjunct to, or in place of, CDT. PMT may attenuate the morbidity of CDT by permitting a dose reduction in thrombolytic drug administration. A number of devices exist and the emerging data have not been subject to critical analysis. The aim of this review was to appraise the growing evidence base for PMT in the treatment of CDT.

Methods

The objective of this article was to review the case selection, technical aspects, safety outcomes and procedural outcomes reported after PMT in patients with DVT. An electronic search was performed using the Embase and Medline databases. The free-text search terms “thrombolysis”, “thrombectomy”, “DVT” and “percutaneous” and MeSH headings “Surgical Procedures, Minimally Invasive”[-MeSH], “Thrombectomy/”[MeSH], “Thrombolytic Therapy/”[MeSH] and “Venous Thrombosis/”[MeSH] were used in combination with the Boolean operators AND or OR. The reference lists of articles obtained were also searched to identify further relevant citations. Finally, the search included the Current Controlled Trials Register (www.controlled-trials.com), the DARE database and the Cochrane Database of Controlled Trials.

Studies reporting open surgical thrombectomy rather than endovenous thrombectomy were excluded. One study was withdrawn from publication for unstated reasons and was therefore excluded. Data published previously by the same group were excluded, and studies in which data for PMT were not discernible from data for patients undergoing CDT without PMT were excluded.

The literature review conformed to PRISMA statement standards. Quantitative pooled meta-analysis was not performed due to the heterogeneity of study design, treatment methodology and patient population in studies that were included in qualitative review. Data were collected regarding case selection (age of thrombus, incidence of PCD, mean age of patients, co-morbidity), technique (veins treated, access vessel, device used) safety outcomes (PE, death, stroke and bleeding requiring transfusion) and procedural outcomes (clinical success, technical success, DVT recurrence, post-thrombotic syndrome, reduction in the dose of, or need for, thrombolysis).

Results and Discussion

The literature search identified 66 articles, of which 50 were excluded (Fig. 1, PRISMA Flowchart). A total of 16 retrospective case series of PMT were analysed, which reported 511 procedures in 481 patients. 2/16 studies were retrospective comparative (cohort) studies of PMT alongside CDT versus CDT alone. There were no published
randomised controlled trials (RCTs) of PMT (with or without CDT) compared to standard treatment (anticoagulation alone). No prospective or population level data were available. Four ongoing studies were identified, which have not published their results to date: the PEARL registry (NCT00778336), the ATTRACT trial28 (NCT00790335), the CAVA trial (NCT00970619) and the SONIC I Safety and Efficacy study (NCT00640731).

**Case selection**

Guidelines from the American College of Chest Physicians (ACCP) suggest that PMT provides greatest benefit in young and functionally active patients, with extensive and proximal thrombus (IVC and ilio-femoral), who have an acute presentation of DVT (<14 days, or with phlegmasia caerulea dolens).29 The mean age of patients selected for PMT in the literature supported this recommendation and ranged from 43 to 57 years, with few reported co-morbidities (Table 1). The prevalence of malignancy (8–42%) reflects the prothrombotic nature of the disease, which leads to DVT in 15% of cancer sufferers,30 although few data are available to examine the effect of malignancy on success or long-term benefit after PMT. Despite recommendations that clot removal is limited to proximal IVC and iliofemoral DVT,29,31 many studies reported a mixed cohort of IVC and proximal iliofemoral DVT with femoropopliteal DVT, or included arm DVT in case selection (Table 1). Although the anatomical site of DVT is important and expert consensus suggests that DVT behaves differently at different sites,29 the heterogeneity and poor quality of available data prevented specific analysis of the effect of DVT location on outcomes from PMT.

