Antithrombotic therapy after venous stents

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Disclosure

Dr. Raghu Kolluri reports following –

- **Uncompensated Consultant/Advisor**—Boston Scientific, Intact Vascular, InterVene, Medtronic, Pedra, Philips, Thrombolex, Vesper Medical
- **Executive Board Member** – VIVA Physician Inc, a 501c3 Corp
Antithrombotic Therapy Following Venous Stenting: International Delphi Consensus

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Edema + Varicose Veins + May Thurner

DVT/ Post Lysis + May Thurner

VLU + PTS + Long seg Iliac V Occlusion
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)

Circulation 2011; 123: 1788-1830
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 iliofemoral 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.
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.
Outcomes of endovascular venous stenting in patients on direct oral anticoagulants and antiplatelet therapy at a tertiary referral center

Katherine Hays, DNP, Michael Jolly, MD, Mitch Silver, MD, John Phillips, MD, Christopher Huff, MD, Michelle Secic, MS, Gary Ansel, MD, and Raghu Kolluri, MD, Columbus and Chardon, Ohio

ABSTRACT

Background: Endovenous revascularization is the standard in the management of acute thrombotic, chronic post-thrombotic iliocaval or iliofemoral obstruction, and nonthrombotic iliac vein lesions. The purpose of this study is to describe our single-center experience of postprocedure anticoagulation and antiplatelet regimens used after endovenous revascularization for a variety of venous occlusive conditions.

Methods: We conducted a retrospective analysis of 100 consecutive patients who underwent endovenous stenting for iliocaval or iliofemoral obstruction from January 1, 2014, to April 30, 2018. Patients treated with direct oral anticoagulants, warfarin, or low-molecular-weight heparin (LMWH) with or without antiplatelet therapy were identified. Demographic, procedural, patency, and follow-up data were collected. Stent patency was evaluated using duplex Doppler ultrasound examination or contrast venography.

Results: Seventy-one of 100 patients were treated with direct oral anticoagulant therapy (DOAC). Sixteen (23%) were lost to follow-up, leaving 55 (77%) available for analysis. The mean follow-up was 14 months (range, 1-43 months) with 32 patients (58%) followed for 12 months or longer. Primary, primary-assisted, and secondary-assisted patency rates were 87%, 97%, and 98%, respectively, at 12 months. In the non-DOAC group (patients treated with warfarin or LMWH), these rates were 87%, 93%, and 95%, respectively, at 12 months. Antiplatelet therapy, including clopidogrel, aspirin, or both, was used in 53 of 55 patients in the DOAC cohort and 18 of 19 patients in the non-DOAC group.

Conclusions: Our single-center retrospective analysis demonstrates acceptable primary patency rates when using DOAC therapy compared with those treated with warfarin or LMWH. (J Vasc Surg: Venous and Lym Dis 2020:1-7.)

Keywords: Direct oral anticoagulant; Warfarin; Vitamin K antagonist; Low-molecular-weight heparin; Endovenous stent; Venous stent; Iliocaval obstruction; Iliofemoral obstruction; Iliofemoral deep venous thrombosis
OhioHealth/Riverside Methodist DOAC experience

- 100 Patient Cohort
- 2 Patients not stented
- 27 Non-DOAC
  - 19 followed (Range 1-43 Months)
    - Primary Patency 12 months 87%
    - Secondary Intervention 2 (13%)
  - 19 followed (Range 1-43 Months)
    - Primary Patency 12 months 87%
    - Secondary Intervention 7 (13%)
- 71 DOAC
  - 55 on DOAC followed (Range 1-43 months)

- 37 (67%) – apixaban
- 17 (31%) – rivaroxaban
- 1 (2%) – dabigatran.
Etiology – Acute Vs Chronic Vs NIVL

Primary Patency DOAC Vs Non-DOAC
Extended LMWH Rationale

- Steady state AC
- Anti-inflammatory effects
- Prior DOAC failures/ Standard AC failure
- Avoids issues with narrow therapeutic window of warfarin

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%

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<th>Anti-Xa Level (U/mL)</th>
<th>≤0.8</th>
<th>&gt;0.8 ≤1.0</th>
<th>&gt;1.0</th>
<th>P Value</th>
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<td>All patients</td>
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<td>Bleeding present/absent</td>
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<td>3/2</td>
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<td>Risk (%)</td>
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<td>14</td>
<td>60</td>
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<td>Heparin group</td>
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<td>Bleeding present/absent</td>
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<td>1/9</td>
<td>2/1</td>
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<tr>
<td>Risk (%)</td>
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<td>10</td>
<td>67</td>
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<td>Fragmin group</td>
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<td>1/1</td>
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<tr>
<td>Risk (%)</td>
<td>8</td>
<td>18</td>
<td>50</td>
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- 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
- 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.

Treatment
- For patients initiating treatment with parenteral anticoagulation, LMWH is preferred over UFH for the initial 5-10 days of anticoagulation for the patient with cancer who has been diagnosed with VTE who does not have severe renal impairment.

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.

ASCO Guidelines

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. Bülher, M.D., for the Hokusai VTE Cancer Investigators*


Original Article

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

J Thromb Haemost. 2019;00:1–11.
DOACs in “aggressive clotters”

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.

SPECIAL ARTICLE

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 Dorm, S Clawson, BJ Hunt, D Isenberg, M Khamashita, and N Muirhead on behalf of the RAPS Trial Protocol Collaborators

1Department of Haematology, University College London Hospitals NHS Foundation Trust, London, UK; 2Haemostasis Research Unit, Department of Haematology, University College London, London, UK; 3University College London Comprehensive Clinical Trials Unit, Gower Street, London, UK; 4Department of Haematology, Guy’s and St Thomas’ NHS Foundation Trust, London, UK; 5Department of Rheumatology, Guy’s and St Thomas’ NHS Foundation Trust, London, UK; 6Department of Haematology, Kings College London, London, UK; 7Centre for Rheumatology Research, Division of Medicine, University College London, London, UK; and 8Department of Rheumatology, Kings College London, London, UK.
Summary

PTS
• 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

NIVL
• Have we not exposed that endothelium/intrinsic pathway?
• ? 3 months of AC as situational DVT?
• Our Practice
  • Enoxaparin X 1 in cath lab
  • AC with Rivaroxaban or Apixaban X3 month
  • Clopidogrel X 3 months
  • After 3 months, ASA only