Managing Anticoagulation in the Hospitalized Patient

Tracy Minichiello, MD
Chief Anticoagulation and Thrombosis Services
San Francisco, VA Medical Center

Conflicts of Interest

- I have no actual or potential conflicts of interest in relation to this program or presentation to disclose.

Objectives

- Summarize management of bleeding on DOAC
- Review available reversal agents
- Outline perioperative management of DOACs
- Antithrombotic therapy for AFIB with stable CAD

Case

75 yo man with HTN, remote CAD s/p PCI/DES in 2015, NVAF on metoprolol, rivaroxaban 20 mg QD and ASA 81 mg daily presents with syncope. He was in his usual state of health until the morning of admission when he suddenly fainted on his way from the kitchen to the bathroom. He recalls feeling urgency to move his bowels then woke up on the floor. He was able to get himself to the bathroom where he had black tarry stools. His wife called 911 and he is brought to the ED.

1. This is a fascinating case. I have never heard of anything like this.
2. Do we have to talk about melena so early in the morning?
3. Exactly how old is Bob?

Case

In the ED his BP is 110/70, HR 110, O2 sat 99%

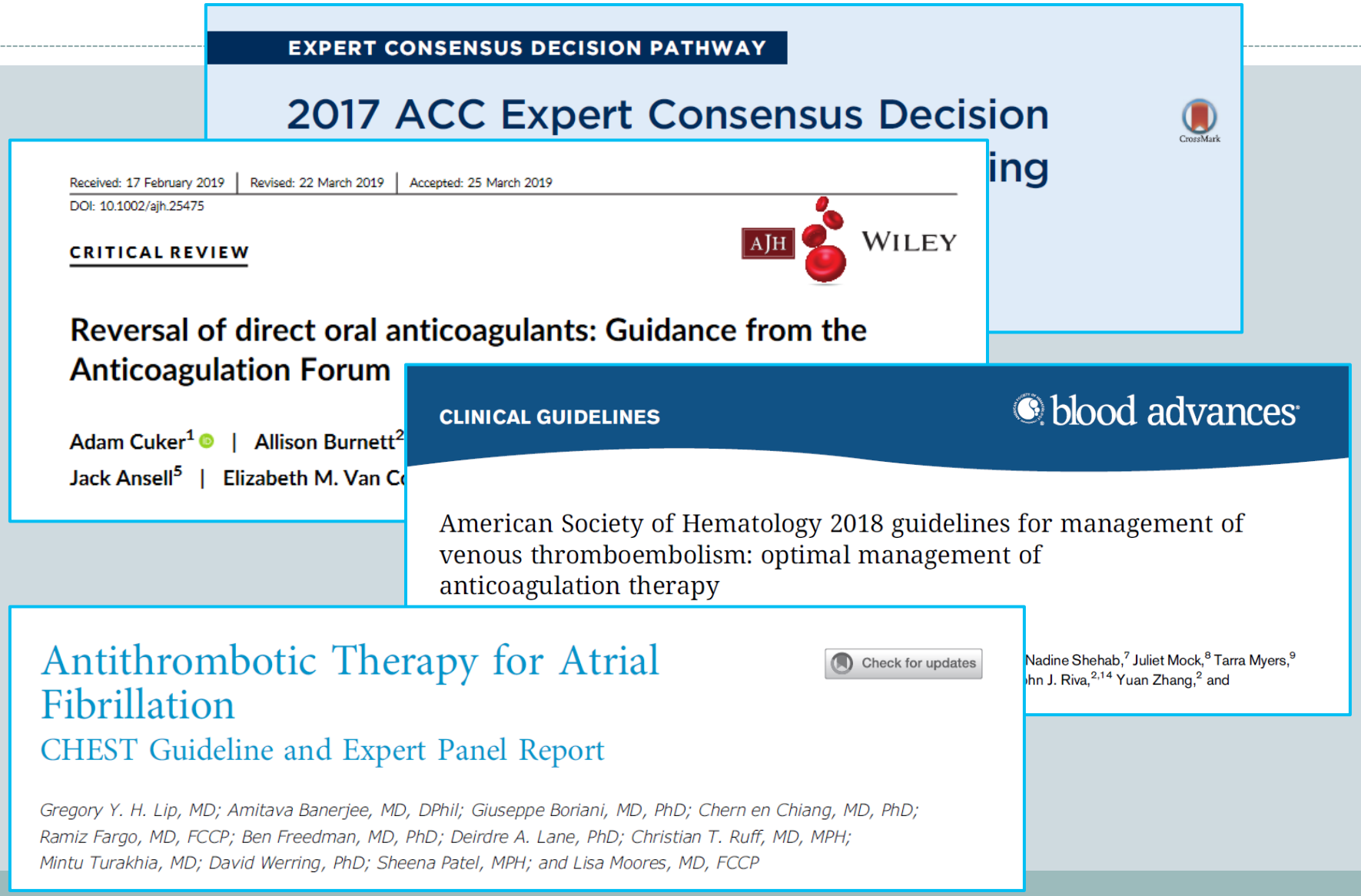
On exam his lungs are clear, heart is tachy irregular rhythm without murmur; abdomen is soft and non tender, he has no peripheral edema, rectal exam show melena

His HGB/HCT is 7.5 g/dL/24 %. his baseline is 12g/dL/36 %.

Creatinine is 1.3 mg/dL, baseline 0.8 mg/dL, LFTS are normal

INR 1.9 PT 18.7

Guidance on DOAC Bleeding Management/Reversal



EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision

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Received: 17 February 2019 | Revised: 22 March 2019 | Accepted: 25 March 2019

DOI: 10.1002/ajh.25475

CRITICAL REVIEW

AJH WILEY

Reversal of direct oral anticoagulants: Guidance from the Anticoagulation Forum

Adam Cuker[1] | Allison Burnett[2]

Jack Ansell[5] | Elizabeth M. Van C

CLINICAL GUIDELINES

blood advances

American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy

Nadine Shehab,[7] Juliet Mock,[8] Tarra Myers,[9]

hn J. Riva,[2,14] Yuan Zhang,[2] and

Antithrombotic Therapy for Atrial Fibrillation

CHEST Guideline and Expert Panel Report

Check for updates

Gregory Y. H. Lip, MD; Amitava Banerjee, MD, DPhil; Giuseppe Boriani, MD, PhD; Chern en Chiang, MD, PhD; Ramiz Fargo, MD, FCCP; Ben Freedman, MD, PhD; Deirdre A. Lane, PhD; Christian T. Ruff, MD, MPH; Mintu Turakhia, MD; David Werring, PhD; Sheena Patel, MPH; and Lisa Moores, MD, FCCP

The Joint Commission Has Revised Anticoagulation-Related National Patient Safety Goals-JULY 2019

- 8 new or revised Elements of Performance (EP) include DOACs and are applicable to:
  - Acute Care Hospitals
  - Critical Access Hospitals
  - Nursing Care Centers
  - Medical Centers (accredited under Ambulatory Health Care Programs)

Why did JC Update the NPSGs for Anticoagulation?