Thrombus age appeared to correlate negatively with the success of lysis and many studies reported poorer clinical and technical outcomes in patients with thrombi of more than 10–14 days age32–34 with better outcomes in patients with acute clots. However, none of the cohort studies was powered, or designed, to assess the effect of the duration of DVT on outcome from PMT. It has previously been suggested that thrombolysis for DVT should commence within 10 days of symptoms to ensure optimal venous recanalisation, preservation of valve function and symptom relief.29 This suggestion was not supported by the results of a recent randomised controlled trial: the CaVenT study demonstrated a significant increase in patency at 6 months’ follow-up after CDT for iliofemoral DVT in patients treated up to 21 days after the onset of symptoms.35 Furthermore, the ATTRACT trial, which will report on outcomes of
| Author, year | No. of patients | Age Median (range) or mean ± s.d. (years) | Follow-up | Co-morbidity | % Phlegmasia | Age of clot | Vein treated | Access vessel | Device | % Lysis, technical and clinical success | % Post-thrombotic syndrome | DVT recurrence | % Needing concurrent thrombolysis or dose reduction in thrombolysis | Length of stay |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gandini, 1999<sup>30</sup> | 8 | 57.4 (24 – 75) | 3–24 months | 25% Hypertension (2/8) 12.5% Recent Myocardial Infarction (1/8) 12.5% Obesity (1/8) 12.5% Cerebral metastasis (1/8) | 12.5% (1/8) | Clinical history < 2 weeks | 62.5% Unilateral Iliac Vein Thrombosis + IVC Thrombosis (5/8) 37.5% IVC Thrombosis (3/8) | Right IJV | ATD | 75% Complete (6/8) 12.5% Partial (1/8) 12.5% Failure (1/8) | 12.5% (1/8) | 0 | — |
| Delomez, 2001<sup>14</sup> | 18 | 37.6 ± 16/1 | 29.6 months | 16.7% Malignancy (3/18) 22.2% Hypercoagulability (4/18) 22.2% Oral contraceptive pill (4/18) | 0 | 45.3 ± 76.3d (Excluding 3 old clots > 2 months 11.3 ± 6.9d) | 16.7% Iliofemoral (3/18) 27.8% IVC (5/18) 55.6% IVC + Iliac (10/18) | 83.3% ATD CFV (15/18) 16.7% PV (3/18) | 56% (10/18) symptom resolution 85% technical success | 5.6% (1/18) | 0 | — |
| Kasirajan, 2001<sup>17</sup> | 17 | 41 ± 20 | 8.9 ± 5.3 months | 41.2% Malignancy (7/17) 5.9% Hypercoagulability (1/17) 17.6% May-Thurner (3/17) | 0 | — | 5.9% IVC (1/17) 52.9% Iliofemoral (9/17) 5.9% Iliofemoropopliteal (1/17) 17.6% IVC + Iliofemoral (3/17) | CFV or PV Angiojet with UK, rt-PA or reteplase | 82% technical and clinical success Grade III: 24% Grade II: 35% Grade I: 41% | 0 | 49% recurrence at 11 months CDT used for 9/13 patients with <90% thrombolysis by PMT alone | — |
| Vedantham, 2002<sup>22</sup> | 20 (22 procedures, 28 limbs) Group A: (n = 4) acute thrombus during stent placement Group B: (n = 9) PMT before CDT Group C: (n = 15) PMT after CDT | 52.6 ± 16.4 | — | — | — | 18% (4/22) Oedema (14/22) 57% One leg (16/28) 75% PV (21/28) | 75% (21/28) 11% CFV (3/28) 32% IVC involved (9/28) 43% Unilateral Iliofemoral (12/28) 4% Unilateral Femoropopliteal (1/28) | 7 Angiojet 2 Tretorola 1 Oasis with UK, rt-PA or reteplase | 24 ATD 7 Angiojet 2 Tretorola 1 Oasis 12.5% | Group C treated with PMT after CDT | 1/28 (4%) | 1/28 (4%) | — |

