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)

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CHEST 2012; 141(2)(Suppl):e152S-e184S
CHEST 2016;149(2):315-352

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)

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Circulation 2011; 123: 1788-1830

score [32]. 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 anti-platelet 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 iliocaval 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.

Cardiovasc Intervent Radiol (2014) 37:889–897
DOI 10.1007/s00270-014-0875-4

CIRSE

CIRSE STANDARDS OF PRACTICE GUIDELINES

CIRSE Standards of Practice Guidelines on Iliocaval Stenting

Andreas H. Mahnken · Ken Thomson ·
Michiel de Haan · Gerard J. O'Sullivan

Cardiovasc Intervent Radiol 2014;37:889-897

Data for AC/ Antiplatelet treatment?

TABLE 5 Stent and recurrent thrombosis outcomes

Article (year)	Acute DVT management procedure	A/C drug after treatment	A/C duration	Antiplatelet therapy after treatment	# MTS patients with acute DVT treated with stent placement	# Of pts evaluable at 12 months	# Of events by 12 months[a]	# Of patients events free at 12 months	Stent patency and event free at 12 months (of those evaluable at 12 months)
Goldman (2017)	Catheter directed thrombolysis or pharmocomechanical thrombolysis	Variable, but delineated for each patient	Variable	No	6	5/6	2	3	3/5, 60%
Husman (2007)	Surgical thrombectomy and Thrombolysis and AV fistula formation	Warfarin	6 months	No	11	9/11	2	7	7/9, 78%
Kim (2017)	Pharmocomechanical thrombolysis	Warfarin	6 months	Asprin and clopidogrel prescribed for 1 year, after warfarin	25[b]	25/25	1	24	24/25, 96%
Matsuda (2014)	Catheter-directed thrombolysis	Warfarin	Variable	No	13	10/13	2	8	8/10, 80%
Roy (2017)	Pharmocomechanical thrombolysis + stent, or angioplasty + stent	Warfarin	"Long-term"	No	6	6	0	6	6/6, 100%

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.

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Res Pract Thromb Haemost. 2019;3:70–78.

Original Article

Phlebology

Long-term antithrombotic therapy after venous stent placement

Phlebology
0(0) 1–7

DOI: 10.1177/0268355519893819
journals.sagepub.com/home/phl
SAGE

Chenyu Lin[1], Karlyn A Martin[1], Mei Wang[2], Brady L Stein[1] and Kush R Desai[3]

- 87 patients ivc or iliocaval stents
- Warfarin (n=42); enoxaparin (n=14); DOAC (n=19); DAPT (n=8)

Table 2. In-stent restenosis/thrombosis and bleeding events by anticoagulant regimen.

	TX ($n=52$)	APAC ($n=16$)	ACT ($n=11$)	DAPT ($n=8$)
Stent restenosis[a]	6 (14%)	2 (18%)	1 (33%)	4 (50%)
Major bleeding	4 (8%)	1 (6%)	1 (9%)	0
Minor bleeding	9 (17%)	4 (25%)	0	0
Any bleeding	11 (21%)	5 (31%)	1 (9%)	0

TX, triple therapy; APAC, anticoagulation with single antiplatelet; DAPT, dual antiplatelet therapy; ACT, anticoagulation only.
[a]Percentage out of patients who had follow-up venograms performed.

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

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

Nicolas Langwieser, Isabell Bernlochner, Isabel Wustrow, Ralf J Dirschinger, Juliane Jaitner, Michael Dommasch, Christian Bradaric, Karl-Ludwig Laugwitz, Tareq Ibrahim

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

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

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

Tim Sebastian[a,1], Lawrence O. Hakki[b,1], David Spirk[c,1], Frederic A. Baumann[a], Daniel Périard[d], Martin Banyai[a], Rebecca S. Spescha[a], Nils Kucher[a,*], Rolf P. Engelberger[b,d]

Thrombosis research. 2018 Dec 1;172:86-93.