- DOACs already among top 10 drugs contributing to ER visits and hospitalization[1]
- Evidence of ADEs and suboptimal quality across care settings[2,3]
- Under-utilization in AF population persists[4]
- "Off-label" dosing of DOACs is common[5,6,7,8]
- 1 in 8 anticoagulated patients undergo invasive procedures requiring interruption each year[9]
- Long-term patient adherence inadequate[10]

NPSG.03.05.01:

New or Amended Elements of Performance:*

- EP-1: Initiation and maintenance of anticoagulants
- EP-2: Reversal and bleeding events
- EP-3: Perioperative management
- EP-4: Laboratory monitoring to monitor and adjust
- EP-5: Identify, respond to, and report ADEs
- EP-6: Patient and family education

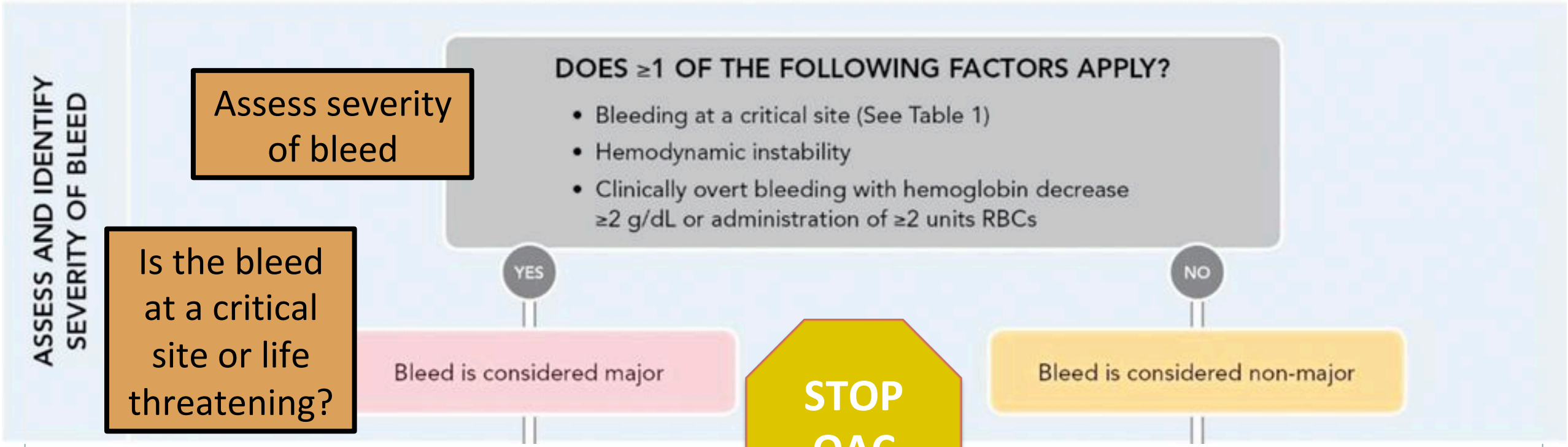
*Including DOACs

EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

J Am Coll Cardiol. 2017 Dec 19;70(24):3042-30



- Critical Site Bleeds
  - Intracranial hemorrhage
  - Other CNS bleeding
  - Pericardial tamponade
  - Airway (including posterior epistaxis)
  - Hemothorax, intra-abdominal bleeding, retroperitoneal hematoma
  - Extremity bleeds

J Am Coll Cardiol. 2017 Dec 19;70(24):3042-3

Case

In the ED his BP is 110/70, HR 110, O2 sat 99%

On exam his lungs are clear, heart is tachy irregular rhythm without murmur; abdomen is soft and non tender, he has no peripheral edema, rectal exam show melena

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INR 1.9 PT 18.7

Major bleeding if ≥1 of factors apply

- Bleeding in critical site
- Hemodynamic instability
- Overt bleeding with HGB drop ≥2g/dL or admin ≥2 u PRBCs

Critical Steps in Anticoagulant Related Bleeding

- Stop oral anticoagulation
- If on a VKA, consider 5-10 mg IV Vitamin K
- Provide local therapy/manual compression
- Provide supportive care (e.g. transfusion, antifibrinolytics)
- Consider holding antiplatelet agents-manage contributors to PLTS (uremia/liver disease)
- Consider surgical/procedural management of bleeding sites

Case

IN ED his BP drifts to 100/60. He receives 3 u lactated ringers and 2 u PRBCs. He continues to have melena. GI is called for urgent evaluation and he is transferred to the ICU. His last dose of rivaroxaban was at 6 am this morning with breakfast. It is now 11 am. Should he receive a reversal agent?

1) Yes

2) No

3) Do we have one of those?

Received: 17 February 2019 | Revised: 22 March 2019 | Accepted: 25 March 2019

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CRITICAL REVIEW

Reversal of direct oral anticoagulants: Guidance from the Anticoagulation Forum

Adam Cuker[1] | Allison Burnett[2] | Darren Trill

Jack Ansell[5] | Elizabeth M. Van Cott[6] | Diane W

Anticoagulation FORUM

Cuker A, et al. Am J Hematol 20

DOAC Reversal Guidance Statements 1,2,3: IF, WHEN, and WHAT to give for Bleeding

TABLE 1 Prioritized questions and guidance statements on DOAC reversal

Question	Guidance statement
(1) When should reversal agents be used to manage DOAC-associated bleeding?	In all patients with DOAC-associated major bleeding, we suggest treatment with supportive measu suggest administration of a reversal agent only if bleeding is life-threatening, into a critical organ controlled with maximal supportive measures and there is demonstration or reasonable expecta patient has clinically relevant plasma DOAC levels.
(2) How should reversal agents be	In patients with dabigatran-associated major bleeding in whom a reversal agent is warranted, we s

Bleeding on DOAC

- Is drug still present?
  - *What is the t ½ of the agent*
  - *When was last dose of drug?*
  - *What is patient's renal function?*
  - *Will laboratory data help?*

Assessing Residual DOAC Effect

Property	Dabigatran[1]	Rivaroxaban[2]	Apixaban[3]	Edoxaban[4]
Est t ½ hrs **Crcl > 80** **CrCl 30-79** **CrCl 15-30**	14 17-19 28	8 9 10	7-8 17-18	8-9 9-10 17
Renal clearance of absorbed dose	80%	35%	27%	50%
Approximate anticoagulation resolution[a] (nml renal fxn)	Day 2.5–3.5 after last dose	Day 1.5–3.5 after last dose	Day 1–2 after last dose	Day 1.3–2 after last dose

[a]Estimated as the time it takes for 5 half-lives to elapse since the last dose

When specialized assays are available

DRUG	CLINICAL OBJECTIVE		
	Exclude Clinically Relevant Drug Level		**Measure Therapeutic Drug Levels**
	Test	***Interpretation***	***Suggested Test***
Dabigatran	Dilute Thrombin Time	Normal probably excludes clinically relevant levels	Dilute Thrombin Time
	Ecarin Clotting Time		Ecarin Clotting Time
	Ecarin Chromogenic Assay		Ecarin Chromogenic Assay
Apixaban, edoxaban, and rivaroxaban	Anti-Xa	Absent chromogenic anti-Xa assay activity probably excludes clinically relevant levels	Anti-Xa (with calibrated reagents)

NATF
North American Thrombosis Forum

When specialized assays not available

DRUG	CLINICAL OBJECTIVE		
	Exclude Clinically Relevant Drug Level		**Suggests Clinically Relevant Drug Level Therapeutic Drug Levels**
	Test	***Interpretation***	***Suggested Test***
Dabigatran	Normal aPTT	Normal does NOT exclude clinically relevant levels	Elevated a PTT
Apixaban, edoxaban, and rivaroxaban	Anti-Xa (LMWH)	Absent chromogenic anti-Xa assay activity probably excludes clinically relevant levels	Elevated Anti-Xa (with calibrated reagents)
	PT/INR	Normal PT/INR does NOT exclude clinically relevants levels	Elevated PT/INR

NATF North American Thrombosis Forum

J Am Coll Cardiol. 2017 Dec 19;70(24):3042-3

Assessing Residual Effect of DOAC in Lab

<u>No clinically relavent drug if:</u>

- On dabigatran and dilute thrombin time normal
- On anti Xa and drug specific anti Xa level (riva, apix, betrix or edox) negative
- Negative LMWH anti-Xa level and on riva, apix, edox
- Normal PT, INR, PTT DOES NOT exclude residual apixaban, edoxaban, rivaroxaban

<u>Residual DOAC Present if:</u>

- PTT elevated-dabigatran
- INR/PT elevated-apix,riva, edox, betrix

INITIAL LABS
PT/INR
PTT
CBC
Specialized assays
Cr/LFTs

Dosing of Reversal Agents for DOAC-Induced Major Bleeding

	Idarucizumab	Andexanet Alfa	APCC	4-factor PCC
Dabigatran-induced bleeding	5 g IV	n/a	50 units/kg	n/a
Rivaroxaban- or **Apixaban**-induced bleeding	n/a	See table	n/a	2000 units
Edoxaban- or **Betrixaban**-induced bleeding*	n/a	High-dose		2000 units