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<table>
<thead>
<tr>
<th>Author, year</th>
<th>No. of patients</th>
<th>Age Median (range) or mean ± s.d.</th>
<th>Follow-up</th>
<th>Co-morbidity</th>
<th>% Phlebitis</th>
<th>Age of clot</th>
<th>Vein treated</th>
<th>Access vessel</th>
<th>Device</th>
<th>% Lysis, technical and clinical success</th>
<th>Post-thrombotic syndrome</th>
<th>% Needing concurrent thrombolysis or dose reduction in thrombolysis</th>
<th>Length of stay</th>
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<tbody>
<tr>
<td>Vedantham, 2004</td>
<td>33</td>
<td>18 (23 limbs)</td>
<td>11.1% Factor V Leiden (2/18)</td>
<td>11.1% malignancy (2/18)</td>
<td>27.8% oral contraceptive pill (5/18)</td>
<td>78% (14/18) symptoms &lt;10d</td>
<td>22% (4/18) symptoms &gt;10d</td>
<td>43.5% Unilateral iliofemoral (10/23)</td>
<td>21.7% IVC + bilateral 8.7% LV iliofemoral (5/23)</td>
<td>13% IVC + Unilateral iliofemoral (3/23)</td>
<td>87% PV (20/23)</td>
<td>Helix, Routine placement of Wallstent, reteplase</td>
<td>100% technical success</td>
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<tr>
<td>Lin, 2006</td>
<td>93 (98 procedures)</td>
<td>45 ± 12 (PMT) 49 ± 10 (CDT)</td>
<td>13 ± 6.2 months</td>
<td>PMT vs. CDT: Malignancy 9/49 (18%) vs. 6/64 (1%) Hypercoagulable state 6/49 (12%) vs. 8/44 (18%) May-Thurner syndrome 10/49 (20%) vs. 9/44 (20%) Recent operation 5/49 (10%) vs. 3/44 (7%) Oral contraceptive 4/49 (8%) vs. 6/44 (14%)</td>
<td>7.7% (4/52) PMT 10.9% (5/46) CDT</td>
<td>From US diagnosis to intervention: PMT 15d (0–34) CDT 13d (0–31)</td>
<td>100% Iliac or Iliofemoral thrombosis 0% solitary IVC thrombus</td>
<td>100% CFV</td>
<td>Angiojet with reteplase, rt-PA, or UK</td>
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<td>Lee, 2006</td>
<td>52 (25 with CDT)</td>
<td>56 (28–64)</td>
<td>16months (12–33)</td>
<td>80% May-Thurner syndrome (20/25) 8% Malignancy (2/25)</td>
<td>4% (1/25)</td>
<td>100% extensive iliofemoral</td>
<td>100% PV</td>
<td>Trerotola</td>
<td></td>
<td></td>
<td></td>
<td>100% clinical and technical success 85% one-year patency</td>
<td>100% technical success</td>
</tr>
<tr>
<td>Arko, 2007</td>
<td>30</td>
<td>50.9 ± 18</td>
<td>6.2 months (3–24)</td>
<td>33% (10/30) hypercoagulable state</td>
<td>–</td>
<td>5.7d (3–14d) after diagnosis</td>
<td>47% iliofemoral (14/30) 20% iliopopliteofemoral (6/30) 17% femoropopliteal (5/30) 17% subclavian (5/30)</td>
<td>83% PV (25/30) 17% CV (5/30)</td>
<td>18 Trellis-8 12 Angiojet 17/30 wallstent</td>
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<td>Bush, 2004</td>
<td>23</td>
<td>52 ± 6</td>
<td>10.2 months (3–26)</td>
<td>21.7% Malignancy (5/23) 17.4% May-Thurner (4/23) 13% Hypercoagulable state (3/23)</td>
<td>–</td>
<td>14d (0–34d) after USS diagnosis</td>
<td>100% PV (23/23)</td>
<td>Angiojet with UK, rt-PA or reteplase</td>
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<td></td>
<td>74% Clinical Success (17/23) Grade III lysis 65% (15/23) Grade I/II lysis 35% (8/23)</td>
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<td>Cynamon, 2006&lt;sup&gt;46&lt;/sup&gt;</td>
<td>24</td>
<td>43 (16–86)</td>
<td>5.3 months — (minimum 1 month)</td>
<td>12.5% (3/24)</td>
<td>83% (20/24) symptoms &lt;14d 17% (4/24) &gt;14d 86% (12/14) symptoms &lt;14d (median 5d, range 2–14) 14% &gt;14d (median 18d, range 15–21) 72% symptoms &lt;14d, 18% &gt;14d</td>
<td>62.5% (15/24) unilateral Iliac + IVC 37.5% (9/24) Iliofemoropopliteal 3% Femoropopliteal (1/14) 7% Iliofemoropopliteal (3/14)</td>
<td>CFV or PV</td>
<td>Angiojet, rt-PA, urokinase</td>
<td>Grade III 50% (12/24) Grade II or I 50% (12/24)</td>
<td>8.3% (2/24) 33.3% (8/24) required CDT</td>
