Anticoagulation after Ilio-femoral intervention

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Disclosure Statement of Financial Interest

I, Raghu Kolluri, have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

• Consultant/ Advisor – UNCOMPENSATED
  • Bard/ BD, Boston Scientific, BTG, Inari, Innovein, Intervene, Janssen, Medtronic, Philips IGT/ Ultrasound, Vascular Insights, Vesper Medical, Thrombolex

• Board Member – VIVA Physicians Inc, 501c

• Medical Director – Syntropic Core lab, 501c
What Do Guidelines & Societies Tell Us?
9th / “10th ” ACCP Guidelines

• **No mention** of anticoagulant/antiplatelet therapy after venous stenting (2012/2016)
AHA Guidelines

• After venous stent placement, the use of therapeutic anticoagulation with **similar dosing, monitoring and duration** as for iliofemoral DVT patients without stents is reasonable. (Class IIa; Level of Evidence C)

• After venous stent placement, the use of **antiplatelet therapy** with concomitant anticoagulation in patients perceived to be at high **risk of rethrombosis** may be considered (Class IIb; level of Evidence C)
Continuous anticoagulation with warfarin aiming at a target International Normalized Ratio (INR) range of 2.5–3 is strongly recommended, although there is no evidence from controlled studies on this issue. Platelet aggregation is known to be important in high-flow, high-shear environment, such as in the coronary arteries, whereas coagulation may be more important in the fibrin-rich thrombi characteristic of the low-flow, low-shear venous circulation [42]. The relative importance of antiplatelet agents versus anticoagulants has never been evaluated in clinical trials and is largely based on extrapolation from the arterial system and an understanding of the venous system. Based on clinical data on stenting of chronic iliacal occlusions, long-term warfarin is recommended in patients with long occlusions, underlying thrombophilia, suprarenal occlusions, and previous long-term anticoagulation and poor inflow on completion angiogram [43, 44]. With postthrombotic lesions being more prone to restenosis, the use of anticoagulants appears to be useful in this subgroup. Thus, although the use of antiplatelet agents and anticoagulants has not been studied systematically, there seems to be a role for these drugs.
Data for AC/ Antiplatelet treatment?

<table>
<thead>
<tr>
<th>Article [year]</th>
<th>Acute DVT management procedure</th>
<th>A/C drug after treatment</th>
<th>A/C duration</th>
<th>Antiplatelet therapy after treatment</th>
<th># MTS patients with acute DVT treated with stent placement</th>
<th># Of events evaluated at 12 months</th>
<th># Of events by 12 months*</th>
<th># Of patients events free at 12 months</th>
<th>Stent patency and event free at 12 months (of those evaluable at 12 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldman (2017)</td>
<td>Catheter directed thrombolysis or pharmacomechanical thrombolysis</td>
<td>Variable, but delineated for each patient</td>
<td>Variable</td>
<td>No</td>
<td>6</td>
<td>5/6</td>
<td>2</td>
<td>3</td>
<td>5/5; 60%</td>
</tr>
<tr>
<td>Husman (2007)</td>
<td>Surgical thrombectomy and Thrombolysis and AV fistula formation</td>
<td>Warfarin</td>
<td>6 months</td>
<td>No</td>
<td>11</td>
<td>9/11</td>
<td>2</td>
<td>7</td>
<td>7/9; 78%</td>
</tr>
<tr>
<td>Kim (2017)</td>
<td>Pharmacomechanical thrombolysis</td>
<td>Warfarin</td>
<td>6 months</td>
<td>Aspirin and clopidogrel prescribed for 1 year, after warfarin</td>
<td>25%</td>
<td>25/25</td>
<td>1</td>
<td>24</td>
<td>24/25; 95%</td>
</tr>
<tr>
<td>Maitsoeda (2014)</td>
<td>Catheter-directed thrombolysis</td>
<td>Warfarin</td>
<td>Variable</td>
<td>No</td>
<td>13</td>
<td>10/13</td>
<td>2</td>
<td>8</td>
<td>8/10; 80%</td>
</tr>
<tr>
<td>Roy (2017)</td>
<td>Pharmacomechanical thrombolysis + stent, or angioplasty + stent</td>
<td>Warfarin</td>
<td>“Long-term”</td>
<td>No</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>6/6; 100%</td>
</tr>
</tbody>
</table>

