Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis – a systematic review and meta-analysis

Michael K. W. Lichtenberg¹, Stefan Stahlhoff¹, Katarzyna Młyńczak^{2,3}, Dominik Golicki^{2,3}, Paul Gagne⁴, Mahmood K. Razavi⁵, Rick de Graaf⁶, Raghu Kolluri⁷, and Katarzyna Kolasa⁸

¹ Angiology Clinic, Venous Center Klinikum Arnsberg, Arnsberg, Germany

² Department of Experimental and Clinical Pharmacology, Medical University of Warsaw, Warsaw, Poland

³ HealthQuest, Warsaw, Poland

⁴ The Vascular Experts, Darien, CT, USA

⁵ Heart and Vascular Center, St Joseph Hospital, Orange, CA, USA

⁶ Clinic for Diagnostic and Interventional Radiology/Nuclear Medicine, Clinical Center of Friedrichshafen, Friedrichshafen, Germany

⁷ Ohio Health Heart and Vascular, Columbus, Ohio, USA

⁸ Health Economics and Healthcare Management Division, Kozminski University, Warsaw, Poland

Summary: *Background:* This study sought to compare effectiveness and safety of percutaneous mechanical thrombectomy (PMT) and thrombolysis alone (THR) in patients with acute or subacute iliofemoral deep vein thrombosis (IfDVT). *Patients and methods:* Observational and randomized trials, published between January 2001 to February 2019 were identified by searching MEDLINE. Studies on deep venous thrombosis (DVT) treated with either THR or PMT adjunctive to conventional anticoagulation and compressive intervention were included. Meta-analysis of proportions was conducted to assess effectiveness outcomes of successful lysis and primary patency, post-thrombotic syndrome (PTS), valvular reflux, recurrent DVT, as well as safety outcomes of major bleeding, hematuria, and pulmonary embolism. *Results:* Of 77 identified records, 17 studies including 1417 patients were eligible. Pooled proportion of successful lysis was similar between groups (THR: 95 % [$I^2 = 68.4\%$], PMT 96 %, [$I^2 = 0\%$]; Q_{bet} [Cochran's Q between groups] 0.3, $p = 0.61$). However, pooled proportion of 6-month primary patency was lower after THR than after PMT (68 % [$I^2 = 15.6\%$] versus 94 %; Q_{bet} 26.4, $p < 0.001$). Considerable heterogeneity within groups did not allow for between-group comparison of PTS and recurrent DVT. Major bleeding was more frequent after THR than after PMT (6.0 % [$I^2 = 0\%$] versus 1.0 % [$I^2 = 0\%$]; Q_{bet} 12.3, $p < 0.001$). Incidence of hematuria was lower after THR as compared to PMT (2 % [$I^2 = 56\%$] versus 91.3 % [$I^2 = 91.7\%$]; Q_{bet} 714, $p < 0.001$). Incidences of valvular reflux and pulmonary embolism were similar across groups (THR: 61 % versus PMT: 53 %; Q_{bet} 0.7, $p = 0.39$ and THR: 2 % versus PMT: 1 %; Q_{bet} 1.1, $p = 0.30$, respectively). *Conclusions:* In patients with iliofemoral DVT, percutaneous mechanical thrombectomy was associated with a higher cumulative 6-month primary patency and a lower incidence of major bleeding compared to thrombolysis alone. Risk of hemolysis from mechanical thrombectomy needs further consideration.

Keywords: Thrombectomy, iliofemoral deep venous thrombosis, thrombolytic therapy, hematuria, hemolysis, post-thrombotic syndrome, pulmonary embolism

Introduction

Ilio-femoral deep vein thrombosis (IfDVT) accounts for about 25 % of lower limb DVT. Patients with acute IfDVT carry a high risk to develop the potentially chronic debilitating post-thrombotic syndrome (PTS) [1]. Residual thrombus may increase the risk of PTS as well as recurrent DVT, and pulmonary embolism. Whether early thrombus

removal in addition to standard care of anticoagulation and compressive therapy decreases the risk of PTS has not been clarified as yet [2–5]. Subsequent angioplasty and stent implantation may contribute to improvement of outflow.