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<td>Gasparis, 2009&lt;sup&gt;45&lt;/sup&gt;</td>
<td>14</td>
<td>40 (19–58)</td>
<td>24 months (13–69)</td>
<td>21% hypercoagulable (3/14)</td>
<td>83% (20/24) symptoms &lt;14d 17% (4/24) &gt;14d 86% (12/14) symptoms &lt;14d (median 5d, range 2–14) 14% &gt;14d (median 18d, range 15–21) 72% symptoms &lt;14d, 18% &gt;14d</td>
<td>62.5% (15/24) unilateral Iliac + IVC 37.5% (9/24) Iliofemoropopliteal 3% Femoropopliteal (1/14) 7% Iliofemoropopliteal (3/14)</td>
<td>CFV or PV</td>
<td>Angiojet, rt-PA, urokinase</td>
<td>Grade III lysis 64% (9/14) Grade II or I lysis 36% (5/14) 100% technical success 86% clinical success (12/14)</td>
<td>7% (1/14) 57% required CDT (8/14)</td>
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<tr>
<td>Jackson, 2005&lt;sup&gt;52&lt;/sup&gt;</td>
<td>28 (21 thrombectomy)</td>
<td>Range 22–80</td>
<td>Mean 15.5 months —</td>
<td>—</td>
<td>62% symptoms &lt;14d, 18% &gt;14d</td>
<td>63% iliofemoral, 57% infrainguinal</td>
<td>PT/PT + CDT: 30%/35% Brachiosubclavian 70%/65% Iliofemoral</td>
<td>PT/PT + CDT: 28.5%/30% Iliofemoral 28% (6/21) 90% thrombus removal 19% (4/21) 60–90% thrombus removal 52.4% (11/21) &lt;60% thrombus removal</td>
<td>28.5% (6/21) 0 0 21/28 CDT + PMT 7/28 CDT alone</td>
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<td>Kim, 2006&lt;sup&gt;46, 27&lt;/sup&gt;</td>
<td>67 limbs (57 patients)</td>
<td>PMT 43.1 ± 13.8 CDT 45 ± 16.3</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>PMT/CDT: Cancer 28%/59% Thrombophilia 18%/7% Symptoms &lt;14d</td>
<td>—</td>
<td>—</td>
<td>Symptoms &lt;14d PMT/CDT: 30%/35% Brachiosubclavian 70%/65% Iliofemoral</td>
<td>PT/PT + CDT: Grade III 81%/73% p = 0.395 Grade II 19%/15% p = 0.704 Grade I 0%/13% p = 0.056 91% &gt; 50% lysis</td>
<td>0 0 Significant reduction in urokinase dose with PMT p = 0.008 (2.7 ± 1.8 vs. 5.6 ± 5.3 million units)</td>
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<td>Rao, 2009&lt;sup&gt;51&lt;/sup&gt;</td>
<td>43</td>
<td>48.4 ± 16.6</td>
<td>5 ± 4.8 months</td>
<td>19% malignancy (8/43) 35% hypercoagulable (15/43) 9.3% (4/43) 35 lower limb (8/35 IVC involvement) 8 upper limb</td>
<td>35 lower limb (8/35 IVC involvement) 8 upper limb</td>
<td>77% PV, 14% BV, 7% LJ, 2% SV</td>
<td>Angiojet (12) Trellis-8 (13) Both (17) With rt-PA ATD (10/16) Straub (6/16) with UK</td>
<td>0 0 Significant lysis 91% &gt; 50% p = 0.056</td>
<td>0 37% underwent — CDT after PMT due to incomplete lysis with PMT</td>
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<tr>
<td>Shi, 2009&lt;sup&gt;51&lt;/sup&gt;</td>
<td>16 (18 limbs)</td>
<td>53.3 ± 15.6</td>
<td>—</td>
<td>18.8% Malignancy (3/16) 25% Hypercoagulability (4/16) 4.9 ± 3.9d</td>
<td>Iliofemoropopliteal 14/16 IVC + Iliofemoropopliteal 2/16</td>
<td>PV</td>
<td>Angiojet (12) Trellis-8 (13) Both (17) With rt-PA ATD (10/16) Straub (6/16) with UK</td>
<td>55.5% Grade III (10/18) 33% Grade II (6/18) 11% Grade I (2/18) 75% clinical success (12/16)</td>
<td>1/18 (5.6%) 1/18 (5.6%) 100% received concurrent urokinase</td>
<td>7 ± 2.5 d</td>
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combined PMT and CDT in the United States, has used 14 days as the cut-off for recruitment. However, the duration of symptoms is known to be a poor measure of thrombus volume and characteristics. Furthermore, thrombus itself may be heterogeneous, with older and fresher components. Although the ATTRACT trial will add to consideration of optimal timing for intervention in the setting of acute proximal thrombosis based on symptom duration, the effect of thrombus heterogeneity and actual thrombus age may be difficult to elucidate.