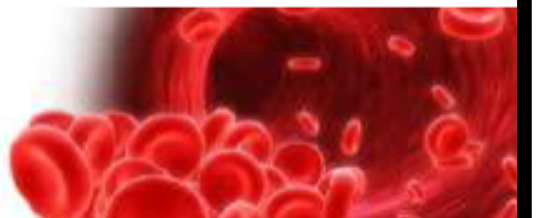
TABLE 2 Dosing and administration of andexanet alfa according to the United States Food and Drug Administration package insert

Drug	Last Dose	Time from last dose	
		<8 h or unknown	≥8 h
Rivaroxaban	≤10 mg	Low dose[a]	Low dose[a]
	>10 mg or unknown	High dose[b]	
Apixaban	≤5 mg	Low dose[a]	
	>5 mg or unknown	High dose[b]	

[a]Initial 400 mg IV bolus at target rate of 30 mg/min followed by continuous infusion at 4 mg/min for up to 120 min.
[b]Initial 800 mg IV bolus at target rate of 30 mg/min followed by continuous infusion at 8 mg/min for up to 120 min.

Cuker A, et al. Am J Hematol 2019;94:697-709.

Anticoagulation FORUM



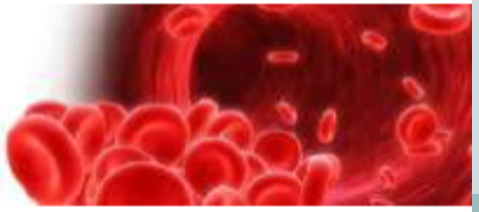
DOAC Reversal Guidance Statements 4,5,6: IF, WHEN, and WHAT to give for Urgent Procedures

(4) When should reversal agents be used before an invasive procedure?	In DOAC-treated patients who require an invasive procedure, we suggest that a reversal agent be administered only if the procedure cannot be safely performed while the patient is anticoagulated, cannot be delayed, and there is demonstration or reasonable expectation that the patient has clinically relevant plasma DOAC levels.
(5) How should reversal agents be...	In dabigatran-treated patients who require an urgent procedure and in whom a reversal agent is warranted, we...

- ONLY IF PROCEDURE CANNOT BE DONE ON AC
- CANNOT BE DELAYED
- DEMOSTRATION OF CLINICALLY RELEVANT LEVELS OF DOAC

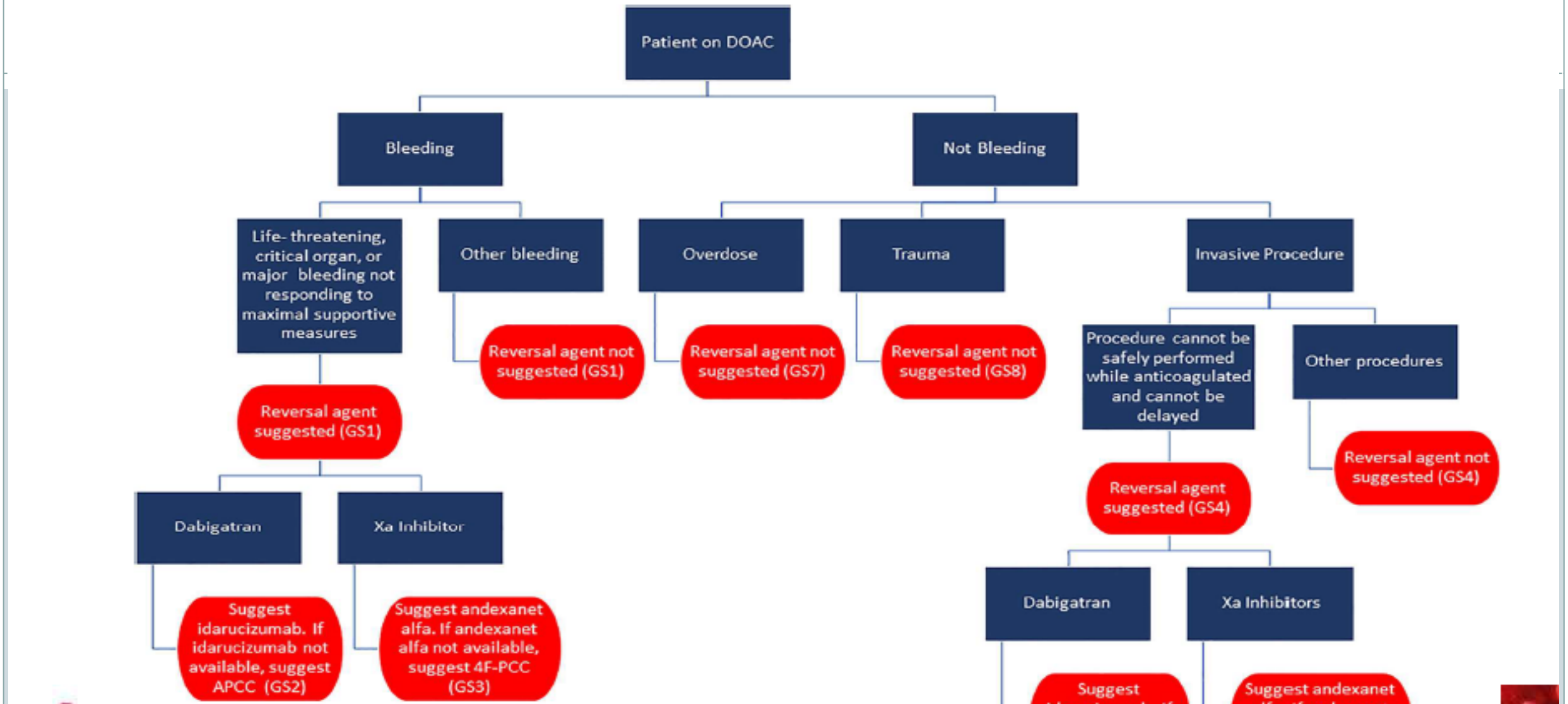
Anticoagulation FORUM

Cuker A, et al. Am J Hematol 2019;94:697-709.



For life threatening bleeding during oral direct Xa inhibition ASH suggests
4 factor PCC OR andexanet alpha plus cessation of anticoagulant OR cessation alone.
no preference for either reversal agent

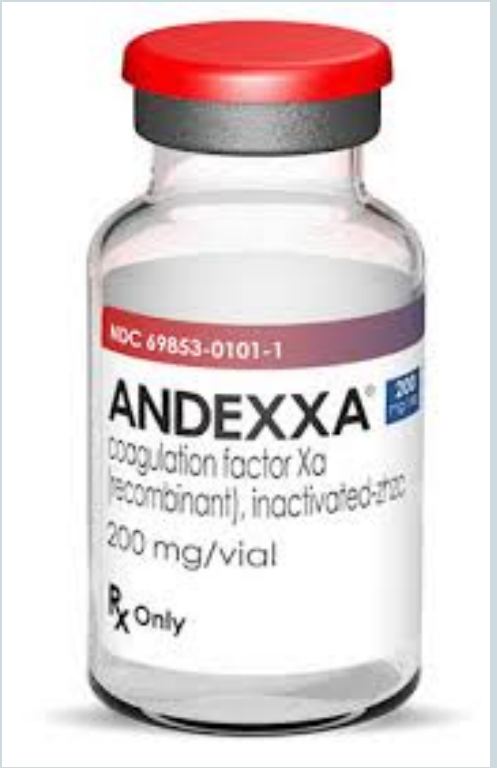
Witt et al Blood Advances 2018



Cuker A, et al. Am J Hematol 2019;94:697-709.

