Rapid Fire-Top Articles You Need to Know

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- Financial Disclosures-NONE
This Year in Guidelines...
This Year in Guidelines...
ASH VTE Guidelines
Case

A 65 year old man with metastatic lung cancer presents with unilateral lower extremity edema. An ultrasound shows occlusive thrombus in the common femoral, deep femoral and popliteal veins. He has no SOB, CP, and VS are stable. What anticoagulant regimen do you recommend?

1. LMWH
2. Edoxaban
3. Rivaroxaban
4. Whatever Dr. Garcia says
What’s New in Cancer-Associated VTE?

Rascob NEJM 2018; Young AM et al, Journal of Clinical Oncology; Carrier M NEJM 2019
<table>
<thead>
<tr>
<th>agent</th>
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<tbody>
<tr>
<td>LMWH</td>
<td>Preferred 2017</td>
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<tr>
<td>edoxaban</td>
<td>with LMWH lead in</td>
</tr>
<tr>
<td>rivaroxaban</td>
<td></td>
</tr>
<tr>
<td>apixaban</td>
<td>Limited to those with compelling reason to avoid LMWH</td>
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Guidelines list urinary or GI tract lesions, pathology, or instrumentation as relative contraindications to DOACs in patients with cancer.
ISTH DOACS in CANCER GUIDEDANCE

- We suggest the use of specific DOAC for active cancer patients with an acute VTE, low risk of bleeding & no drug–drug interactions with current systemic therapy. LMWHs constitute an acceptable alternative.
- Currently, edoxaban and rivaroxaban are the only DOACs that have been compared with LMWH in RCTs in cancer.
- Inform patients regarding potential reduction in recurrence but higher bleeding.

Khorana et al. Journal of Thrombosis and Haemostasis, 16: 1891–1894
We suggest the use of LMWHs for cancer patients with acute diagnosis of VTE and a high risk of bleeding (GI cancers with intact primary, cancers at risk of bleeding from the GU tract, bladder, or nephrostomy tubes, active GI mucosal abnormalities such as duodenal ulcers, gastritis, esophagitis, or colitis.)

Specific DOACs (edoxaban and rivaroxaban) are acceptable alternatives if there are no drug–drug interactions with current systemic therapy.

Khorana et al. Journal of Thrombosis and Haemostasis, 16:1891–1894
The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

Jan Steffel, Peter Verhamme, Tatjana S. Potpara, Pierre Albaladejo, Matthias Antz, Lien Destege, Karl Georg Haeusler, Jonas Oldgren, Holger Reinecke, Vanessa Roldan-Schilling, Nigel Rowell, Peter Sinnaeve, Ronan Collins, A. John Camm, and Hein Heidbüchel

Vasquez S. Drug-drug interactions in an era of multiple anticoagulants: a focus on clinically relevant drug interactions DDIs. Hematology 2018
“Skilled drug interaction management is critical, consult multiple resources”

A 65 year old man with metastatic lung cancer presents with unilateral lower extremity edema. An ultrasound shows occlusive thrombus in the common femoral, deep femoral and popliteal veins. He has no SOB, CP, and VS are stable. What anticoagulant regimen do you recommend?

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Case

A 35 year old woman with lupus presents with unprovoked bilateral pulmonary embolism. Baseline coags are significant for a prolonged aPTT raising concern for antiphospholipid syndrome. What anticoagulation regimen do you recommend?

1) LMWH → warfarin
2) Rivaroxaban VTE dosing
3) IV heparin → warfarin
4) Whatever Dr Garcia says
Anticoagulation in APS

- Pathophysiology
- Diagnostic criteria
  - Thrombosis
  - Persistently lupus anticoagulant, positive acL, and/or B2gp1 abs (separated by at least 12 weeks)
- Laboratory interpretation

Anticoagulation in APS

Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome


Intervention-Rivaroxaban 20 mg QD (15 mg if CrCl 30-50 ml/min) v warfarin (INR 2-3) for SECONDARY prevention in triple positive APS
Primary outcome -Cumulative incidence of TE, major bleeding, vascular death
Rivaroxaban in high risk patients with APS was associated with excess of arterial events compared to warfarin. Trial stopped early.

Cumulative incidence of death, thromboembolism, major bleeding

A 35 year old woman with probably lupus presents with unprovoked bilateral pulmonary embolism? Baseline coags are significant for a prolonged aPTT raising concern for APS. What anticoagulation regimen do you recommend?