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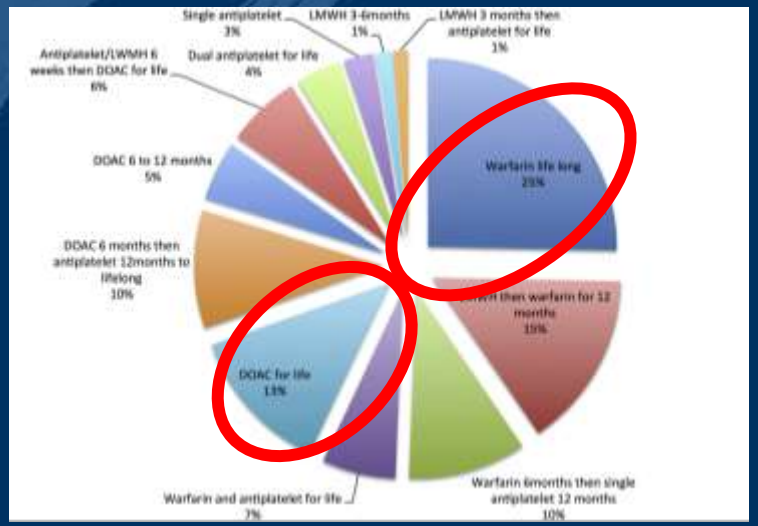
Eur J Vasc Endovasc Surg (2018) 55, 537–544

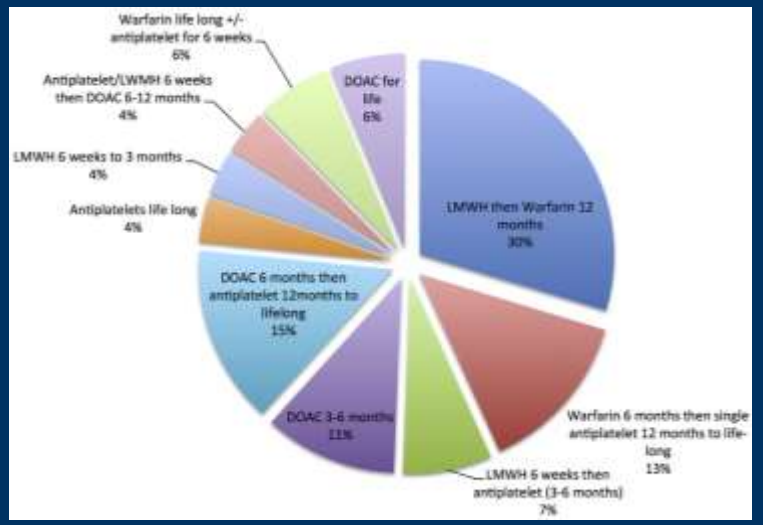
Antithrombotic Therapy Following Venous Stenting: International Delphi Consensus

Kristijonas Milinis [a], Ankur Thapar [b], Joseph Shalhoub [c], Alun H. Davies [a,*]

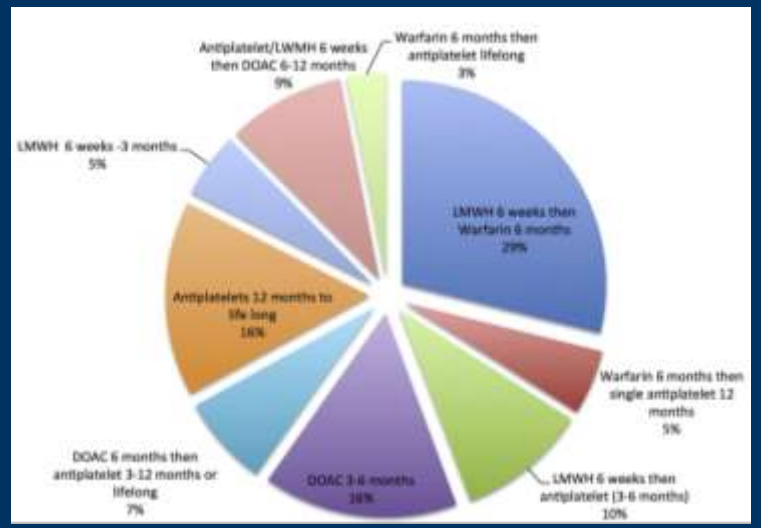
[a] Imperial College London, London, UK
[b] London Postgraduate School of Surgery and Imperial College London, London, UK
[c] Imperial College Healthcare NHS Trust and Imperial College London, London, UK