Andexanet (ANDEXXA)

- AKA: Coagulation Factor Xa [recombinant], inactivated zhzo
- Recombinant, modified Factor Xa (FXa) decoy molecule that binds and inactivates FXa inhibitors
- Received accelerated FDA approval for the reversal of **apixaban** and **rivaroxaban** in patients with life-threatening or uncontrolled **bleeding**
- High cost: $27,500 - $49,500 per patient*



WAC=wholesale acquisition cost

Andexanet: BOXED WARNING

Andexanet is associated with serious and life-threatening adverse events including:

- **Arterial and venous thromboembolic events**
- **Ischemic events, including MI, ischemic stroke**
- **Cardiac arrest**
- **Sudden death**

- Monitor patients for s/sx
- Resume anticoagulant therapy as soon as appropriate
- Safety not evaluated in patients who received other reversal agents or with recent thromboembolic event
- Anti-FXa activity returns to placebo levels ~2 hrs after stopping andexanet

What about 4F-PCC (off-label)?

- Most extensively studied agent for FXa inhibitor reversal
- Evidence limited to:
  - Human volunteer studies– correction of laboratory parameters (not entirely consistent) and bleeding on punch biopsy (variable)
  - Case series
  - Meta-analysis of case series*
- Cannot conclude whether stopping FXa inhibitor plus 4F-PCC is superior to stopping FXa inhibitor alone without comparator group
- **Reserve for the most severe, life-threatening cases**

*Blood Adv. 2019;3(2):158-67.

Summary of Outcomes with Reversal Agents

	Andexanet	Idarucizumab	4F-PCC-OFF LABEL
Study	ANNEXA-4	REVERSE-AD	Meta-analysis
Effective mgmt of bleed	82%	68%	~69-77%
TE events	10%	4.8%	4%
Mortality	14%	13%	16%

- NOTE: For informational purposes only; outcomes cannot be directly compared to each other
- Many differences between studies: population, design, outcomes definitions

When to consider a reversal agent?

- **Mainstay of managing bleeding in patients on DOACs is temporary discontinuation of DOAC and supportive care**
- Major bleed that is in a critical site (e.g., intracranial) or life-threatening

  AND
- Confident that therapeutic anticoagulant is present
  - Often established by patient history, as specific assays are often not rapidly or readily available
- Concerns:
  - Reversal exposes patients to baseline or possibly additional thromboembolic risk
  - Improvement in outcomes is low quality or lacking
  - Some agents are high cost

Case

IN ED his BP drifts to 100/60. He receives 3 u lactated ringers and 2 u PRBCs. He continues to have melena. GI is called for urgent evaluation and he is transferred to the ICU. His last dose of rivaroxaban was at 6 am this morning with breakfast. It is now 11 am. Should he receive a reversal agent?

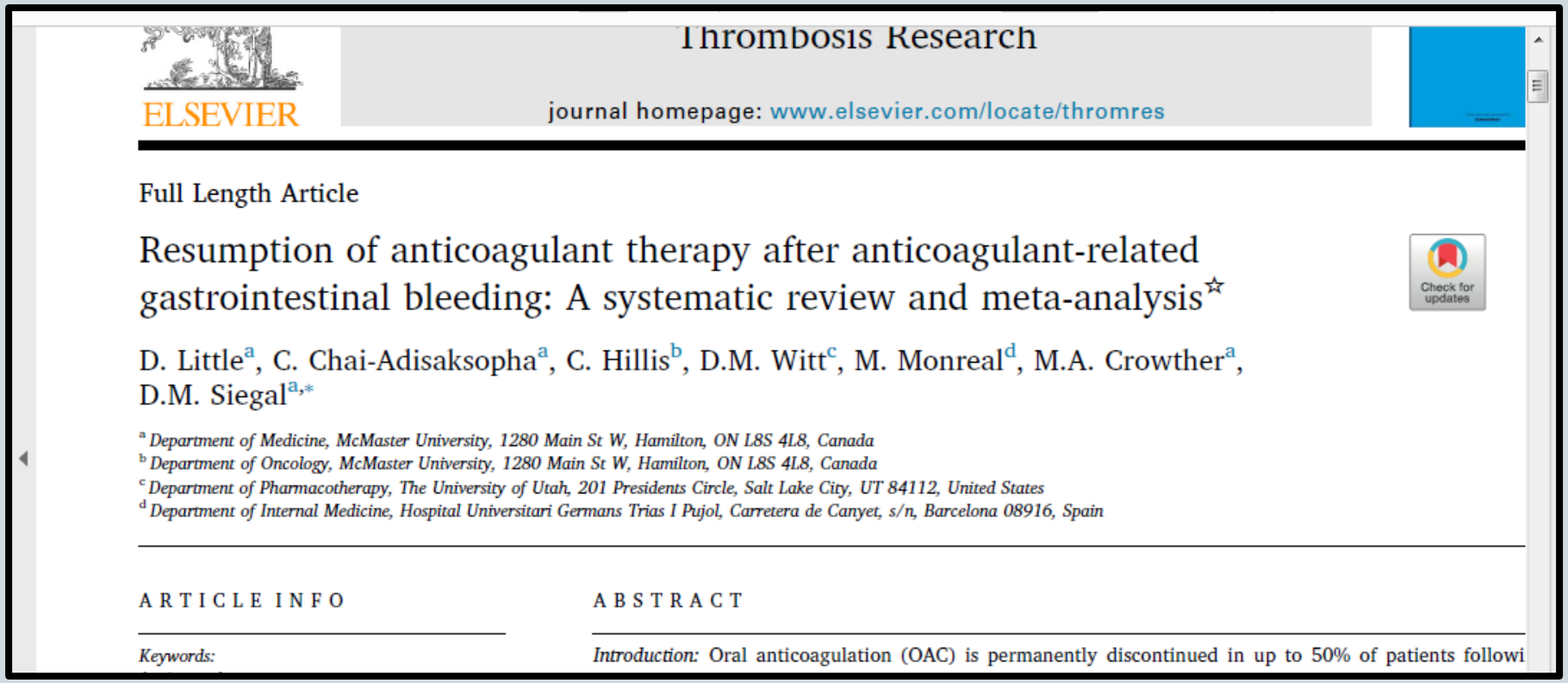
a) Yes
b) No
c) Do we have one of those?

Case

He has EGD and is found to have peptic ulcer. He is placed on high dose PPI and GI says he can resume anticoagulation in 2 weeks. In two weeks he should

1) Resume rivaroxaban and ASA
2) Start rivaroxaban only
3) Start apixaban only
4) Start ASA only
5) Talk with his PCP because in two weeks he is no longer on my service

What To Do After the Bleed



Thrombosis Research

ELSEVIER

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

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

D. Little[a], C. Chai-Adisaksopha[a], C. Hillis[b], D.M. Witt[c], M. Monreal[d], M.A. Crowther[a], D.M. Siegal[a,*]

[a] Department of Medicine, McMaster University, 1280 Main St W, Hamilton, ON L8S 4L8, Canada
[b] Department of Oncology, McMaster University, 1280 Main St W, Hamilton, ON L8S 4L8, Canada
[c] Department of Pharmacotherapy, The University of Utah, 201 Presidents Circle, Salt Lake City, UT 84112, United States
[d] Department of Internal Medicine, Hospital Universitari Germans Trias I Pujol, Carretera de Canyet, s/n, Barcelona 08916, Spain

