Innovations in DVT Treatment: An Evidence-Based Review of Proximal and Distal Approaches

Farbod Fazlollahi[1,2], BS; Mina S. Makary[1,2], MD
College of Medicine[1]; Division of Vascular and Interventional Radiology, Department of Radiology, The Ohio State University Wexner Medical Center[2], Columbus, OH 43210, United States

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Purpose

- Deep vein thrombosis (DVT) of the lower limbs is a prevalent and serious condition, affecting 9.3 per 10,000 individuals annually.
- Cancer patients are at particular risk due to hypercoagulability, prolonged immobility, endothelial injury from oncotherapy, and catheterization.
- DVT is categorized as proximal (inferior vena cava to popliteal vein) or distal (below the knee), with treatment goals focused on symptom resolution, quality of life improvement, and minimizing adverse events.
- This work presents an evidence-based review of the current data on effectiveness and long-term outcomes by treatment modality for proximal DVT (PDVT) and distal DVT (DDVT).

Materials and Methods

- A comprehensive review of guidelines and clinical data was conducted, focusing on management approaches to PDVT and DDVT.
- Data were collected from PubMed-indexed literature, recent and ongoing clinical trials, and guidelines from multiple clinical societies.

Results

- Current guidelines from SIR and ASH encourage prompt systemic or catheter-directed anticoagulation for PDVT based on severity and bleeding risk, while urgency for DDVT treatment varies.
- Mechanical thrombectomy (MT) is generally not recommended due to uncertain efficacy compared to pharmacologic methods but may be viable for limb-threatening DVT.

Clinical Society	UK National Institute of Healthcare Excellence (2020)	American Society of Hematology (2020)
Guideline	CDT– symptomatic for <14d, good functional status, life expectancy >1 yr, and low bleeding risk.	AC first. If DVT extensive and thrombolysis appropriate, CDT >> systemic.
European Society of Vascular Surgery (2021)	**American College of Chest Physicians (2021)**	**Society of Interventional Radiology (2023)**
Early MT recommended if symptomatic. DDVT - systemic AC >> early MT.	Acute DDVT - systemic AC. If limb-threatening - MT, thrombolysis (systemic or CDT).	Therapeutic AC first, then interventional techniques in severely symptomatic patients with low bleeding risk, few comorbidities, and high pre-DVT functional status.

Table 1. Societal Iliofemoral DVT Management Guidelines. Review of clinical societal recommendations for management of acute iliofemoral DVT as a demonstration of general agreement between different societies on management of the same condition. (CDT: catheter directed thrombolysis; AC: anticoagulation; MT: mechanical thrombectomy)

Technique	Technologies
Mechanical Clot Engagement and/or Aspiration	• *ICHOR Percutaneous Reperfusion System (ICHOR Vascular)* • *Laguna Thrombectomy System (Innova Vascular)* • Artix (Inari Medical) • SmartClaw Thrombectomy Catheter (Boston Scientific) • *Pounce Thrombectomy Systems (Surmodics)** • *ClotTriever (Inari Medical)*
Mechanical Clot Disruption/Maceration and Aspiration	• Cleaner Rotational Thrombectomy System (Argon Medical Devices)* • Aspirex Mechanical Aspiration System (BD/Bayer)* • D*Clot HD Thrombectomy System (Mermaid Medical)* • Symphony Thrombectomy System (Imperative Care Vascular) • Prodigy Thrombectomy System (Imperative Care Vascular) • FlowTriever Catheter (Inari Medical)
Rheolytic Clot Disruption and Aspiration	• Jeti (Walk Vascular/Abbott)* • *AngioJet (Boston Scientific)*
Thrombus Aspiration	• AlphaVac (AngioDynamics) • Control Mechanical Thrombectomy System (Control Medical Technology) • Lightning Flash/Bolt Thrombectomy System (Penumbra) • QuickClear Mechanical Thrombectomy System (Philips)
Catheter-Directed Thrombolysis (± Aspiration)	• EKOS Endovascular System (BTG/Boston Scientific)* • ZelanteDVT Catheter (Boston Scientific) • Bashir Endovascular Catheters (Thrombolex)* • Cleaner Rotational Thrombectomy System (Argon Medical Devices)* • Multi-Sideport Catheter Infusion Set (Multiple Companies)

Table 2a. Currently available interventional technologies for the treatment of peripheral thrombosis. Mechanical clot engagement typically relies on Nitinol mesh. Rheolytic devices use liquid to macerate and fragment thrombi. Catheter-Directed Thrombolysis devices have the functionality to deliver thrombolytic agents at the thrombus with or without additional functionality. * - indicates unique mechanism of action compared to other devices in the same class. *Italicized* – indicates utility in both acute AND chronic clot.