### Device selection and technical considerations

PMT devices are categorised as rotational, rheolytic, or ultrasound-enhanced and were most commonly inserted into the ipsilateral popliteal vein (Table 1), although a variety of access vessels have been reported successfully including the posterior tibial vein.

Rotational devices, such as the Amplatz Thrombectomy Device (ATD, or Helix, Amplatz Thrombectomy Device (ATD); Microvena, White Bear Lake, Minneapolis, USA), Straub Rotarex (Straub Medical, Wangs, Switzerland) and the Tretorotola Device (Tretorotola Percutaneous Thrombectomy Device; Arrow International, Reading, Philadelphia, USA) employ a high-velocity rotating helix or nitinol cage to macerate thrombus. The Trellis device (Trellis-8; Bacchus Vascular, Santa Clara, California, USA) employs a sinusoidal nitinol wire to disintegrate thrombus infused with thrombolytic agent between proximal and distal balloons for control and to prevent PE. This category of PMT device has the potential for endothelial damage, though no comparative studies have been performed to analyse whether this translates to a higher risk of recurrent thrombosis in clinical practice compared to rheolytic devices.

The Angiojet device (Angiojet; Possis, Minneapolis, USA) uses a rheolytic mode of action. The "Power Pulse" technique is used to spray the thrombus with thrombolytic drug. The device then generates a high-pressure saline jet to create a pressure gradient, resulting in rheolytic thrombectomy with aspiration of the softened thrombus into the catheter, where it is fragmented by the saline jets. A possible advantage of the Angiojet device is that there is no contact of a rotational component with the vessel wall. However, its use of high-pressure saline jets carries a theoretical risk of haemolysis and the release of adenosine and potassium. This has been linked to the incidence of bradyarrhythmia in cardiac applications of the device, or haemoglobinuria. Presentation of the mid-term results of the PEARL registry revealed that 1/332 patients experienced a serious adverse bradycardic episode, which was classified as "possibly related" to the use of the Angiojet system by the investigating physician. To lessen the risk of haemolysis, a shorter duration of action has been recommended; some authors advise multiple shorter activations with each pass limited to 5 s. Isolated reported of secondary pancreatitis and renal failure further caution against prolonged device use.

Ultrasound-enhanced devices, such as the EKOS Endwave (EKOS Corporation, Bothell, WA, USA) and Omniwave (Omnisonics Medical Technologies, Wilmington, MA, USA)
utilise catheters containing multiple ultrasound transducers, which radially emit high-frequency, low-energy ultrasound energy. The ultrasonic energy expands and thins the fibrin component of thrombus, exposing plasminogen receptor sites, which enhances the transport of thrombolytic agents within target thrombus.45 Although this technique may be associated with fewer haemolytic effects than rheolytic thrombectomy46 and has a lower potential for endothelial damage than rotational thrombectomy devices, the omission of a mechanical mode of action may lead to longer thrombolytic infusion times.

The importance of PMT device selection requires focussed investigation to determine any contribution of differences in endothelial damage on DVT recurrence, of differences in haemolysis on cardiac side-effects and of differences in mechanism on the extent to which thrombolytic times can be minimised. The benefit of differences in mechanism on the extent to which thrombolytic times can be minimised. The benefit of differences in mechanism on the extent to which thrombolytic times can be minimised. The benefit of differences in mechanism on the extent to which thrombolytic times can be minimised.

Procedural outcomes

Early procedural outcomes were encouraging and the series reviewed reported technical success of 82–100% (Table 1), demonstrating the feasibility of PMT. The early clinical success of CDT or PMT has been quantified by a 3-tiered grade to reflect postoperative luminal patency. Grades II or III represent a satisfactory therapeutic outcome of at least 50% luminal patency post-lysis,47 because this value has been shown to correlate with significantly improved 1-year patency.47 Grade II or III patency was reported in 83–100% of patients who underwent the combined use of PMT with CDT. This provides encouraging evidence for PMT, although there was significant heterogeneity in the methodology used to report thrombus lysis by different studies (Table 1).

An important drawback of phlebographic patency as an indicator of procedural success is that this scale does not account reliably for the potential effect of residual thrombus load; the associated partial luminal obstruction which is difficult for physicians to quantify.48 Intravascular ultrasound allows the detection of residual stenosis and external compression after treatment of DVT, yet was not reported in the series reviewed. Furthermore, data to report clinical outcome, using validated systems such as the Villalta score,49 or quality of life, are lacking. Further evidence is required to ascertain the effects of PMT on these important clinical outcomes.

Early studies reported the use of PMT without adjunctive CDT44,50 and two later studies noted successful lysis in the subgroup of patients treated solely with PMT due to contraindications to thrombolysis.51,52 Both Rao et al and Lee et al acknowledged that administering CDT alongside PMT was preferable to PMT alone as it facilitated thrombectomy. Significant improvements in thrombus removal have been demonstrated using CDT in combination with PMT compared to the use of PMT alone (62.4% ± 24.9 vs. 26% ± 24.1, p = 0.006),51 and there is consensus that CDT should be utilised alongside PMT unless there is a specific contraindication to thrombolysis or anti-coagulation.53,54 Ultrasound-enhanced devices such as the EKOS Endowave (EKOS Corporation, Bothell, WA, USA) require obligatory adjunctive CDT due to their mode of action, which improves penetration of thrombolytic drugs but does not mechanically remove thrombus. Such devices are associated with longer treatment times than mechanical PMT devices, with a median of 22 h reported.55 Iliac vein stenting was performed adjunctively according to individual clinical judgement in the reported studies, with no specific criteria outlined for the use of stents in any of the analysed studies (Table 1). This methodological heterogeneity represented a potential confounding factor in analysis of PMT devices. Future studies must record both