ARTICLE INFO

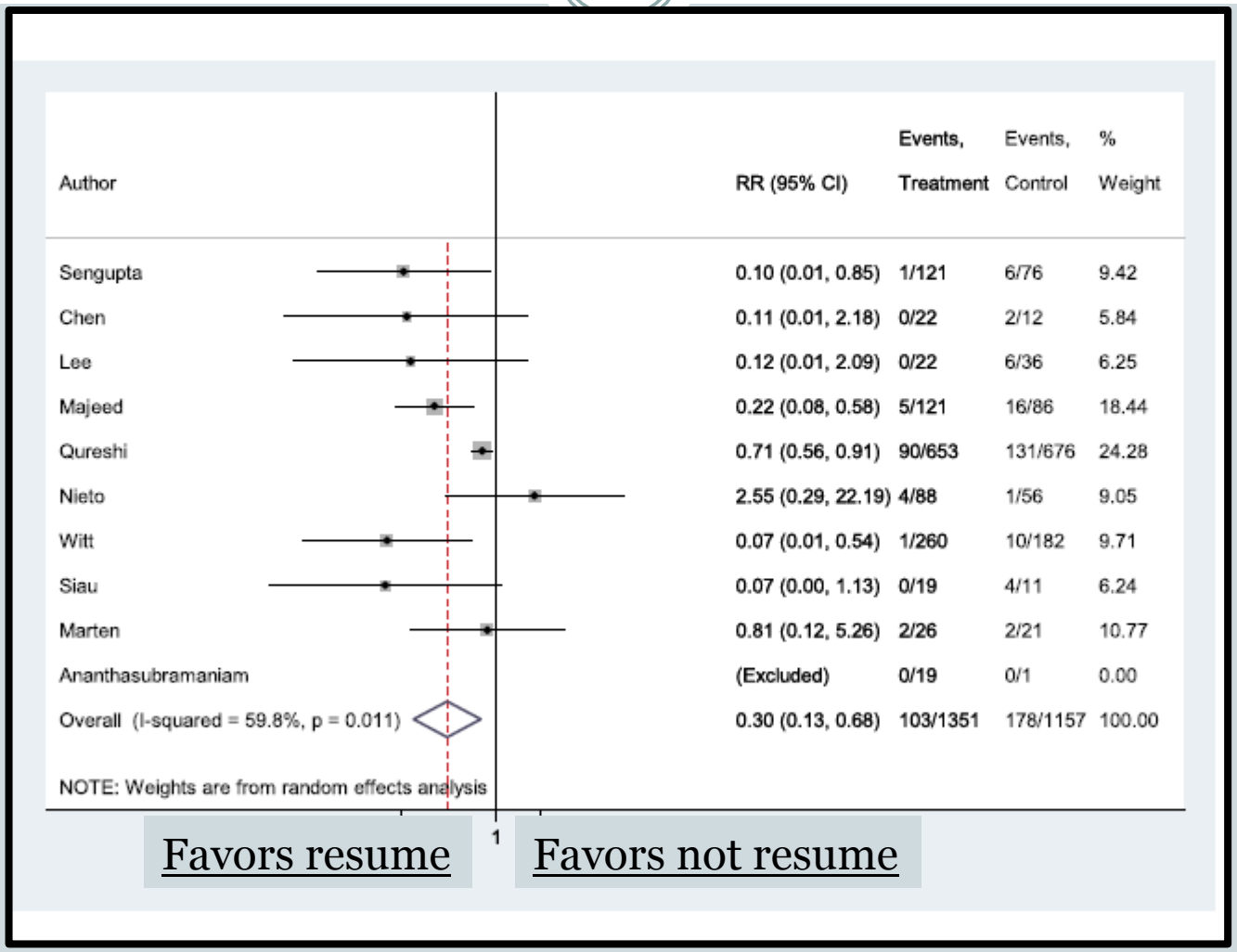
Keywords:

ABSTRACT

Introduction: Oral anticoagulation (OAC) is permanently discontinued in up to 50% of patients followi

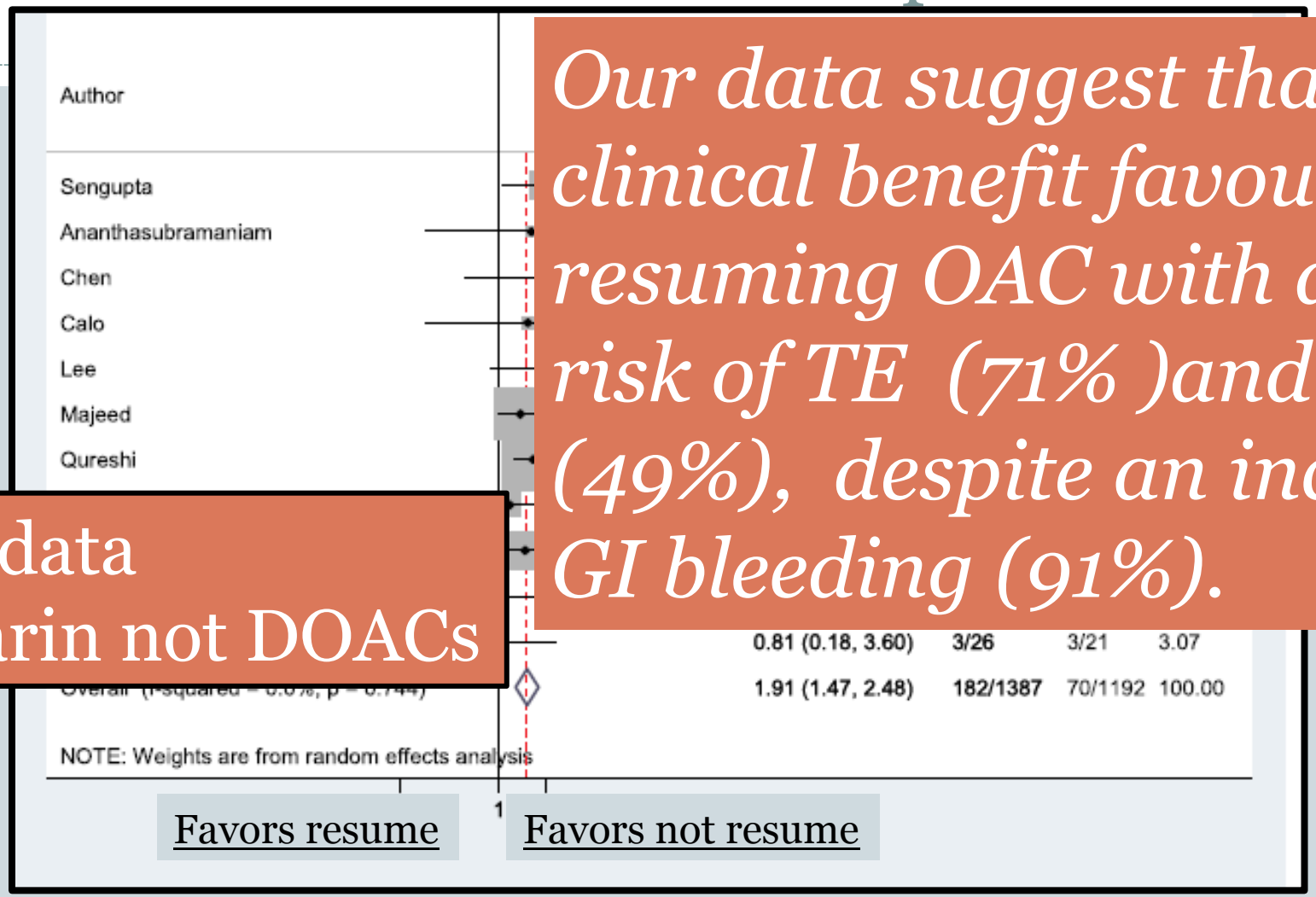
Little et al. Thrombosis Research 2018

Thromboembolism After Resumption of AC



Little et al. Thrombosis Research 2018

Recurrent GIB After Resumption of AC



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%).