**Essentials**

- May-Thurner syndrome (MTS) is an anatomical variant that may be associated with deep vein thromboembolism (DVT).
- Optimal antithrombotic management in patients with MTS and DVT who undergo endovascular stenting is unknown.
- The available evidence on antithrombotic management in this setting is reviewed and discussed.
- Optimal systemic management in this setting remains uncertain and further high-quality, prospective studies are needed.
87 patients ivc or iliocaval stents
Warfarin (n=42); enoxaparin (n=14); DOAC (n=19); DAPT (n=8)
DOAC studies

- 10 procedures for iliofemoral post-thrombotic obstruction
- Rivaroxaban 20mg once daily and clopidogrel 75mg daily or QOD for 6 mo.
- Mean f/u 14 mo. 100% patency

- Rivaroxaban (n=78); VKA (n=38)
- Mean f/u 24 mo (3-77 mo)
- Primary patency rivaroxaban 87% (76-94%); VKA 95% (85-98%)

Combination of factor Xa inhibition and antiplatelet therapy after stenting in patients with iliofemoral post-thrombotic venous obstruction


First Published July 15, 2015; pp. 430–437

Rivaroxaban or vitamin-K antagonists following early endovascular thrombus removal and stent placement for acute iliofemoral deep vein thrombosis

Tim Sebastian, Lawrence O. Hakki, David Spirk, Frederic A. Baumann, Daniel Périard, Martin Banyai, Rebecca S. Spescha, Nils Kucher, Rolf P. Engelberger

Thrombosis research. 2018 Dec 1;172:86-93.
Antithrombotic Therapy Following Venous Stenting: International Delphi Consensus

Kristijonas Milinis, Ankur Thaper, Joseph Shallhoub, Alan H. Davies

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2 Imperial College Healthcare NHS Trust and Imperial College London, London, UK

Edema + Varicose Veins + May Thurner

DVT/ Post Lysis + May Thurner

VLU + PTS + Long seg Iliac V Occlusion
OhioHealth/ Riverside Methodist Hospital DOAC experience

- **71 DOAC**
  - 16 Lost to Follow up
  - 55 on DOAC followed (Range 1-43 months)
    - 100% Patency 48 (87%)
    - Secondary Intervention 7 (13%)
Patency Rates
LMWH to Warfarin is the best

No Way! LMWH for 4 weeks

DOAC is ok people!
Extended LMWH Rationale

• Steady state AC
• Anti-inflammatory effects
• Prior DOAC failures/ Standard AC failure

• Caution
  • HIT possibility
  • 0.5% absolute risk
  • ? Platelet monitoring
LMWH Rationale

• Bleeding
• ANTI-XA
  • Pregnancy
  • Extreme body weights
  • Children
  • Renal insufficiency
  • Elderly (weight based) –
    • Hemorrhagic complications 12%

• Blood, Vol78, No9(November), 1991;pp 2337-2343
• Thromb Haemost 2000; 84(04): 559-564
Venous Thromboembolism Prophylaxis and Treatment in Patients with Cancer

High-risk outpatients with cancer may be offered thromboprophylaxis with Apixaban, Rivaroxaban, or LMWH provided there are no significant risk factors for bleeding and no drug interactions.

Consideration of such therapy should be accompanied by a discussion with the patient about the relative benefits and harms, drug cost, and duration of prophylaxis in this setting.

Initial Anticoagulation

Initial anticoagulation may involve LMWH, UFH, Fondaparinux, or Rivaroxaban.

Long-Term Anticoagulation

For long-term anticoagulation, LMWH, Edoxaban, or Rivaroxaban for at least 6 months are preferred because of improved efficacy over VKA. VKA are inferior, but may be utilized if LMWH or direct oral anticoagulants (DOAC) are not accessible.

There is an increase in major bleeding risk with DOAC, particularly observed in GI and potentially GU malformations. Caution with DOAC is also warranted in other settings with high risk for mucosal bleeding. Drug-drug interaction should be checked prior to using a DOAC.