Edema + Varicose Veins + May Thurner



DVT/ Post Lysis + May Thurner



VLU + PTS + Long seg Iliac V Occlusion

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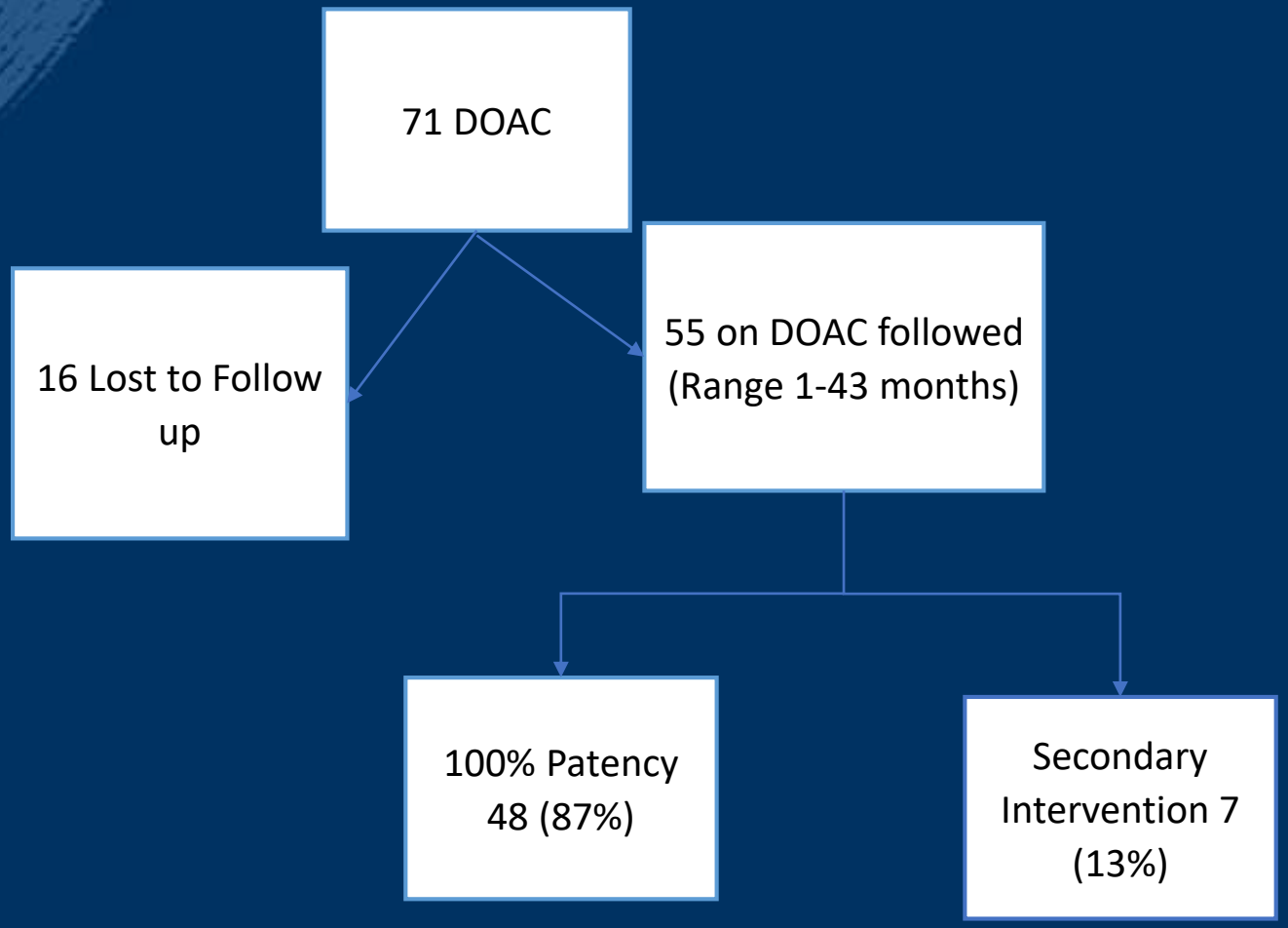
OhioHealth/ Riverside Methodist Hospital DOAC experience