### Table 2  Mid-term outcomes from PMT.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Clinical follow-up</th>
<th>Radiological follow-up</th>
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<tbody>
<tr>
<td>Gandini, 199990</td>
<td>75% (6/8) symptom free at 24 months</td>
<td>75% (6/8) negative CT venogram at 24 months</td>
</tr>
<tr>
<td>Delomez, 200114</td>
<td>93% (14/15) symptom free at mean 29.6 months</td>
<td>93% (14/15) negative duplex ultrasound (US) at 6 months</td>
</tr>
<tr>
<td>Kasirajan, 200157</td>
<td>51.8% Recurrence-free survival at 11 months</td>
<td>77% (13/17) US patency at 8.9 ± 5.3 months</td>
</tr>
<tr>
<td>Vedantham, 200232</td>
<td>89% (16/18) symptom free or mild symptoms only at mean 19.8 ± 11.6 months</td>
<td>—</td>
</tr>
<tr>
<td>Lin, 200656</td>
<td>5/23 limbs (3/18 patients) lost to follow-up</td>
<td>—</td>
</tr>
<tr>
<td>Lee, 200652</td>
<td>92% 1-year clinical success</td>
<td>68% primary patency at 1 year in PMT cohort</td>
</tr>
<tr>
<td>Arko, 200758</td>
<td>—</td>
<td>64% primary patency at 1 year in CDT cohort</td>
</tr>
<tr>
<td>Bush, 200449</td>
<td>82% reported symptom improvement at 10.2 ± 0.3 months</td>
<td>85% 1-year patency (CT venography)</td>
</tr>
<tr>
<td>Cynamon, 200660</td>
<td>90% (19/21) symptom-free at mean 5.3 months</td>
<td>90% patent ultrasound (US) at mean 6.2 months (range 3–24)</td>
</tr>
<tr>
<td>Gasparis, 200951</td>
<td>93% (13/14) symptom-free or mild symptoms only at median 24 months (range 13–69)</td>
<td>74% free from US evidence of segmental reflux at median 24 months (range 13–69)</td>
</tr>
<tr>
<td>Jackson, 200552</td>
<td>—</td>
<td>80% long-term USS patency at mean 15.5 months</td>
</tr>
<tr>
<td>Kim, 2006510,27</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rao, 200951</td>
<td>98% complete symptom resolution or significant symptom improvement at 5 ± 4.8 month follow-up</td>
<td>95% Kaplan–Meier freedom from DVT recurrence or re-intervention at 9 months</td>
</tr>
<tr>
<td>Shi, 200963</td>
<td>—</td>
<td>75% venous patency at 13 months</td>
</tr>
<tr>
<td>Parikh, 200855</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>
indications for stenting, stent use and long-term follow-up after stent placement. Many studies reported mid-term follow-up, with encouraging clinical and radiological results (Table 2). 75–98% of patients demonstrated significant mid-term improvement in symptoms with similar radiological findings, although loss to follow-up was a disadvantage of the retrospective nature of the existing evidence for PMT.

Safety outcomes

The different devices all appeared to be safe, with no reported procedure-related deaths or strokes, and <1% incidence of symptomatic PE (Table 3). 10/16 studies reported the use of prophylactic IVC filters, although indications for their use were diverse due to the retrospective nature of the evidence base (Table 3). The majority of studies reported no major bleeding complications, though 6/16 studies reported the need for transfusion in 4.2%—14% of 130 patients. However, these data should be interpreted with caution as all studies to date report retrospective data in highly selected groups of patients, with small sample sizes. Selective reporting cannot be discounted and a degree of publication bias should therefore be assumed. It has been suggested that procedure-related mortality is a poor choice of outcome measure for evaluation of CDT or PMT and that a greater focus on patient-related outcome measures, including quality of life analysis, would be beneficial. There was significant methodological heterogeneity between the studies (Table 1), with a variety of PMT devices and a range of adjunctive thrombolytic drugs employed. Future research should provide methodological standards to enable comparison of results between different centres.