1) LMWH → warfarin
2) Rivaroxaban VTE dosing
3) IV heparin → warfarin
4) Whatever Dr Garcia says
Case

66 year old man with DM and HTN, ESRD on HD is found to be in AFIB after presenting with TIA. His CHADS2-VASc is 5. He is referred to your clinic to start anticoagulation. He tells you “There is NO way I am taking that rat poison. But I will take one of those new drugs, the ones I hear about on television.” You:

1) Start apixaban 5 mg BID
2) Start apixaban 2.5 mg BID
3) Tell him warfarin is his only option
4) Quickly update your profile on LinkedIn...you really need a new gig.
Apixaban in ESRD


Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States

**ORIGINAL RESEARCH ARTICLE**

**BACKGROUND:** Patients with end-stage kidney disease (ESKD) on dialysis were excluded from clinical trials of direct oral anticoagulants for atrial fibrillation (AF). Recent data have raised concerns regarding the safety of

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**Editorials, see p 1530 and p 1534**

Konstantinos C. Siontis, MD
Xiaosong Zhang, MS
Ashley Eckard, MS
Nicole Bhave, MD
Apixaban in ESRD

In AF patients with a CHA2DS2-VASc score ≥2 in men or ≥3 in women and a creatinine clearance <15 ml/min or who are on dialysis, it is reasonable to use warfarin or apixaban for oral anticoagulation.

EHRA-routine use of NOACs best avoided in CrCl < 15 ml/min & HD; given lack of strong evidence for VKA decision to anticoagulate remains an individualized one.
66 year old man with DM and HTN, ESRD on HD is found to be in AFIB after presenting with TIA. His CHADs-vasc score is 5. He is referred to anticoagulation clinic to start anticoagulation. He tells you “There is NO way I am taking that rat poison. But I will take one of those new drugs, the ones I hear about on television.” You:

1) Start apixaban 5 mg BID
2) Start apixaban 2.5 mg BID
3) Tell him warfarin is his only option
4) Quickly update your profile on LinkedIn...you really need a new gig.
76 yo man s/p PCI 2015, AFIB CHADS2-VASc=4 on warfarin and ASA is admitted with UGIB. INR is 3.0. He requires 3u PRBCs, vit K and FFP. EGD shows peptic ulcer disease. He is started on high dose PPI therapy, bx for H Pylori done. When should his anticoagulation and antiplatelet regimen be restarted?

1) Three weeks- resume anticoagulation and antiplatelet
2) Three weeks-resume anticoagulation only
3) Resume ASA only when GI says ok
4) Are we seriously going to do this again???
What To Do After the Bleed

Resumption of anticoagulant therapy after anticoagulant-related gastrointestinal bleeding: A systematic review and meta-analysis

D. Little, C. Chai-Adisaksoph, C. Hillis, D.M. Witt, M. Monreal, M.A. Crowther, D.M. Siegal

Keywords: Introduction: Oral anticoagulation (OAC) is permanently discontinued in up to 50% of patients followi
Thromboembolism After Resumption of AC

<table>
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<th>Author</th>
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<th>% Weight</th>
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<td>Overall (I-squared = 59.8%, p = 0.011)</td>
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NOTE: Weights are from random effects analysis

Favors resume
Favors not resume

Little et al. Thrombosis Research 2018
Our data suggest that the net clinical benefit favours resuming OAC with a reduced risk of TE (71%) and death (49%), despite an increase in GI bleeding (91%).

Little et al. Thrombosis Research 2018
“In patients with prior GIB apixaban or dabigatran 110 mg BID may be preferable”
EHRA 2018 AFIB DOAC Guidelines

In AF patients requiring OAC undergoing elective PCI/stenting, where bleeding risk is high (HASBLED ≥ 3), we suggest triple therapy for 1 month, followed by dual therapy with OAC plus single antiplatelet (preferably clopidogrel) for 6 months, following which OAC monotherapy can be used (Weak recommendation, low quality evidence).
Canadian AFIB Guidelines

AF Patients with Coronary or Peripheral Arterial Disease and an Indication for OAC (Age ≥ 65 years or CHADS₂ ≥ 1)

- Elective PCI without High Risk features for thrombotic CV events
- ACS with PCI or Elective PCI with High Risk features for thrombotic CV events
- ACS without PCI

- Dual Therapy (OAC + Clopidogrel)
  - Duration: 1 to 12 months post PCI 9 to 12 months post DES

- Triple Therapy (OAC + ASA + Clopidogrel)
  - Duration: 1 to 3 months

- Dual Therapy (OAC + Clopidogrel)
  - Duration: Up to 12 months post PCI

- Stable CAD/PAD

OAC³

OAC⁴

OAC⁴

Antithrombotic Therapy in AFIB on OAC

WHITE PAPER

Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention
A North American Perspective—2018 Update

ABSTRACT: The optimal antithrombotic treatment for atrial fibrillation undergoing percutaneous intervention with stent implantation represents a challenge. In 2016, an updated opinion of selected experts on the treatment of patients with atrial fibrillation undergoing percutaneous coronary intervention was reported. This American consensus statement on the management of antithrombotic therapy in patients with atrial fibrillation undergoing percutaneous coronary intervention is a direct follow-up to that effort.

