

EVIDENCE BASED STATEMENT

DOMAIN **06**, Statement **08**

TOPIC: “**Pharmaco-mechanical thrombolysis indications and complications management**”

SEARCH TERMS & SOURCES

("pharmaco-mechanical thrombolysis" OR "pharmacomechanical thrombolysis") OR
("deep venous thrombosis" AND "thrombolysis") AND ("meta analysis" OR "systematic review" OR "guidelines")

INCLUSION CRITERIA

Systematic review or meta-analysis (2012-2022)
Focused on PMT
Last ten years

SEARCH RESULT BEFORE - AFTER SELECTION

72 – 13

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Goldhaber SZ, Magnuson EA, Chinnakondepalli KM, et al. Catheter-directed thrombolysis for deep vein thrombosis: 2021 update. *Vascular Medicine*. 2021 Dec;26(6):662-9.
2. Broderick C, Watson L, Armon MP. Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb. *Cochrane Database Syst Rev*. 2021 Jan 19;1(1):CD002783. doi: 10.1002/14651858.CD002783.pub5. PMID: 33464575; PMCID: PMC8094969
3. Mazzolai, L., Ageno, W., Alatri, A., et al. (2021) Second consensus document on diagnosis and management of acute deep vein thrombosis: updated document elaborated by the ESC Working Group on aorta and peripheral vascular diseases and the ESC Working Group on pulmonary circulation and right ventricular function. *European Journal of Preventive Cardiology*.
4. Kahn SR, Julian JA, Kearon C, et al. Quality of life after pharmacomechanical catheter-directed thrombolysis for proximal deep venous thrombosis. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*. 2020 Jan 1;8(1):8-23.
5. Comerota AJ. Pharmacologic and Pharmacomechanical Thrombolysis for Acute Deep Vein Thrombosis: Focus on ATTRACT CME. *Methodist DeBakey Cardiovascular Journal*. 2018 Jul;14(3):219.
6. Vedantham S. Thrombectomy and thrombolysis for the prevention and treatment of postthrombotic syndrome. *Hematology 2014, the American Society of Hematology Education Program Book*. 2017 Dec 8;2017(1):681-5.
7. Liu D, Peterson E, Dooner J, Baerlocher M, Zypchen L, Gagnon J, Delorme M, Sing CK, Wong J, Guzman R, Greenfield G. Diagnosis and management of iliofemoral deep vein thrombosis: clinical practice guideline. *CMAJ*. 2015 Nov 17;187(17):1288-96.