Comparative evidence for PMT versus CDT

The development of endovascular technology focussed attention on less invasive ways of removing the thrombus load in DVT, principally catheter-directed thrombolysis (CDT). Younger patients with acute onset of extensive, proximal (ilio-femoral) DVT, who may have underlying anatomical abnormalities or acute limb compromise, appeared most likely to derive benefit. Disadvantages of

<table>
<thead>
<tr>
<th>Author, year</th>
<th>PE</th>
<th>Death</th>
<th>Use of prophylactic IVC filter</th>
<th>Stroke</th>
<th>Bleeding complication requiring transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gandini, 1999</td>
<td>0</td>
<td>12.5% (1/8) from MI (unrelated to PMT)</td>
<td>Yes 6/8 temporary filter 2/8 permanent filter</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Delomez, 2001</td>
<td>0</td>
<td>16.7% (3/18) from cancer or MI (unrelated to PMT)</td>
<td>Yes 16/18 temporary filter 2/18 permanent filter</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kasirajan, 2001</td>
<td>0</td>
<td>17.6% (3/17) from cancer unrelated to PMT</td>
<td>No</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vedantham, 2002</td>
<td>0</td>
<td>0</td>
<td>No</td>
<td>0</td>
<td>3/22 (14%)</td>
</tr>
<tr>
<td>Vedantham, 2004</td>
<td>0</td>
<td>11% (2/18) — unrelated to PMT</td>
<td>No 28/52 temporary filter 15/52 permanent filter</td>
<td>0</td>
<td>Decreased blood transfusion requirement in PMT group vs CDT group (0.2 units vs 1.2 units, p &lt; 0.05)</td>
</tr>
<tr>
<td>Lin, 2006</td>
<td>0</td>
<td>0</td>
<td>Yes Selective in 4/25 with contraindication to adjunctive CDT</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lee, 2006</td>
<td>0</td>
<td>0.5/30 (17%) detectable on CT only. None symptomatic.</td>
<td>Yes 21/25 temporary filter</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arko, 2007</td>
<td>0</td>
<td>0</td>
<td>Yes 4/23 temporary filter 3/23 permanent filter</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bush, 2004</td>
<td>0</td>
<td>0</td>
<td>Yes 19/24 temporary filter</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cynamon, 2006</td>
<td>0</td>
<td>0</td>
<td>Yes Temporary in 6/23 with free-floating IVC thrombus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gasparis, 2009</td>
<td>0</td>
<td>0</td>
<td>No 16 had pre-existing permanent filter Temporary filter used before PMT if caval involvement.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jackson, 2005</td>
<td>0</td>
<td>0</td>
<td>Yes PMT/CDT 4%/3%, p = 0.818</td>
<td>0</td>
<td>PMT/CDT 5.3%/7.7%, p = 0.749</td>
</tr>
<tr>
<td>Kim, 2006</td>
<td>0</td>
<td>0</td>
<td>Yes PMT/CDT 4%/3%, p = 0.818</td>
<td>0</td>
<td>4/43 (9.3%) required transfusion</td>
</tr>
<tr>
<td>Rao, 2009</td>
<td>0</td>
<td>0</td>
<td>Yes PMT 4%/3%, p = 0.818</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Shi, 2006</td>
<td>0</td>
<td>0</td>
<td>Yes PMT/CDT 4%/3%, p = 0.818</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Parikh, 2008</td>
<td>0</td>
<td>0</td>
<td>Yes Temporary IVC filters in all patients</td>
<td>0</td>
<td>24/43 (4.2%) required transfusion</td>
</tr>
</tbody>
</table>
CDT have precluded its universal implementation but may be ameliorated by adjunctive PMT; these include medical contraindications to thrombolysis, the risk of bleeding complications in up to 11%, long infusion times (on average 53.4 h) and significant economic cost incurred by the need for close monitoring during treatment. Two retrospective cohort studies reported comparative analysis of rheolytic PMT with CDT in 150 patients (165 limbs), providing convincing evidence in favour of rheolytic PMT with the Angiojet device as an adjunct to CDT. Lin et al found no difference in thrombus clearance, but identified that PMT using the Angiojet device for rheolytic thrombectomy was associated with a significantly shorter length of stay in ITU (0.6 days vs. 2.4 days, \( p < 0.04 \)) and hospital (4.6 days vs. 8.4 days, \( p < 0.02 \)). There was a significantly shorter treatment time for PMT (mean 76 min) than CDT (mean 18 h), and a lower requirement for interval venograms (0.4 vs. 2.5, \( p < 0.001 \)) with the ensuing benefits of lower radiation dose, nephrotoxicity and cost.

This resulted in significant savings in the total hospital cost of PMT compared to CDT, which was calculated from the sum of the operating room, radiological and hospital room costs ($47,742 ± $19,247 per PMT patient vs. $85,301 ± $24,832 per CDT patient, \( p < 0.01 \)). These findings were in accordance with those of Kim et al, who reported the clinical and economic findings of a retrospective institutional series using the Angiojet device for rheolytic thrombectomy. They demonstrated a significant reduction in treatment duration with PMT (26.3 ± 16.6 h vs. 48 ± 27.1 h, \( p = 0.0004 \)) and in urokinase dose (2.7 ± 1.8 million units vs. 5.6 ± 5.3 million units, \( p = 0.008 \)). In a separate economic analysis of patients treated during the same time period, the mean urokinase and equipment cost per patient was cheaper for PMT than CDT ($5128 vs. $10,127, \( p = 0.026 \).