Thrombus removal may be performed in various ways. Catheter directed thrombolysis (CDT) by means of direct delivery of fibrinolytic plasminogen activator into the

thrombus provides a high local drug concentration, however increases the risk of bleeding [6]. CDT can be enhanced with ultrasound assistance (UA CDT) to improve drug dispersion. However, to date, for this complement, no effect on relevant clinical outcomes is evident [7]. Percutaneous mechanical thrombectomy (PMT) with or without adjunctive thrombolysis may reduce residual thrombus burden and shorten procedure time. Additionally, PMT allows to lower the dose of plasminogen activator. An earlier randomized trial found a similar incidence but lower severity of PTS after mechanical thrombectomy plus concomitant thrombolysis (PCDT) compared to anticoagulation alone without an effect on early major bleeding [1, 4]. However, little is known about differences in outcomes between thrombolysis alone and PMT with or without adjunctive thrombolysis.

We conducted this meta-analysis to indirectly compare effectiveness and safety of systemic or catheter directed thrombolysis (THR-studies) with that of mechanical thrombectomy with or without supplemental thrombolysis (PMT-studies) in patients with acute IfDVT who receive adjunctive anticoagulation and compression therapy and optional subsequent angioplasty with or without venous stent implantation.

Patients and methods

Search strategy and selection criteria

Randomized and observational studies reporting on treatment of iliac and/or common femoral DVT with catheter-directed (CDT) or systemic thrombolysis or PMT with or without thrombolysis were included. CDT was conducted with or without ultrasound assistance (UA CDT). Eligible endovascular thrombectomy systems for PMT were the AngioJet™ Rheolytic thrombectomy system (Boston Scientific Corporation, Marlborough, MA, USA), the Trellis peripheral infusion system (Covidien Inc., Mansfield, MA, USA), Penumbra's Indigo System (Penumbra, Inc., Alameda, CA, USA), and the Aspirex®S catheter (Straub Medical, Wangs, Switzerland). Studies on thrombolysis with adjunctive PMT (PCDT) were allocated to the PMT-group. Detailed description of thrombectomy systems are provided in electronic supplementary material (ESM) 1, Table.

Reviewers searched MEDLINE and web-based platforms of specialized journals. Search period was January 2001 to February 2019. No language restriction was imposed. Titles and abstracts were screened by two reviewers who subsequently assessed full-text versions of selected articles for eligibility. Our study was conducted according to Preferred Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

Data analysis

Extracted data included study characteristics, treatment strategies, and effectiveness and safety outcomes as

assessed by investigators. Effectiveness outcomes were pooled proportions of successful thrombolysis, 6-month primary patency, PTS, valvular reflux, and recurrent overall DVT. Safety outcomes were pooled proportions of major bleeding, hematuria, and pulmonary embolism at any time. Lysis grade was determined by venography. Grade I indicated < 50 %, grade II 50–99 %, and grade III 100 % thrombolysis. Grade II and III were considered as successful thrombolysis. Primary patency referred to the absence of recurrent diameter stenosis of ≥ 30 % [8], ≥ 50 % [9], or without defined threshold [10, 11] PTS and recurrent DVT were followed-up for up to 65 months (median). Severity of PTS was stratified by means of Villalta scale considering symptoms (pain, cramps, heaviness, paresthesia, pruritus) and clinical signs (pretibial edema, skin induration, hyperpigmentation, redness, venous ectasia, pain on calf compression, venous ulcer), by the revised venous clinical severity score (rVCSS), or the clinical, etiologic, anatomic, and pathophysiologic (CEAP) classification.

Validity of included studies was determined according to ROBINS-I tool for assessing risk of bias in non-randomized studies of interventions [12]. To assess publication bias, symmetry of funnel plot was visually evaluated, and Egger test applied for effectiveness and selected safety outcomes.