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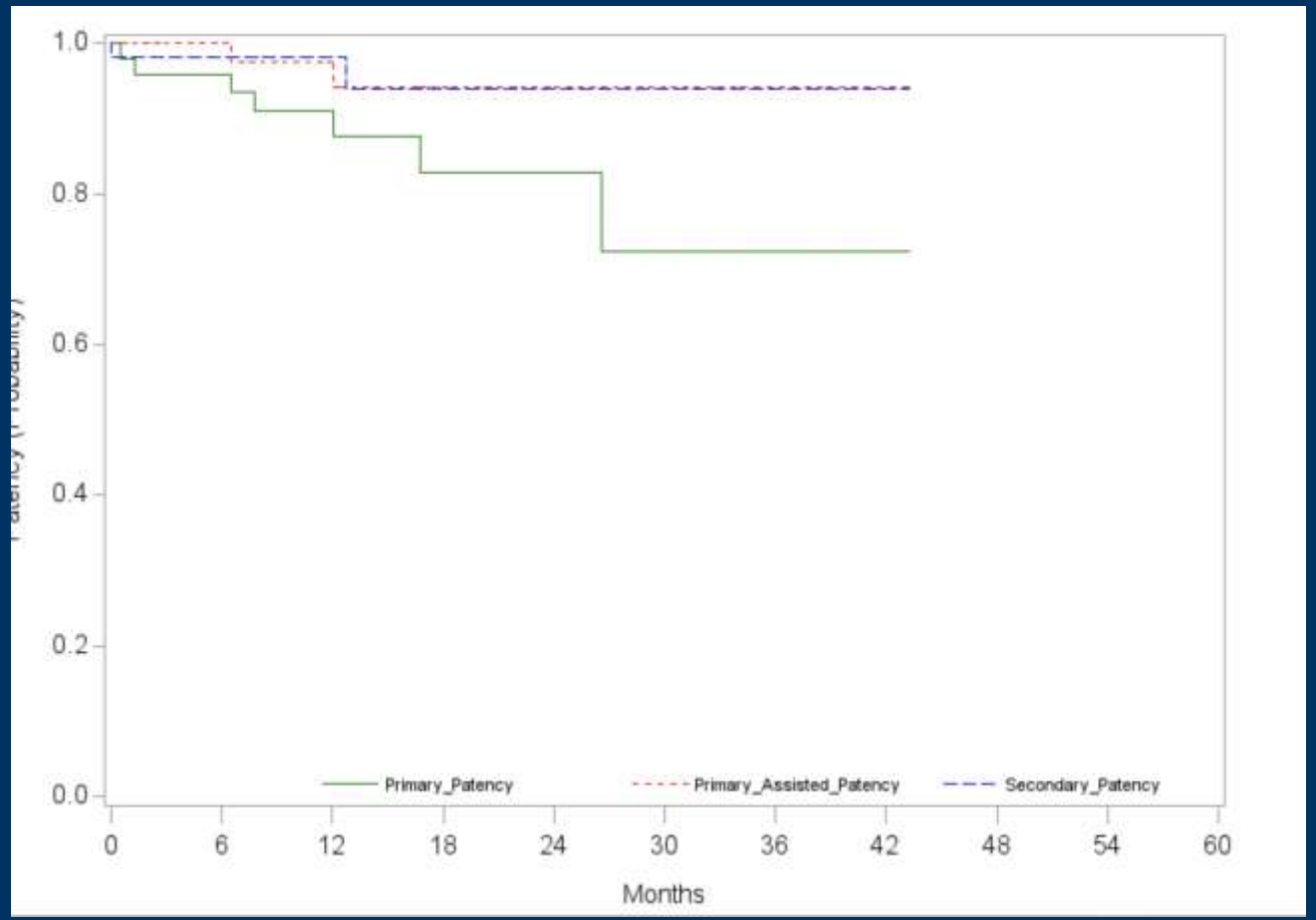
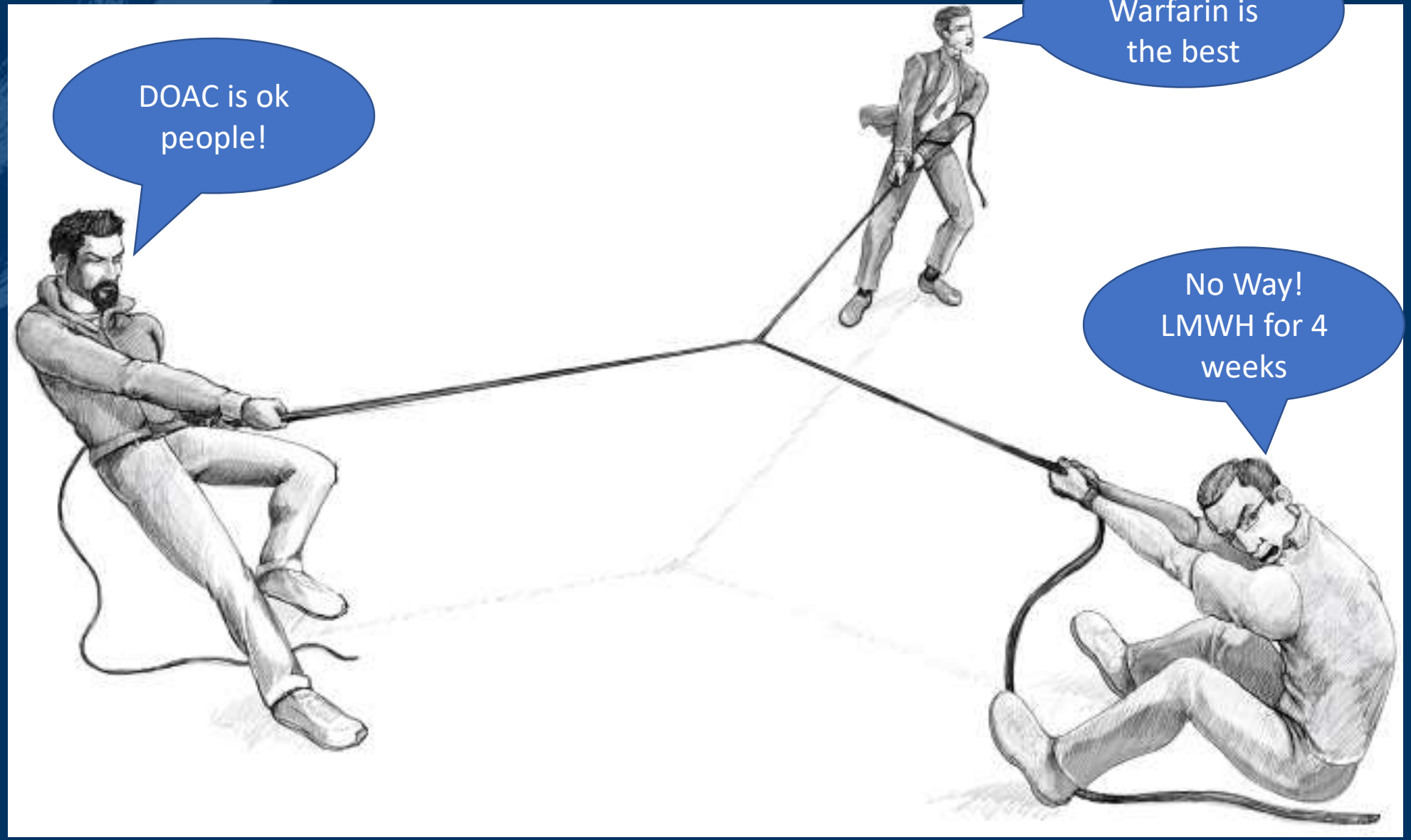
Patency Rates