EVIDENCE BASED STATEMENT

Domain 6; Statement 8

IDENTIFIED REFERENCES

1. Broderick C, Watson L, Armon MP. Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb. *Cochrane Database Syst Rev.* 2021 Jan 19;1(1):CD002783. doi: 10.1002/14651858.CD002783.pub5. PMID: 33464575; PMCID: PMC8094969.
2. Lichtenberg MKW, Stahlhoff S, Młyńczak K, et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. *Vasa.* 2021 Jan;50(1):59-67. doi: 10.1024/0301-1526/a000875. Epub 2020 May 25. PMID: 32449481.
3. Hansrani V, Moughal S, Elmetwally A, et al. A review into the management of May-Thurner syndrome in adolescents. *J Vasc Surg Venous Lymphat Disord.* 2020 Nov;8(6):1104-1110. doi: 10.1016/j.jvsv.2020.05.006. Epub 2020 May 28. PMID: 32474151.
4. Diniz J, Coelho A, Mansilha A. Endovascular treatment of iliofemoral deep venous thrombosis: is there enough evidence to support it? A systematic review with meta-analysis. *Int Angiol.* 2020 Apr;39(2):93-104. doi: 10.23736/S0392-9590.19.04298-6. Epub 2019 Nov 25. PMID: 31782288.
5. Tang T, Chen L, Chen J, et al. Pharmacomechanical Thrombectomy Versus Catheter-Directed Thrombolysis for Iliofemoral Deep Vein Thrombosis: A Meta-Analysis of Clinical Trials. *Clin Appl Thromb Hemost.* 2019 Jan-Dec;25:1076029618821190. doi: 10.1177/1076029618821190. PMID: 30808224; PMCID: PMC6715002.
6. Thomas M, Hollingsworth A, Mofidi R. Endovascular Management of Acute Lower Limb Deep Vein Thrombosis: A Systematic Review and Meta-analysis. *Ann Vasc Surg.* 2019 Jul;58:363-370. doi: 10.1016/j.avsg.2018.12.067. Epub 2019 Feb 13. PMID: 30769054.
7. Xing Z, Tang L, Zhu Z, Hu X. Effects of thrombolysis on outcomes of patients with deep venous thrombosis: An updated meta-analysis. *PLoS One.* 2018 Sep 25;13(9):e0204594. doi: 10.1371/journal.pone.0204594. PMID: 30252917; PMCID: PMC6155544.
8. Wang W, Sun R, Chen Y, Liu C. Meta-analysis and systematic review of percutaneous mechanical thrombectomy for lower extremity deep vein thrombosis. *J Vasc Surg Venous Lymphat Disord.* 2018 Nov;6(6):788-800. doi: 10.1016/j.jvsv.2018.08.002. PMID: 30336908.
9. Elbasty A, Metcalf J. Safety and Efficacy of Catheter Direct Thrombolysis in Management of Acute Iliofemoral Deep Vein Thrombosis: A Systematic Review. *Vasc Specialist Int.* 2017 Dec;33(4):121-134. doi: 10.5758/vsi.2017.33.4.121. Epub 2017 Dec 31. PMID: 29354622; PMCID: PMC5754069.
10. Robertson L, McBride O, Burdess A. Pharmacomechanical thrombectomy for iliofemoral deep vein thrombosis. *Cochrane Database Syst Rev.* 2016 Nov 4;11(11):CD011536. doi: 10.1002/14651858.CD011536.pub2. PMID: 27814432; PMCID: PMC6464782.
11. Meissner MH, Gloviczki P, Comerota AJ, et al; Society for Vascular Surgery; American Venous Forum. Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg.* 2012 May;55(5):1449-62. doi: 10.1016/j.jvs.2011.12.081. Epub 2012 Apr 1. PMID: 22469503.
12. Dasari TW, Pappy R, Hennebry TA. Pharmacomechanical thrombolysis of acute and chronic symptomatic deep vein thrombosis: a systematic review of literature. *Angiology.* 2012 Feb;63(2):138-45. doi: 10.1177/0003319711410050. Epub 2011 May 20. PMID: 21602252.
13. Karthikesalingam A, Young EL, Hinchliffe RJ, et al. A systematic review of percutaneous mechanical thrombectomy in the treatment of deep venous thrombosis. *Eur J Vasc Endovasc Surg.* 2011 Apr;41(4):554-65. doi: 10.1016/j.ejvs.2011.01.010. Epub 2011 Feb 1. PMID: 21288745.

EVIDENCE BASED STATEMENT

Domain 6; Statement 8

TEXT FOR INCLUSION IN THE DOCUMENT

DOMAIN 06, Statement 08, TOPIC: “**Pharmaco-mechanical thrombolysis indications and complications management**”

Catheter-directed thrombolysis may be used alongside endovascular techniques to remove thrombus, such as mechanical thrombectomy, catheter aspiration, balloon maceration, balloon venoplasty, or stenting. This combined approach is known as pharmacomechanical thrombolysis (PMT)(**Broderick C, Watson L, Armon MP. Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb. Cochrane Database Syst Rev. 2021 Jan 19;1(1):CD002783. doi: 10.1002/14651858.CD002783.pub5. PMID: 33464575; PMCID: PMC8094969**).