Summary estimates were proportions with their corresponding 95 % confidence intervals (CI). Pooled proportions for the two comparison groups of thrombolysis only (THR) and percutaneous mechanical thrombectomy (PMT) were assessed using random or fixed effects subgroup meta-analysis. I^2 -statistic in case of more than two studies per group and Cochran Q test were applied to evaluate heterogeneity within comparison groups. I^2 indicated heterogeneity that might not be important (0 – 40 %), or that may represent moderate (30 – 60 %), substantial (50 – 90 %), or considerable (75 – 100 %) heterogeneity. Importance of I^2 depends on magnitude, strength, and evidence of the treatment effect. Q formed part of the DerSimonian-Laird random effects pooling method. Heterogeneity between treatment groups was indicated by Cochran's Q_{bet} ($Q_{bet} = Q_{all} - [Q_{THR} + Q_{PMT}]$) [13]. Considering a low power of Cochran's Q test in case of small numbers of studies and small-scale studies, a two-sided p-value of < 0.1 was considered statistically significant. In addition, forest plot indicates a statistically significant difference if 95 % CIs of point estimates don't overlap. Data were analyzed using StatsDirect Statistics (Version 2.7.9, StatsDirect Ltd., Cambridge, UK).

Results

Twenty articles based on 17 randomized or observational studies published between January 2001 and February 2019 were included in this systematic review and meta-analysis (Figure 1) [1, 7–11, 14–25]. Eligible studies conducted in nine countries evaluated 1417 patients who were treated with CDT or systemic thrombolysis alone

Figure 1. Study selection process.

(17 cohorts) or with PMT (12 cohorts). Three CDT cohorts included ultrasound assistance and 14 did not. Adjunctive anticoagulation and compressive intervention were carried out in each group. Eleven studies (6 THR-studies, 5 PMT-studies) reported on adjunctive venoplasty (ESM 2, Table).

Four observational studies that evaluated multiple study cohorts assigned to different interventions were subjected to serious risk of confounding bias [18, 19, 21, 23]. Moderate risk of selection bias resulted from the absence of comparability between THR- and PMT-groups within studies and thus, was present in all studies. Serious risk of misclassification bias was present in one study that assigned multi-sidehole CDT to PMT [1]. Serious information bias regarding safety outcomes was introduced by different follow-up periods, selection of reported results, and inconsistent outcome definitions. Visual inspection of funnel plots and Egger test for asymmetry revealed evidence of publication bias for proportions of total PTS (Egger test: $p < 0.001$) (ESM 3, Figure c) and major bleeding (Egger test: $p = 0.03$), (ESM 4, Figure a).

Effectiveness outcomes

Data on successful thrombolysis (grade II or III) were available from 4 studies (7 cohorts) including 300 limbs [10, 19, 22, 24]. Pooled proportion was 95.0 % (95 %CI: 88 to 99 %) in the THR-group with substantial heterogeneity ($I^2 = 68.4$ %), and 96 % (95 %CI 91 to 99 %) in the PMT-group without heterogeneity ($I^2 = 0$ %). There was no evidence of heterogeneity between treatment groups ($Q_{\text{bet}} 0.3$, $p = 0.61$) implying similar effectiveness regarding lysis with THR or PMT (Figure 2a).

Primary patency at 6 months was reported from 5 studies including 215 patients [8–11, 18] Forest plot showed that

pooled proportion of primary patency in THR-studies differed significantly from the proportion in the single PMT study (68 % versus 94 %). Cochran's Q test confirmed the difference ($Q_{\text{bet}} 26.3$, $p < 0.001$), (Figure 2b).

Proportion of PTS manifestation was reported in 9 studies (14 cohorts) including 572 patients. Pooled proportion was 31 % (95 %CI: 19 to 45 %) in the THR- and 29 % (95 %CI: 4 to 65 %) in the PMT-group with considerable heterogeneity within each group ($I^2 = 80.7$ % and $I^2 = 96.7$ %, respectively). Thus, validity of pooled proportions of PTS is limited (Figure 3a). Proportion of moderate and severe PTS (5 studies, 7 cohorts, 398 patients) was lower in the THR- compared to the PMT-group (13 % and 26 %, respectively) and Cochran's statistics suggests that treatment strategy modified the proportion of PTS ($Q_{\text{bet}} 4.1$, $p = 0.04$). However, there is substantial unexplained heterogeneity between the studies within each treatment group, (Figure 3b).