What To Do After the Bleed

76 y/o man with CAD (s/p PCI 2015), AFIB CHADS2-VASc=4 on warfarin and ASA. INR is 3.0. He requires 3u PRBC, vit K and FFP. EGD shows peptic ulcer disease. H Pylori bx for H Pylori done. When should his anticoagulation and antiplatelet regimen be restarted?

1) Three weeks - resume anticoagulation and antiplatelet
2) Three weeks - resume anticoagulation only
3) Resume ASA only when GI says ok
4) Are we seriously going to do this again??

2017: “Two weeks may provide the best balance among GI bleed recurrence, thromboembolism and mortality”
A 65 year old man with unprovoked PE that occurred 3 months ago develops SOB and chest pain and is found to have recurrent PE. He is on warfarin. His INR is 2.0. Its Friday afternoon at 4:45 pm. What do you do now?

1) rivaroxaban
2) warfarin with goal INR 3–4
3) IVC filter
4) Low molecular weight heparin
5) Go into an empty room and shout “Why me?”
How I treat recurrent venous thromboembolism in patients receiving anticoagulant therapy

Sam Schulman
Thrombosis and Atherosclerosis Research Institute, Department of Medicine, McMaster University, Hamilton, ON, Canada; and Karolinska Institutet, Stockholm, Sweden

Oral anticoagulant therapy for venous thromboembolism is very effective. When oral anticoagulants are managed well, the risk of recurrence is approximately 2 per 100 patient-years. The main reasons for a breakthrough event are underlying disease and subtherapeutic drug levels. The most common underlying disease that results in recurrence on treatment is cancer. Subtherapeutic drug levels can be caused by poor adherence to the drug regimen, interactions with other drugs or food, or inappropriate dosing. It is important to investigate and understand the cause whenever such an event occurs and to improve management of anticoagulants thereby avoiding further recurrences. Here we present 4 illustrative cases together with a discussion of the underlying pathology. Whereas the mechanisms are usually quite well understood, the management of further anticoagulation after a breakthrough event is based on minimal or no clinical trial evidence. (Blood. 2017; 129(25):3295-3299)
VTE Recurrence on Anticoagulation

1st—is it REAL?

D-dimer

DOAC-acute VTE vs AFIB
No dose reduction for renal insufficiency with DOAC except edox
Warfarin overlap

1 in 3 may have cancer

MPO-JAK 2
Other exon mutations

APLS-beware the INR

PNH-hemolysis cytopenias and clots in weird places

Underlying condition or disease
1. Cancer
   a. Consider CT chest-abdomen-pelvis
   b. Age- and sex-appropriate work-up
2. Vasculitis, specifically Behçet
3. Antiphospholipid syndrome
   a. History, pregnancy complications?
   b. Antibodies against cardiolipin and beta2-glycoprotein I**
4. Paroxysmal nocturnal hemoglobinuria
5. Pregnancy
6. Vascular malformation
7. Heparin-induced thrombocytopenia

DOAC-on anticoagulant treatment

Is the patient taking the drug?

Yes

No

Inappropriate dosing?

The patient is on:
Heparin VKA NOAC

Antithrombin deficiency?

INR below 2.0
Drug interaction?
Carbamazepine?
Phenytoin?
Rifampin?
Post-anthelarone?
Increased vitamin K intake?
Compliance?

Inappropriate dose reduction?
Rivaroxaban not taken with food?
CYP3A4/P-gp inducer?
Morbidly obese?
Compliance?

Shulman Blood 2017
VTE Recurrence on Anticoagulation

NOTICE - NO MENTION OF IVC FILTER!

Shulman Blood 2017
A 65 year old man with unprovoked PE that occurred 3 months ago develops SOB and chest pain and is found to have recurrent PE. He is on warfarin. His INR is 2.0. What anticoagulation regimen do you recommend now?

1) rivaroxaban
2) warfarin with goal INR 3–4
3) IVC filter
4) Low molecular weight heparin
5) Go into an empty room and shout “Why me?”
National Patient Safety Goal for Anticoagulant Therapy
Effective July 1, 2019

- EP 3: The hospital uses approved protocols and evidence-based practice guidelines for perioperative management of all patients on oral anticoagulants.
National Patient Safety Goal for anticoagulant therapy
Effective July 1, 2019

Reversal of DOACs-Guidance from AC Forum
- COMING SOON!!

Cuker et al American Journal of Hematology 2019

PAUSE TRIAL
~3000 patients on DOAC for AFIB
Hold 1 day pre op-low bleed risk
Hold 2 days preop-high bleed risk
< 2% bleed, < 1% TE
Drug levels low in 90%

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