Apixaban, rivaroxaban, and LMWH have not been FDA approved for thromboprophylaxis in outpatients with cancer. Dalteparin is the only LMWH with FDA approval for extended therapy to prevent recurrent thrombosis in patients with cancer.

Key et al J Clin Oncol 2019
asco.org/supportive-care-guidelines

ORIGINAL ARTICLE

Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism

Gary E. Raskob, Ph.D., Nick van Es, M.D., Peter Verhamme, M.D., Marc Carrier, M.D., Marcello Di Nisio, M.D., David Garcia, M.D., Michael A. Grosso, M.D., Ajay K. Kakkar, M.B., B.S., Michael J. Kovacs, M.D., Michele F. Mercuri, M.D., Guy Meyer, M.D., Annelise Segers, M.D., Minggao Shi, Ph.D., Tzu-Fei Wang, M.D., Erik Yeo, M.D., George Zhang, Ph.D., Jeffrey I. Zwicker, M.D., Jeffrey I. Weitz, M.D., and Harry R. Bülle, M.D., for the Hokusai VTE Cancer Investigators*

Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D)

Anne M. Young, Andrea Marchal, Jenny Thirlwall, Oliver Chapman, Arvind Lekar, Catherine Hall, Danielle J. Hall, Janet A. Dunn, Gary H. Lyman, Charles Bachmann, Peter MacCallum, Ajay Kakkar, E.D. Richard Halperin, Steven Pepe, Jenny Cole, Christopher J. Posr, Anthony Marcon, and Mark Leith


ORIGINAL ARTICLE

Apixaban and dalteparin in active malignancy-associated venous thromboembolism: The ADAM VTE trial


J Thromb Haemost. 2019;00:1–11.
Apixaban for the Secondary Prevention of Thrombosis Among Patients With Antiphospholipid Syndrome: Study Rationale and Design (ASTRO-APS)

Scott C. Woller, MD, Scott M. Stevens, MD, David A. Kaplan, MD, D. Ware Branch, MD, Valerie T. Aston, BS, Emily L. Wilson, MS, Heather M. Gallo, BS, Eric G. Johnson, MPH, Matthew T. Rondina, MD, James F. Lloyd, BS, R. Scott Evans, PhD, and C. Gregory Elliott, MD

Rivaroxaban in antiphospholipid syndrome (RAPS) protocol: a prospective, randomized controlled phase II/III clinical trial of rivaroxaban versus warfarin in patients with thrombotic antiphospholipid syndrome, with or without SLE

H Cohen, CJ Dore, S Clowse, BJ Hunt, D Izenberg, M Khamashta, and N Mayhead on behalf of the RAPS Trial Protocol Collaborators

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Lancet (2015) 386, 1087-1094
http://lancetpub.com
Aspirin for Preventing the Recurrence of Venous Thromboembolism

Cecilia Becattini, M.D., Ph.D., Giancarlo Agnelli, M.D., Alessandro Schenone, M.D., Sabine Eichinger, M.D., Eugenio Bucherini, M.D., Mauro Silingardi, M.D., Marina Bianchi, M.D., Marco Moia, M.D., Walter Ageno, M.D., Maria Rita Vandelli, M.D., Elvira Grandone, M.D., and Paolo Prandoni, M.D., Ph.D., for the WAFASA Investigators*

- **Steady state AC**
  - Duration – Based on underlying cause
  - ASA
  - Acute phase?
  - After anticoagulation termination – YES

- **Our practice**
  - Enoxaparin X1 injection in cath lab
  - Apixaban loading dose + ASA 81mg

- **Complex/ Cancer**
  - Enoxaparin 1 mg/kg Q12 (Anti XA adjusted)
  - Followed by Warfarin bridge

- **Have we not exposed that endothelium/ intrinsic pathway?**
  - 3 months of AC as situational

Low-Dose Aspirin for Preventing Recurrent Venous Thromboembolism

Need to collect more data on anticoagulation regimens in interventional trials!

Affects the patency rates
Affects our patients
Anticoagulation after Ilio-femoral intervention

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