Two studies [17, 23] including 3 THR-cohorts and 2 PMT-cohorts with total of 86 patients reported on valvular reflux. Pooled proportion from fixed effects model was 61 % (95 % CI: 48 to 74 %) in the THR-group with moderate heterogeneity ($I^2 = 39.3$ %) and 53 % (95 %CI: 39 to 66 %) in the PMT-group without heterogeneity ($Q_{\text{within}} 0.8$, $df = 1$, $p = 0.37$). There was no evidence of heterogeneity between groups ($Q_{\text{bet}} 0.7$, $p = 0.39$).

Recurrent overall DVT was reported in 6 studies (8 cohorts) including 711 patients. Proportion of DVT was lower in the THR- compared to the PMT-group (2 % and 4 %, respectively) with Q statistics indicating real variance among effects between groups ($Q_{\text{bet}} 14.0$, $p < 0.001$). However, considerable heterogeneity restricts reliability of pooled proportion of recurrent DVT in the PMT group, (Figure 4).

Safety outcomes

Data on major bleeding were available from 11 studies (16 cohorts) including 690 patients. Pooled proportion of major bleeding was 6 % (95 %CI 4 to 9 %) in the THR- and 1 % (95 %CI: 0 to 3 %) in the PMT group without evidence of heterogeneity within either group. Cochran's statistic indicated significant heterogeneity between groups ($Q_{\text{bet}} 12.3$, $p < 0.001$), (Figure 5). Five studies [11, 19, 21, 25] reported on the hemolytic complication of hematuria (4 THR-cohorts, 521 patients; 3 PMT-cohorts, 170 patients). Pooled proportions from random effects models were 2 % (95 %CI: 0 to 4 %) in the THR-group and 91.3 % (95 % CI: 71.5 to 99.9 %) in the PMT group. Heterogeneity within (THR: $I^2 = 56.0$ %, PMT: $I^2 = 91.7$ %) and across groups ($Q_{\text{bet}} 714$, $p < 0.001$) was considerable. Five studies (6 cohorts) including 245 patients reported on pulmonary embolism. Pooled proportions were 2 % (95 %CI: 0 to 5 %) and 1 % (95 %CI: 0 to 3 %) in the THR- and the PMT-group, respectively. There was no evidence of dispersion of effect size across groups ($Q_{\text{bet}} 1.1$, $p = 0.30$), (Figure 6).

Figure 2. Meta-analysis of successful thrombolysis (grade II and III) (a) and 6-month primary patency (b) after iliofemoral deep vein thrombosis by treatment strategy. Pooled proportions are marked with unfilled diamond with an ascending line from the upper point. CDT: catheter-directed thrombolysis; IfDVT: iliofemoral deep vein thrombosis; PMT: percutaneous mechanical thrombectomy; Q_{bet}: Cochran's heterogeneity statistic between THR and PMT subgroups; THR: thrombolysis; UA CDT: ultrasound-assisted, catheter-directed thrombolysis.

Discussion

Our meta-analysis provided an indirect comparison between THR and PMT. It revealed similar proportions of successful lysis in patients with IfDVT with either thrombolysis alone or PMT. Primary patency at 6 months appeared higher after PMT. However, it is to be pointed out that only two PMT-studies provided data on primary patency [9, 18]. Incidence of major bleeding was lower but that of hematuria higher after PMT. Considerable heterogeneity within treatment groups did not allow to draw final conclusions from between-group comparisons of PTS and recurrent DVT. No difference across groups were seen regarding pulmonary embolism and valvular reflux.

On one hand, thrombolysis supports standard treatment of anticoagulation by means of improved thrombus clearance, but on the other, long lasting infusion of up to 72 hours and the need of intensive care unit monitoring due to an increased risk of bleeding is necessary. PMT is shown to accelerate thrombus maceration and removal and to effectively decrease residual thrombus burden by means of aspiration. Thus, with rapid reperfusion by

PMT, thrombolytic medication can be reduced or completely avoided. It is therefore to be expected that the incidence of bleeding decreases without compromising effectiveness.