It should be noted that other healthcare services, such as the English National Health Service, operate through a tariff costing system, in which admissions are reimbursed according to a set tariff making the device costs critical. These differ widely; for example the Angiojet Ultra Console costs £31500 with disposable catheters at £850 to £1250 each (personal communication, MedRad Ltd., Cambridge, United Kingdom), the Trellis-8 device retails at £1250 in the UK (personal communication, Covidien, Hamps., UK) and the Trerotola Device costs £414 to £572 each (personal communication, Teleflex Medical, Bucks., UK). Focussed health economic analysis is required to analyse the fiscal impact of the array of PMT devices used alone or in combination in the UK, including the identification of which patients would derive greatest benefit.

Conclusion

Deep vein thrombosis is a common condition with a significant socioeconomic burden, particularly in the setting of PTS and ulceration. The current standard of treatment remains anticoagulation in the absence of trial data. PMT is an emerging technology that offers promising results as an adjunct to CDT. Early reports suggest that PMT is safe and may be cost-effective with an acceptable safety profile and encouraging mid-term results.

However, the quality of evidence is poor and major RCTs reporting to consensus standards are needed in tandem with registry data to prove the safety, efficacy and compatibility of these devices. These must be combined with formal cost effectiveness analyses. Until these data are available there is little substantial evidence to support the routine use of PMT over CDT alone.

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Disclosures

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Conflict of Interest

None.

References


40. Lookstein R. PEARL Registry Mid-Term Analysis. Paper presented at: ISET; 2009; Florida, USA.


47. Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Haughton S. Catheter-directed thrombolysis
for lower extremity deep venous thrombosis: report of
48 Comerota AJ, Paolini D. Treatment of acute iliofemoral deep
venous thrombosis: a strategy of thrombus removal. Eur J Vasc
Assessment of validity and reproducibility of a clinical scale for
the post-thrombotic syndrome. Haemostasis 1994;24:158a
[abstract].
50 Gandini R, Marsapes F, Sodani G, Masala S, Assegnati G,
Simonetti G. Percutaneous ilio-caval thrombectomy with the
951–8.
Pharmacomechanical thrombectomy for iliofemoral deep vein
thrombosis: an alternative in patients with contraindications to
Mechanical thrombectomy of acute iliofemoral deep vein
thrombosis with use of an Arrow-Trerotola percutaneous
thrombectomy device. J Vasc Interv Radiol 2006;17(3):
487–95.
53 Nazir SA, Ganeshan A, Nazir S, Uberoi R. Endovascular treat-
ment options in the management of lower limb deep venous
54 McLaugherty RB. Endovascular management of deep venous
87–91.
55 Parikh S, Motarjeme A, McNamara T, Raabe R, Hagspiel K,
Benenati JF, et al. Ultrasound-accelerated thrombolysis for the
treatment of deep vein thrombosis: initial clinical experience.
SCVIR reporting standards for the treatment of acute limb
ischaemia with use of transluminal removal of arterial thrombus.
57 Kasirajan K, Gray B, Ouriel K. Percutaneous AngioJet thro-
bectomy in the management of extensive deep venous throm-
58 Arko FR, Davis 3rd CM, Murphy EH, Smith ST, Timaran CH,
Modrall JG, et al. Aggressive percutaneous mechanical thromb-
bectomy of deep venous thrombosis: early clinical results. Arch
Pharmacomechanical thrombectomy for treatment of symp-
tomatic lower extremity deep venous thrombosis: safety and
60 Cynamon J, Stein EG, Dym RJ, Jagust MB, Binkert CA, Baum RA.
A new method for aggressive management of deep vein
thrombosis: retrospective study of the power pulse technique.
61 Gasparis AP, Labropoulos N, Tassiopoulos AK, Phillips B, Pagan J,
Cheng L, et al. Midterm follow-up after pharmacomechanical
thrombolysis for lower extremity deep venous thrombosis. Vasc
62 Jackson LS, Wang XJ, Dudrick SJ, Gersten GD. Catheter-
directed thrombolysis and/or thrombectomy with selective
devascular stenting as alternatives to systemic anti-
coagulation for treatment of acute deep vein thrombosis. Am
63 Shi HJ, Huang YH, Shen T, Xu Q. Percutaneous mechanical
thrombectomy combined with catheter-directed thrombolysis
in the treatment of symptomatic lower extremity deep venous