Most of this data
is with warfarin not DOACs

Little et al. Thrombosis Research 2018

CHEST AFIB Guideline 2018

After bleeding if you are to resume anticoagulation: apixaban, low dose dabigatran 110 mg or edoxaban

Lip et al. CHEST 2018; 154(5):1121-1201;

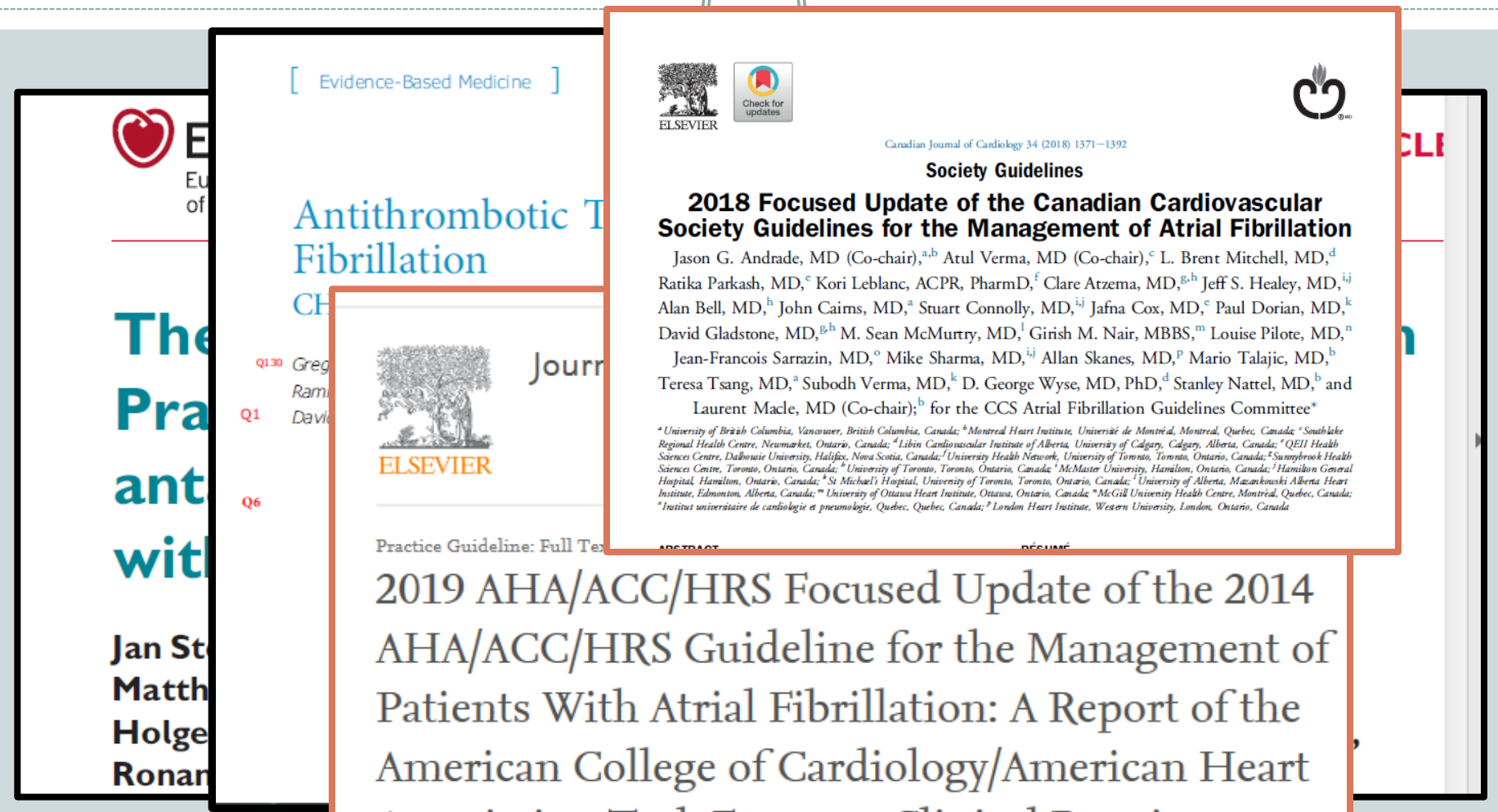
Pearls

- Reassess risk benefit of ongoing AC after every bleed
  - Mechanical valve, high risk AFIB, recurrent VTE→yes
  - Low risk AFIB, single remote VTE→maybe not
- Talk directly with GI to get input on rebleed risk
- Reconsider the anticoagulation regimen-if on warfarin or rivaroxaban consider apixaban; if must stay on warfarin—closer monitoring? Add more kale? if on any DOAC was it right dose, is there compromised renal function or DDI resulting in accumulation?
- If on concomitant ASA…is this REALLY necessary? Consult cardiology and ask them to consider THIS case, not give reflexive answer

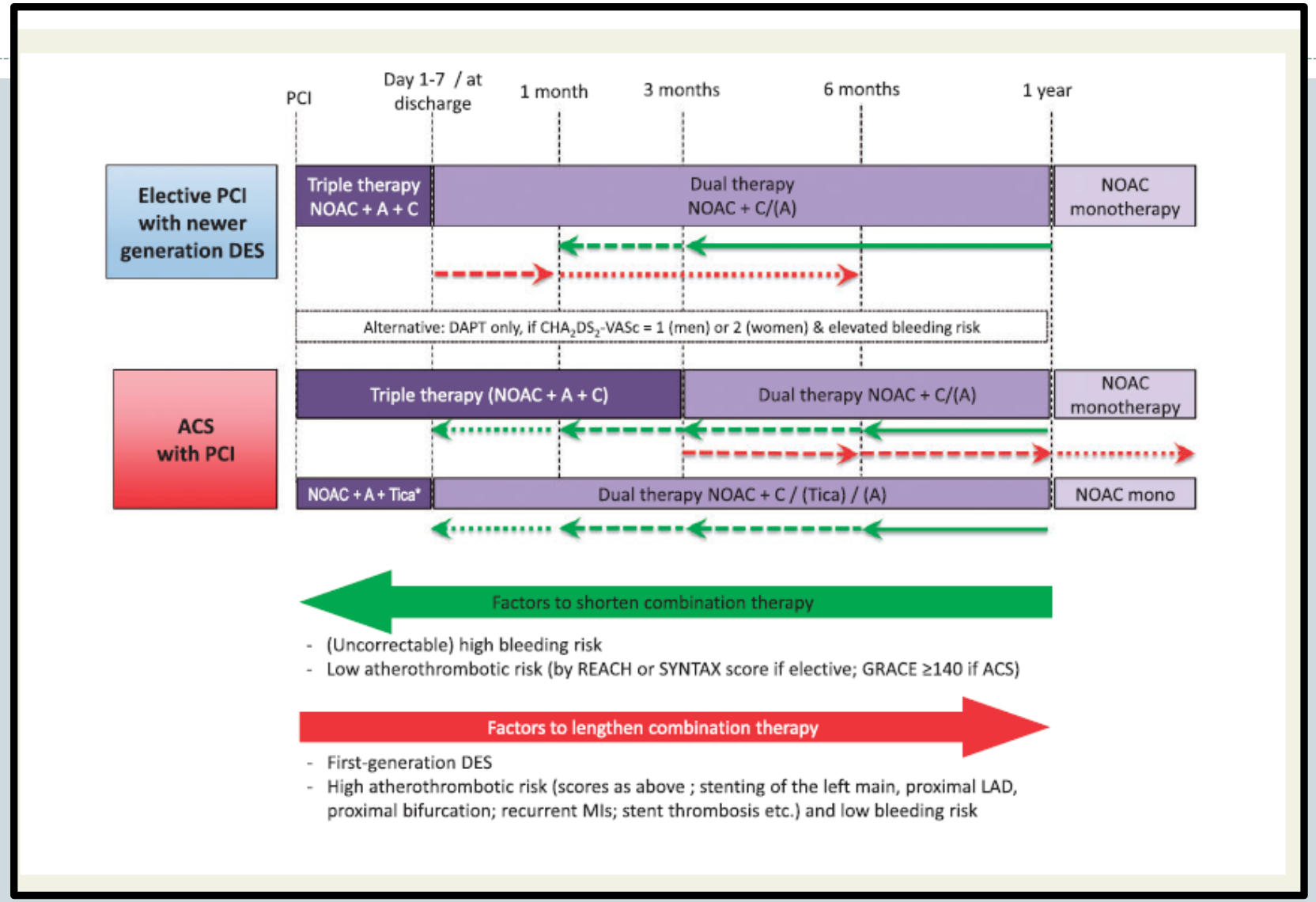
This Year in Guidelines…

WHAT ABOUT ASA
IN ADDITION TO
ANTICOAGULATION
IN AFIB + STABLE CAD?