Balance between successful lysis and risk of bleeding

From early studies it is known that thrombosis-free survival is related to successful lysis [26]. However, conventional anticoagulation resolves only about 30 % of IfDVT [27]. In contrast, our study revealed high incidences of successful lysis after both THR and PMT. Patients who underwent thrombolysis alone might need higher doses of fibrinolytic drug. This in turn can increase the risk of bleeding. This assumption is supported by a significantly lower pooled proportion of major bleeding after PMT compared to THR, however against the background of significant publication bias. The only PMT-study that provided data on primary patency in our meta-analysis evaluated rotational aspiration without any adjunctive thrombolysis [9].

Figure 3. Meta-analysis of any (a) or moderate and severe (b) post-thrombotic syndrome after iliofemoral deep vein thrombosis by treatment strategy. Pooled proportions are marked with unfilled diamond with an ascending line from the upper point. CDT: catheter-directed thrombolysis; IfDVT: iliofemoral deep vein thrombosis; PMT: percutaneous mechanical thrombectomy; Q_{bet}: Cochran's heterogeneity statistic between THR and PMT subgroups; THR: thrombolysis; UA CDT: ultrasound-assisted, catheter-directed thrombolysis.

All patients received dedicated venous stents. In that particular study, cumulative 6-month primary patency was superior compared to the THR-group and no bleeding complications occurred.

Aspects of PTS prevention

Prevention of PTS is crucial because it is the most devastating sequela of IfDVT. A subgroup analysis of the ATTRACT trial for iliofemoral DVT showed no difference in total PTS incidence between 6 and 24 months after PCDT compared to conventional anticoagulation (49 % vs. 51 %, p = 0.59). However, acute leg pain, swelling, and

progression of PTS severity was significantly reduced [1]. In our meta-analysis considerable heterogeneity within groups, and significant publication bias did not allow for comparison of total PTS between groups. Heterogeneity might have been due to different strategies of adjunctive venoplasty and different follow-up periods ranging from 3 to 65 months on average. Finally, PTS is known to progressively increase over time.

Incidence of moderate and severe PTS after thrombolysis alone (13 %) was in the same range as in the ATTRACT trial (18 %) and thus, was superior to that achieved with anticoagulation alone (28 %). However, a comparably high incidence of moderate PTS in the Aspirex registry (36 %)

Figure 4. Meta-analysis of recurrent iliofemoral deep vein thrombosis by treatment strategy. Pooled proportions are marked with unfilled diamond with an ascending line from the upper point. CDT: catheter-directed thrombolysis; IfDVT: iliofemoral deep vein thrombosis; PMT: percutaneous mechanical thrombectomy; Q_{bet}: Cochran's heterogeneity statistic between THR and PMT subgroups; THR: thrombolysis.

Figure 5. Meta-analysis of major bleeding incidence after iliofemoral deep vein thrombosis by treatment strategy. Pooled proportions are marked with unfilled diamond with an ascending line from the upper point. CDT: catheter-directed thrombolysis; IfDVT: iliofemoral deep vein thrombosis; PMT: percutaneous mechanical thrombectomy; Q_{bet}: Cochran's heterogeneity statistic between THR and PMT subgroups; THR: thrombolysis; UA CDT: ultrasound-assisted; catheter-directed thrombolysis.

Figure 6. Meta-analysis of pulmonary embolism after iliofemoral deep vein thrombosis by treatment strategy. Pooled proportions are marked with unfilled diamond with an ascending line from the upper point. CDT: catheter-directed thrombolysis; IfDVT: iliofemoral deep vein thrombosis; PMT: percutaneous mechanical thrombectomy; Q_{bet}: Cochran's heterogeneity statistic between THR and PMT subgroups; THR: thrombolysis.