DOAC is ok people!
LMWH to Warfarin is the best
No Way! LMWH for 4 weeks

Extended LMWH Rationale

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

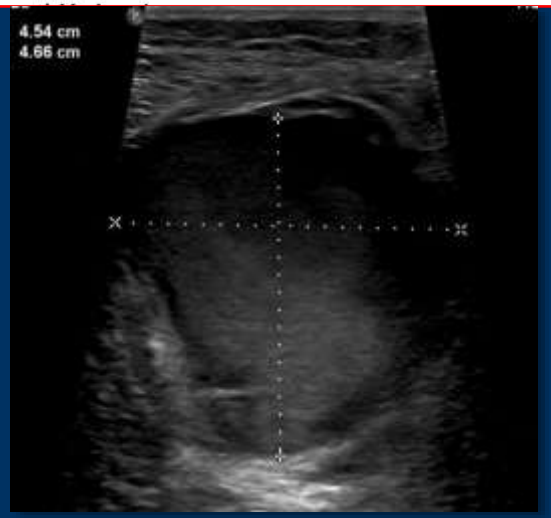
- Caution
  - HIT possibility
  - 0.5% absolute risk
  - ? Platelet monitoring

LMWH Rationale

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

Table 2. Relationship Between Anti-Xa Levels and Major Bleeding

	Anti-Xa Level (U/mL)			
	≤0.8	>0.8-≤1.0	>1.0	*P* Value
First anti-Xa level, 4 h after bolus				
All patients				
Bleeding present/absent	17/150	3/18	3/2	.003
Risk (%)	10	14	60	
Heparin group				
Bleeding present/absent	10/74	1/9	2/1	.022
Risk (%)	12	10	67	
Fragmin group				
Bleeding present/absent	7/76	2/9	1/1	.110
Risk (%)	8	18	50	