This Year in Guidelines…



EHRA 2018 AFIB DOAC Guidelines



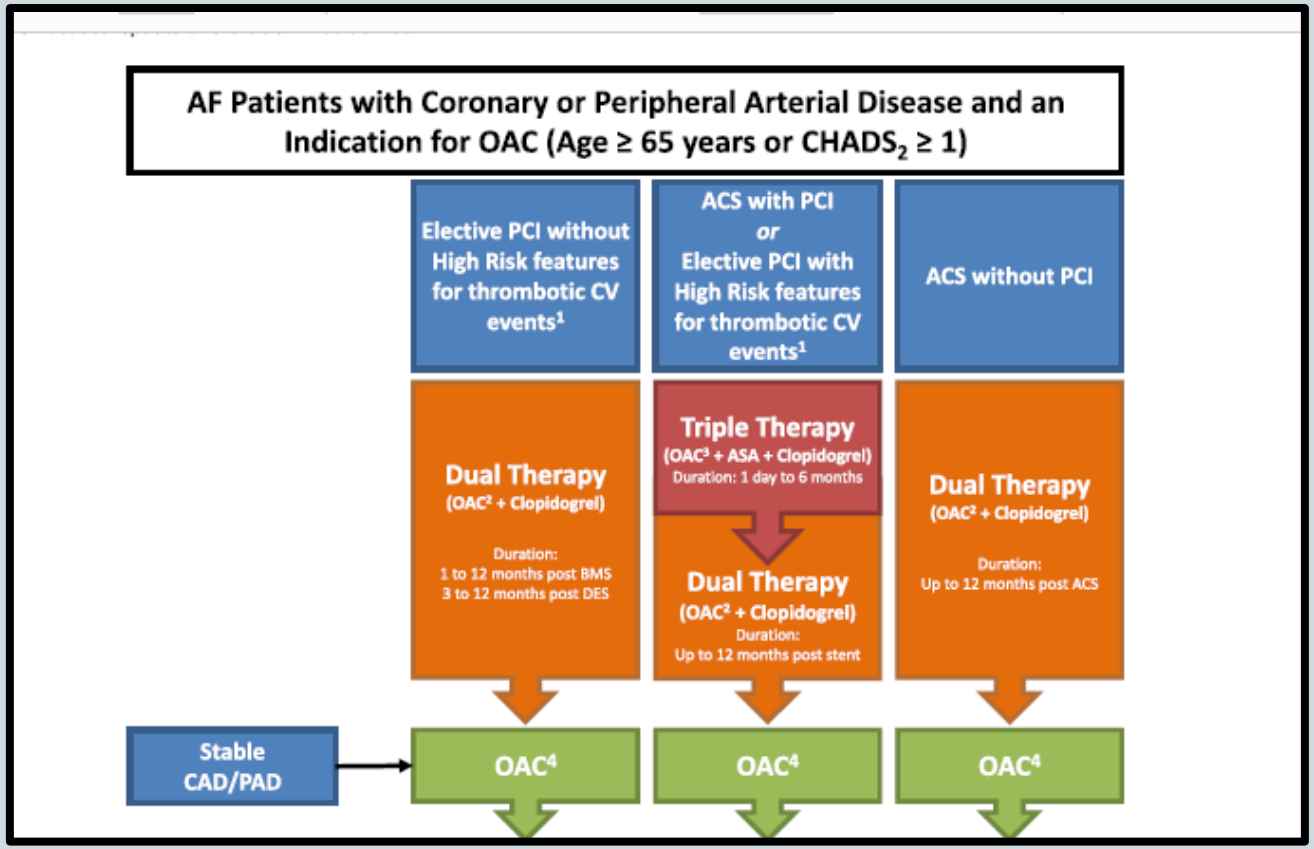
Steffal J et al. European Heart Journal (2018) 39, 1330–1393

CHEST 2018 AFIB 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

Lip et al. CHEST 2018; 154(5):1121-1201;

Canadian AFIB Guidelines



Andrate et al. Canadian Journal of Cardiology 34 (2018) 1371e1392

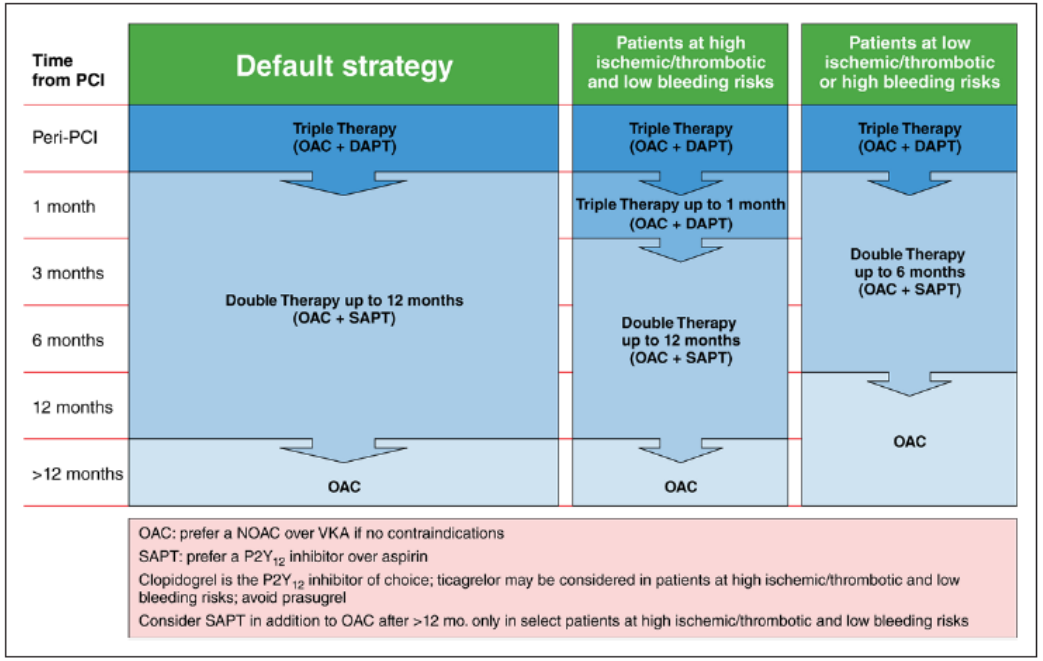
Antithrombotic Therapy in AFIB on OAC

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 treatm
with atrial fibrillation undergoing percutaneou
with stent implantation represents a challenge
2016, an updated opinion of selected experts
Canada on the treatment of patients with atria
percutaneous coronary intervention was repor
American consensus statement on the manage