[9] after mechanical thrombectomy plus venous stent that waived thrombolysis contributed to an increased pooled proportion of PTS in the PMT-group. However, solely in the Aspirex registry, rVCSS score and CEAP classification were used for assessment of PTS severity. Whether thrombolysis prevents PTS beyond acute thrombus clearance and how to further improve factors such as valvular competence to reduce venous hypertension has to be evaluated in future research. Kuo et al. described a continuous decrease of venous obstruction with a nadir at 3 months after intervention, possibly attributed to inflammation related remodeling [28].

Beyond thrombus load and valvular incompetence, venous outflow obstruction and recurrent DVT are important predictors of PTS. Therefore, in case of considerable residual stenosis, particularly in patients with May-Thurner syndrome, dedicated venous stents with larger diameters and higher radial force compared to arterial stents are probably most suitable. Arterial stents and a comparable low rate of stent placement (28 %) might have contributed to recurrent DVT in the ATTRACT trial [1].

Embolic and hemolytic complications

A high incidence of hematuria was seen in PMT-studies that provided respective data. These studies applied AngioJet-PMT [19, 21]. Thus, our meta-analysis revealed a considerably higher pooled proportion of hematuria in PMT- compared to THR-patients. Although, heterogeneity within groups was considerable, these findings support earlier results from Escobar et al. [29] who identified pharmacomechanical thrombectomy (AngioJet-PMT) as independent risk factor for acute kidney disease. Moreover, Morrow et al. found AngioJet.PMT with or without thrombolysis to be associated with renal dysfunction [30].

In our study, incidence of pulmonary embolism was rare and did not differ between group.

Limitations

Our study has several limitations. First, comparison is based on study-level results from small to medium scale studies with different patient and procedure characteristics such as additional stenting in varying frequencies. The PMT group included studies that applied mechanical thrombectomy alone as well as studies that combined mechanical thrombectomy and CDT. This approach might have increased heterogeneity. Outcome definitions including primary patency, recurrent DVT, and severity of PTS as well as follow-up time were not consistent across studies. Evidence is limited by moderate to considerable confounding, selection, misclassification, or information bias of included studies. Due to the small number of studies regarding lysis, primary patency, recurrent DVT, and pulmonary embolism, publication bias must be interpreted with caution. Due to the differences in the mechanisms of action for the analyzed PMT devices, it may not be correct to group the findings and assume the results can be consistently assumed for each device i.e. class effect.

Conclusions

We conclude that our meta-analysis of thrombolysis alone versus mechanical thrombectomy with or without thrombolysis in patients with IfDVT revealed similar incidences of acute successful thrombus removal. However, mechanical thrombectomy increased 6-month cumulative primary

patency and, subject to publication bias, decreased frequency of major bleeding. No differences across groups became obvious with regard to valvular reflux or pulmonary embolism. Level of risk and clinical relevance of hemolysis resulting from mechanical thrombectomy needs to be evaluated in future studies.

Electronic supplementary material

The electronic supplementary material (ESM) is available with the online version of the article at <https://doi.org/10.1024/0301-1526/a000875>

ESM 1. Description of eligible devices for percutaneous, mechanical thrombectomy (Table).

ESM 2. Characteristics of included Studies (Table).

ESM 3. Funnel plot of thrombolysis, primary patency, post-thrombotic syndrome, and recurrent DVT (Figure).

ESM 4. Funnel plot of major bleeding, and pulmonary embolism (Figure).