- Warkentin TE, et al. Chest 2008;133:340S-380S.
- Blood, Vol78, No9(Novemberl), 1991:pp 2337-2343
- Thromb Haemost 2000; 84(04): 559-564

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Venous Thromboembolism Prophylaxis and Treatment in Patients with Cancer

Prevention

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

Treatment

Initial Anticoagulation

Initial anticoagulation may involve

LMWH, UFH, Fondaparinux, or Rivaroxaban

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 with newly diagnosed VTE who does not have severe renal impairment

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 malignancies. 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

ASCO Guidelines

JOURNAL OF CLINICAL ONCOLOGY | RAPID COMMUNICATION

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)

Annie M. Young, Andrea Marshall, Jenny Thirlwall, Oliver Chapman, Anand Lokare, Catherine Hill, Danielle Hale, Janet A. Dunn, Gary H. Lyman, Charles Hutchinson, Peter MacCallum, Ajay Kakkar, F.D. Richard Hobbs, Stavros Petrou, Jeremy Dale, Christopher J. Poole, Anthony Maraveyas, and Mark Levine

J Clin Oncol. 2018 Jul 10.

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

N Engl J Med. 2018;378:615

ORIGINAL ARTICLE

jth

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

J Thromb Haemost. 2019;00:1–11.

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DOACs in “aggressive clotters”

Apixaban for the Secondary Prevention of Thrombosis Among Patients With Antiphospholipid Syndrome: Study Rationale and Design (ASTRO-APS)

Clinical and Applied Thrombosis/Hemostasis
2016, Vol. 22(3) 239-247

DOI: 10.1177/1076029615615960
cat.sagepub.com
SAGE

Scott C. Woller, MD[1,2], Scott M. Stevens, MD[1,2], David A. Kaplan, MD[2], D. Ware Branch, MD[1,3], Valerie T. Aston, BS[1], Emily L. Wilson, MS[4], Heather M. Gallo, BS[1], Eric G. Johnson, MPH[1], Matthew T. Rondina, MD[2], James F. Lloyd, BS[5], R. Scott Evans, PhD[5,6], and C. Gregory Elliott, MD[1,2]

Lupus (2015) 24, 1087–1094
http://lup.sagepub.com

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[1,2], CJ Doré[3], S Clawson[3], BJ Hunt[4,6], D Isenberg[7], M Khamashta[5,8] and N Muirhead[3]
on behalf of the RAPS Trial Protocol Collaborators
[1]Department of Haematology, University College London Hospitals NHS Foundation Trust, London, UK; [2]Haemostasis Research Unit, Department of Haematology, University College London, London, UK; [3]University College London Comprehensive Clinical Trials Unit, Gower Street, London, UK; [4]Department of Haematology, Guy's and St Thomas' NHS Foundation Trust, London, UK; [5]Department of Rheumatology, Guy's and St Thomas' NHS Foundation Trust, London, UK; [6]Department of Haematology, Kings College London, London, UK; [7]Centre for Rheumatology Research, Division of Medicine, University College London, London, UK; and [8]Department of Rheumatology, Kings College London, London, UK

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 24, 2012 VOL. 366 NO. 21

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 WARFASA Investigators*

ve not exposed that
elium/ intrinsic pathway?
ths of AC as situational

- **After anticoagulation terminati**
- Our practice
  - Enoxaparin X1 injection in cath l
  - Apixaban loading dose + ASA 81
- Complex/ Cancer
  - Enoxaparin 1 mg/kg Q12 (Anti X
  - Followed by Warfarin bridge

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 22, 2012 VOL. 367 NO. 21

Low-Dose Aspirin for Preventing Recurrent Venous Thromboembolism

Timothy A. Brighton, M.B., B.S., John W. Eikelboom, M.B., B.S., Kristy Mann, M.Biostat., Rebecca Mister, M.Sc., Alexander Gallus, M.B., B.S., Paul Ockelford, M.B., Harry Gibbs, M.B., Wendy Hague, Ph.D., Denis Xavier, M.Sc., Rafael Diaz, M.D., Adrienne Kirby, M.Sc., and John Simes, M.D., for the ASPIRE Investigators*

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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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