	Anticoagulant	Mechanism of Action	Average Cost Per Month (in USD)	Reversal Agent	Half-Life
Direct Oral Anticoagulants	Dabigatran (Pradaxa)	Direct thrombin inhibitor	~$293	Idarucizumab (Praxbind)	12-17 hours
	Rivaroxaban (Xarelto)	Direct Factor Xa inhibitor	~$625	Andexanet alfa (Andexxa), aPCC	5-9 hours
	Apixaban (Eliquis)	Direct Factor Xa inhibitor	~$700	Andexanet alfa (Andexxa), aPCC	12 hours
	Edoxaban (Savaysa)	Direct Factor Xa inhibitor	~$513	None (aPCC off-label)	10-14 hours
	Unfractionated Heparin	Inhibits thrombin & Factor Xa	Variable ($120 - $319)	Protamine sulfate	1-1.5 hours
Low Molecular Weight Heparins	Enoxaparin (Lovenox)	Primarily inhibits Factor Xa	~$787	Protamine sulfate (partial)	4-7 hours
	Dalteparin (Fragmin)	Primarily inhibits Factor Xa	~$1461	Protamine sulfate (partial)	3-5 hours
	Tinzaparin (Innohep)	Inhibits Factor Xa and thrombin	Variable	Protamine sulfate (partial)	3-4 hours
	Fondaparinux (Arixtra)	Indirect Factor Xa inhibitor	~$3888	None (aPCC/rFVIIa off-label)	17-21 hours
	Warfarin (Coumadin)	Inhibits vitamin K-dependent factors	~$261	Vitamin K, FFP, PCC	20-60 hours

Table 3. Pharmacotherapeutics for Venous Thromboembolism. Anticoagulants currently FDA approved for use in venous thromboembolism. Costs are for 30d supply of brand name medication from commercial pharmacy without insurance. (USD: United States Dollars; aPCC: Activated prothrombin complex concentrate; FFP: Fresh frozen plasma)

Technology	Unique Characteristic
Pounce Thrombectomy Systems (Surmodics)*	• 2 sequential mesh baskets for engagement • DDVT and PDVT specific models
Cleaner Rotational Thrombectomy System (Argon Medical Devices)*	• Vessel wall contact with sinusoidal wire for clot maceration with simultaneous thrombolytic delivery
Aspirex Mechanical Aspiration System (BD/Bayer)*	• Helical aspiration with mechanical augur transport, continuous augur maceration inside catheter tip
D*Clot HD Thrombectomy System (Mermaid Medical)*	• High-speed rotating spiral shaft with steel tip for rapid clot maceration
Jeti (Walk Vascular/Abbott)*	• Saline jet inside catheter directed orthogonal to aspiration axis for rheolytic clot maceration
EKOS Endovascular System (BTG/Boston Scientific)*	• Utilizes ultrasound energy to disrupt clot and expose more surface area to thrombolytics
Bashir Endovascular Catheters (Thrombolex)*	• Deploys mesh-shaped catheter inside clot to simultaneously disrupt clot and greatly increase clot surface area exposed to thrombolytic

Table 2b. Techniques with unique mechanism of action compared to other technologies of the same class.

Results cont…

- Less consensus exists for DDVT management, but recent and ongoing clinical trials have had intriguing results.
- Comparison of data from the ATTRACT trial and CLOUT registry revealed that anticoagulation alone significantly increases risk of post-thrombotic syndrome (PTS), a chronic complication of DVT, compared to MT.
- CAVA, CAVENT, and ATTRACT trials have provided valuable data, but a distinct benefit over standard of care has not yet been shown.
- One example is the RIETE Registry, an ongoing international clinical registry of acute VTE started in 2001, currently with 128,584 cases recorded across 203 hospitals.
- With advances in MT technology and endovascular anticoagulation, improved management protocols for acute PDVT and DDVT are on the horizon.

Conclusions

- Advancements in endovascular approaches to thrombectomy and anticoagulation have broadened treatment options for both PDVT and DDVT.
- DVT and its complication, PTS, represent a substantial global healthcare and economic burden.
- Further research and large-scale trials are essential to optimize treatment paradigms, minimize time to complete VTE resolution, and reduce endothelial damage and systemic anticoagulant exposure.

References

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