References

- Comerota AJ, Kearon C, Gu CS, Julian JA, Goldhaber SZ, Kahn SR, et al. Endovascular thrombus removal for acute iliofemoral deep vein thrombosis. *Circulation*. 2019;139(9):1162–73.
- Watson L, Broderick C, Armon MP. Thrombolysis for acute deep vein thrombosis. *Cochrane Database Syst Rev*. 2016;11:CD002783.
- Haig Y, Enden T, Grotta O, Klow NE, Slagsvold CE, Ghanima W, et al. Post-thrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomised controlled trial. *Lancet Haematol*. 2016;3(2):e64–71.
- Vedantham S, Goldhaber SZ, Julian JA, Kahn SR, Jaff MR, Cohen DJ, et al. Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. *N Engl J Med*. 2017;377(23):2240–52.
- Notten P, Ten Cate-Hoek AJ, Arnoldussen C, Strijkers RHW, de Smet A, Tick LW, et al. Ultrasound-accelerated catheter-directed thrombolysis versus anticoagulation for the prevention of post-thrombotic syndrome (CAVA): a single-blind, multicentre, randomised trial. *Lancet Haematol*. 2020;7(1):e40–e9.
- Bashir R, Zack CJ, Zhao H, Comerota AJ, Bove AA. Comparative outcomes of catheter-directed thrombolysis plus anticoagulation vs anticoagulation alone to treat lower-extremity proximal deep vein thrombosis. *JAMA Intern Med*. 2014;174(9):1494–501.
- Engelberger RP, Stuck A, Spirk D, Willenberg T, Haine A, Periard D, et al. Ultrasound-assisted versus conventional catheter-directed thrombolysis for acute iliofemoral deep vein thrombosis: 1-year follow-up data of a randomized-controlled trial. *J Thromb Haemost*. 2017;15(7):1351–60.
- AbuRahma AF, Perkins SE, Wulu JT, Ng HK. Iliofemoral deep vein thrombosis: conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. *Ann Surg*. 2001;233(6):752–60.
- Lichtenberg M, Stahlhoff WF, Ozkapi A, de Graaf R, Breuckmann F. Safety, procedural success and outcome of the Aspirex®S endovascular thrombectomy system in the treatment of iliofemoral deep vein thrombosis – data from the Arnsberg Aspirex registry. *Vasa*. 2019;48(4):341–6.
- Haig Y, Enden T, Slagsvold CE, Sandvik L, Sandset PM, Klow NE. Determinants of early and long-term efficacy of catheter-directed thrombolysis in proximal deep vein thrombosis. *J Vasc Interv Radiol*. 2013;24(1):17–24.
- Lee CY, Lai ST, Shih CC, Wu TC. Short-term results of catheter-directed intrathrombus thrombolysis versus anticoagulation in acute proximal deep vein thrombosis. *J Chin Med Assoc*. 2013;76(5):265–70.
- Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
- Borenstein M, Hedges LV, Higgins JP, Rothstein HR. *Introduction to meta-analysis*. 2nd ed. Hoboken, NJ: John Wiley & Sons, Ltd.; 2009.
- Elsharawy M, Elzayat E. Early results of thrombolysis vs anticoagulation in iliofemoral venous thrombosis. A randomised clinical trial. *Eur J Vasc Endovasc Surg*. 2002;24(3):209–14.
- Engelberger RP, Spirk D, Willenberg T, Alatri A, Do DD, Baumgartner I, et al. Ultrasound-assisted versus conventional catheter-directed thrombolysis for acute iliofemoral deep vein thrombosis: 1-year follow-up data of a randomized-controlled trial. *Circ Cardiovasc Interv*. 2015;8(1):1351–60.
- Gombert A, Gombert R, Barbati ME, Bruners P, Keszei A, Wittens C, et al. Patency rate and quality of life after ultrasound-accelerated catheter-directed thrombolysis for deep vein thrombosis. *Phlebology*. 2018;33(4):251–60.
- Laiho MK, Oinonen A, Sugano N, Harjola VP, Lehtola AL, Roth WD, et al. Preservation of venous valve function after catheter-directed and systemic thrombolysis for deep venous thrombosis. *Eur J Vasc Endovasc Surg*. 2004;28(4):391–6.
- Dopheide JF, Sebastian T, Engelberger RP, Haine A, Kucher N. Early clinical outcomes of a novel rheolytic directional thrombectomy technique for patients with iliofemoral deep vein thrombosis. *Vasa*. 2018;47(1):56–62.
- Liu G, Qin J, Cui C, Ye K, Shi H, Liu X, et al. Comparison of direct iliofemoral stenting following angiojet rheolytic thrombectomy vs staged stenting after angiojet rheolytic thrombectomy plus catheter-directed thrombolysis in patients with acute deep vein thrombosis. *J Endovasc Ther*. 2018;25(1):133–9.
- Murphy EH, Broker HS, Johnson EJ, Modrall JG, Valentine RJ, Arko FR 3rd. Device and imaging-specific volumetric analysis of clot lysis after percutaneous mechanical thrombectomy for iliofemoral DVT. *J Endovasc Ther*. 2010;17(3):423–33.
- Shen Y, Wang X, Jin SS, Zhang RL, Zhao WJ, Chen G. Increased risk of acute kidney injury with percutaneous mechanical thrombectomy using AngioJet compared with catheter-directed thrombolysis. *J Vasc Surg Venous Lymphat Disord*. 2019;7(1):29–37.
- Tichelaar VY, Brodin EE, Vik A, Isaksen T, Skjeldestad FE, Kumar S, et al. A retrospective comparison of ultrasound-assisted catheter-directed thrombolysis and catheter-directed thrombolysis alone for treatment of proximal deep vein thrombosis. *Cardiovasc Intervent Radiol*. 2016;39(8):1115–21.
- Vogel D, Walsh ME, Chen JT, Comerota AJ. Comparison of vein valve function following pharmacomechanical thrombolysis versus simple catheter-directed thrombolysis for iliofemoral deep vein thrombosis. *J Vasc Surg*. 2012;56(5):1351–4.
- Yoon WJ, Halandras P, Aulivola B, Crisostomo P. Malignancy does not affect outcomes of pharmacomechanical thrombolysis in acute symptomatic iliofemoral deep vein thrombosis. *Ann Vasc Surg*. 2018;51:234–8.
- Zhang X, Ren Q, Jiang X, Sun J, Gong J, Tang B, et al. A prospective randomized trial of catheter-directed thrombolysis with additional balloon dilatation for iliofemoral deep venous thrombosis: a single-center experience. *Cardiovasc Intervent Radiol*. 2014;37(4):958–68.
- Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Houghton SH. Catheter-directed thrombolysis