Like catheter-directed thrombolysis (CDT), PMT is most commonly used in patients with acute (< 14 days since thrombus formation), iliofemoral DVT, good functional status, and low bleeding risk (**Tang T, Chen L, Chen J, et al. Pharmacomechanical Thrombectomy Versus Catheter-Directed Thrombolysis for Iliofemoral Deep Vein Thrombosis: A Meta-Analysis of Clinical Trials. Clin Appl Thromb Hemost. 2019 Jan-Dec;25:1076029618821190**). The best available evidence to support this approach comes from the ATTRACT trial. This trial included 692 patients with acute, proximal DVT and randomized them to either PMT or anticoagulation alone. PMT did not reduce post-thrombotic syndrome but reduced the severity of PTS; in subgroup analyses of iliofemoral DVT patients, PMT also improved venous-specific quality of life (**Broderick C, Watson L, Armon MP. Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb. Cochrane Database Syst Rev. 2021 Jan 19;1(1):CD002783. doi: 10.1002/14651858.CD002783.pub5. PMID: 33464575; PMCID: PMC8094969**). However, meta analyses have indicated that PMT may slightly reduce rates of post-thrombotic syndrome relative to anticoagulation alone. There was also a small but significant increased risk of bleeding associated with the procedure in the ATTRACT trial (1.7% PCDT vs. 0.3% standard therapy; p =0.049). PCDT also did not significantly reduce recurrent VTE (12.5% PCDT vs. 8.5% standard therapy; p = 0.087)(**Kakkos SK et al., European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis, Eur J Vasc Endovasc Surg 2020**).

Both PMT and CDT are associated with increased rates of complete clot lysis compared to standard anticoagulation, although this has not translated to a reduced risk of PE (**Broderick C, Watson L, Armon MP. Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb. Cochrane Database Syst Rev. 2021 Jan 19;1(1):CD002783. doi: 10.1002/14651858.CD002783.pub5. PMID: 33464575; PMCID: PMC8094969**). There are no significant differences between PMT and CDT in rates of PTS, VTE recurrence, or bleeding events. However, meta analyses have suggested that PMT is more effective than CDT at reducing severity of PTS, and the clot lysis time and length of hospital stay are also shorter for PMT. High quality evidence is still lacking to support PMT over catheter-directed thrombolysis alone (**Tang T, Chen L, Chen J, et al. Pharmacomechanical Thrombectomy Versus Catheter-Directed Thrombolysis for Iliofemoral Deep Vein Thrombosis: A Meta-Analysis of Clinical Trials. Clin Appl Thromb Hemost. 2019 Jan-Dec;25:1076029618821190**).

EVIDENCE BASED STATEMENT

Domain 6; Statement 8

STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 06, Statement 08

Pharmaco-mechanical thrombolysis is clot treatment and removal through a catheter. This treatment is safe in expert hands after proper consideration of the risks and benefits. A careful specialist evaluation must be performed to avoid treatment when not appropriate.

4 SELECTED REFERENCES

1. Broderick C, Watson L, Armon MP. Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb. Cochrane Database Syst Rev. 2021 Jan 19;1(1):CD002783.
2. Tang T, Chen L, Chen J, Mei T, Lu Y. Pharmacomechanical Thrombectomy Versus Catheter-Directed Thrombolysis for Iliofemoral Deep Vein Thrombosis: A Meta-Analysis of Clinical Trials. Clin Appl Thromb Hemost. 2019 Jan-Dec;25:1076029618821190.
3. Kakkos SK, Gohel M, Baekgaard N, et al. European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis
4. Robertson L, McBride O, Burdess A. Pharmacomechanical thrombectomy for iliofemoral deep vein thrombosis. Cochrane Database Syst Rev. 2016 Nov 4;11(11):CD011536.

identified LITERATURE BIAS

Few studies comparing CDT to PMT, and even fewer comparing to DOACs.

SUGGESTED NEXT LINES OF RESEARCH

Randomized controlled trials comparing CDT to PMT and comparing PMT/CDT to DOACs.
Need for more research on cutting edge interventional devices for PMT, which have replaced those used in the ATTRACT trial.