- for lower extremity deep venous thrombosis: report of a national multicenter registry. *Radiology*. 1999;211(1):39–49.
27. Vedantham S, Kahn SR, Goldhaber SZ, Comerota AJ, Parpia S, Meleth S, et al. Endovascular therapy for advanced post-thrombotic syndrome: Proceedings from a multidisciplinary consensus panel. *Vasc Med*. 2016;21(4):400–7.
 28. Kuo TT, Huang CY, Hsu CP, Lee CY. Catheter-directed thrombolysis and pharmacomechanical thrombectomy improve midterm outcome in acute iliofemoral deep vein thrombosis. *J Chin Med Assoc*. 2017;80(2):72–9.
 29. Escobar GA, Burks D, Abate MR, Faramawi MF, Ali AT, Lyons LC, et al. Risk of acute kidney injury after percutaneous pharmacomechanical thrombectomy using angiojet in venous and arterial thrombosis. *Ann Vasc Surg*. 2017;42:238–45.
 30. Morrow KL, Kim AH, Plato SA 2nd, Shevitz AJ, Goldstone J, Baele H, et al. Increased risk of renal dysfunction with percutaneous mechanical thrombectomy compared with catheter-directed thrombolysis. *J Vasc Surg*. 2017;65(5):1460–6.

History

Submitted: 01.03.2020

Accepted after revision: 29.04.2020

Published online: 25.05.2020

Acknowledgement

The authors thank Maja Ingwersen, medwing, office for scientific and regulatory writing, Hamburg, Germany, for medical writing support.

Conflicts of interests

Michael Lichtenberg, Rick de Graaf, Katarzyna Kolasa and Dominik Golicki are consultants for Straub Medical AG. All other authors report no conflicts of interest with respect to this article.

Funding

This study was funded by Arnsberg Venous Center.

Correspondence address

Michael Lichtenberg, MD
 Angiology Clinic
 Arnsberg Venous Center
 Klinikum Arnsberg
 Stolte Ley 5
 59759 Arnsberg
 Germany
 klichte@gmx.net