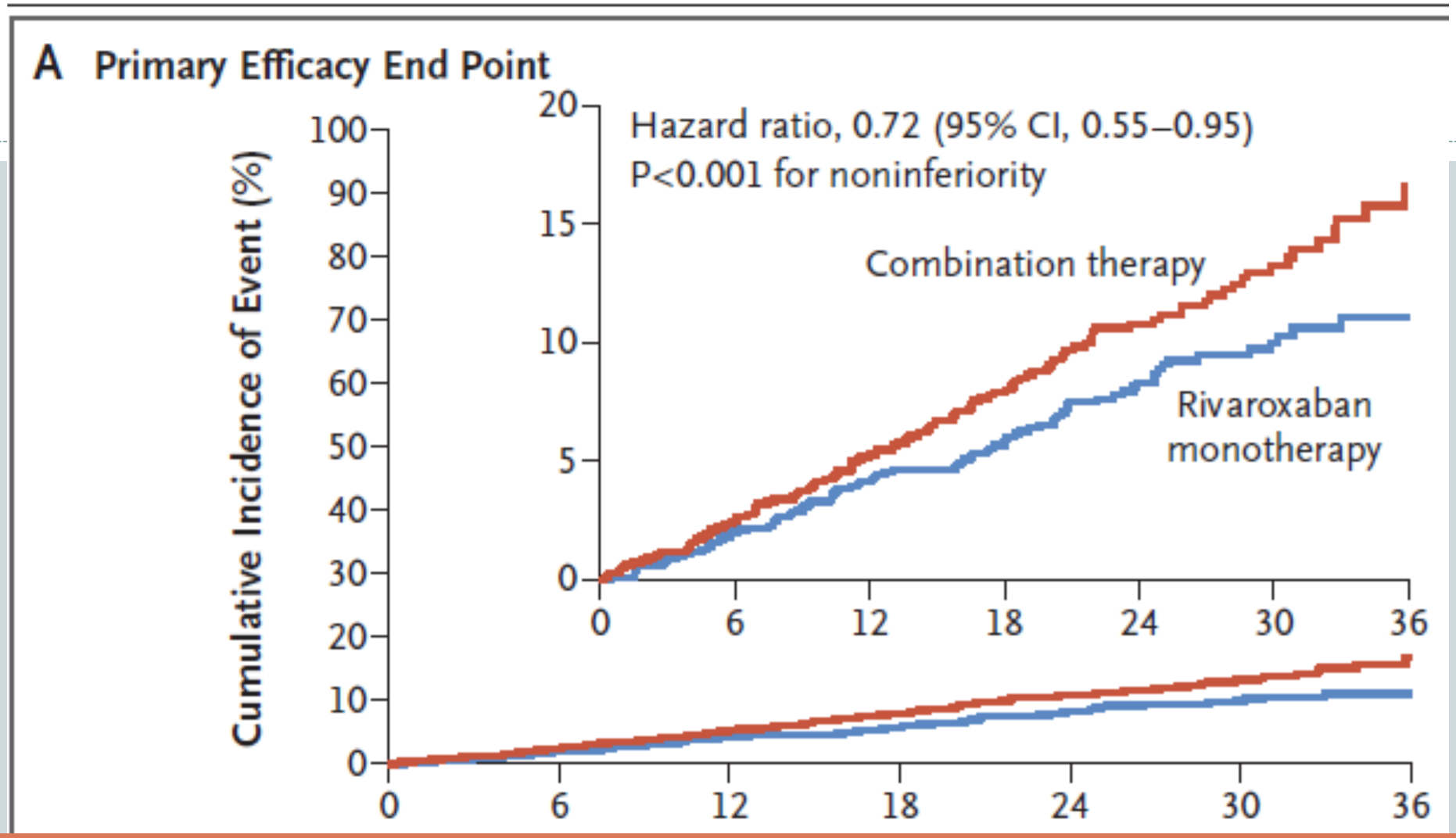
2. Management of antiplatelet therapy in patients with atrial fibrillation undergoing percutaneous coronary intervention (PCI) treated

Angiolillo DJ et al. Circulation. 2018;138:527–536.

AFIRE Results

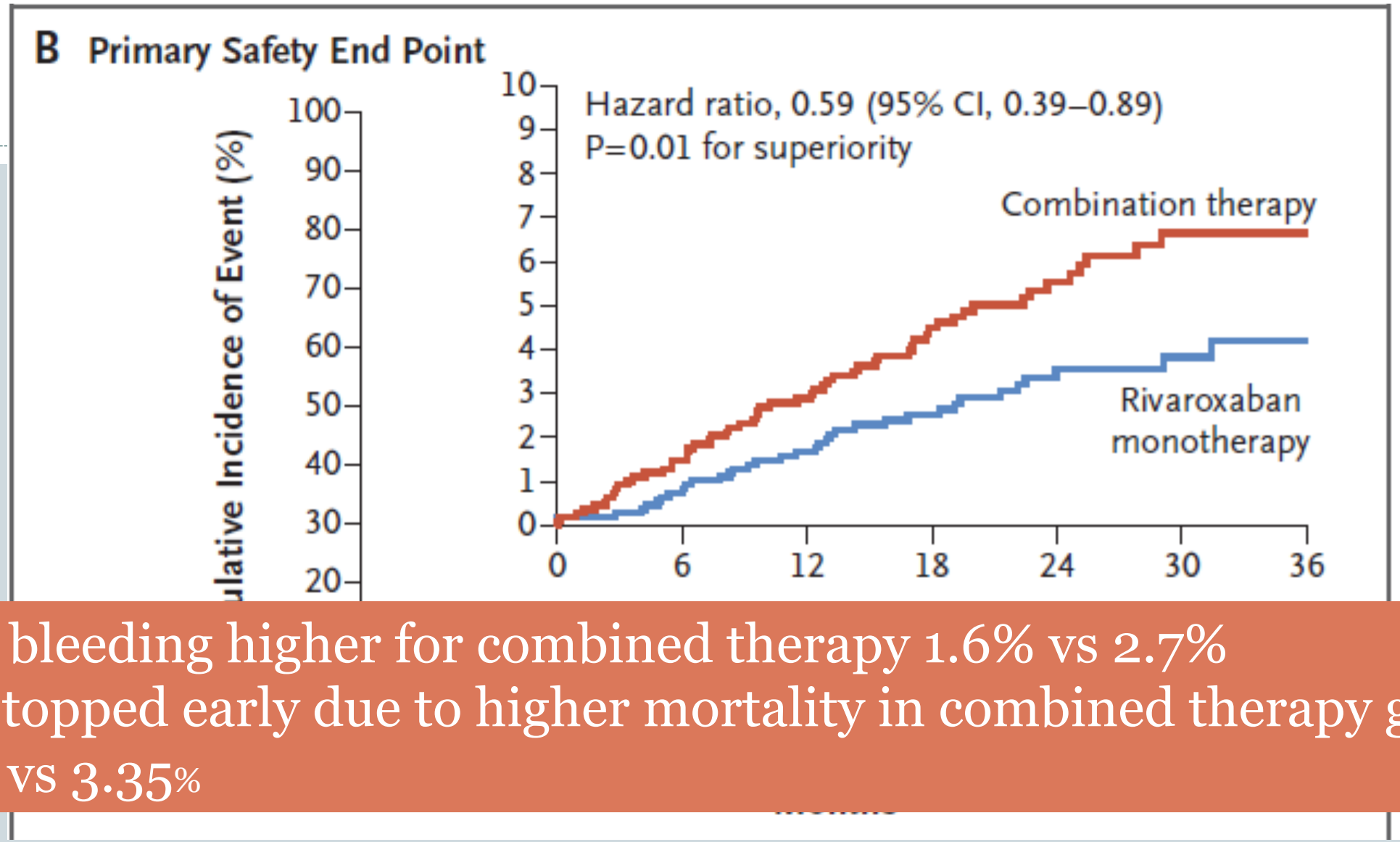
3000 patients with AFIB in Japan with stable CAD, > 1 year out from CABG or PCI
15 mg if CrCl>≥ 50 ml/min; 10 mg if CrCl,< 50 ml/min

Yasuda S. et al NEJM 2019



Monotherapy non-inferior to dual therapy for combined endpoint (CVA, SE< MI, death) ~4% vs ~6%

Yasuda S. et al NEJM 2019



Major bleeding higher for combined therapy 1.6% vs 2.7%
Trail stopped early due to higher mortality in combined therapy group 1.85% vs 3.35%

Yasuda S. et al NEJM 2019

Case

He has EGD and is found to have peptic ulcer. He is placed on high dose PPI and GI says he can resume anticoagulation in 2 weeks. In two weeks he should

1)Resume rivaroxaban and ASA

2) Start apixaban only

3) Start ASA only

4) Talk with his PCP because in two weeks he is no longer on my service

Case

A 75 year old man with HTN, PAD, DM and AFIB on rivaroxaban is admitted with recurrent osteomyelitis of the foot. Given his poor perfusion he will need a TMA. How long should you hold his rivaroxaban before going to the OR?

1) 5-7 days, seemed to work for warfarin

2) Last dose 2 days prior to OR

3) Last dose 3 day prior to OR

4) no hold required

5) I have absolutely no idea but I do know I need more coffee

NPSG.03.05.01:

New or Amended Elements of Performance:*

- EP-1: Initiation and maintenance of anticoagulants
- EP-2: Reversal and bleeding events
- EP-3: Perioperative management
- EP-4: Laboratory monitoring to monitor and adjust
- EP-5: Identify, respond to, and report ADEs
- EP-6: Patient and family education

*Including DOACs

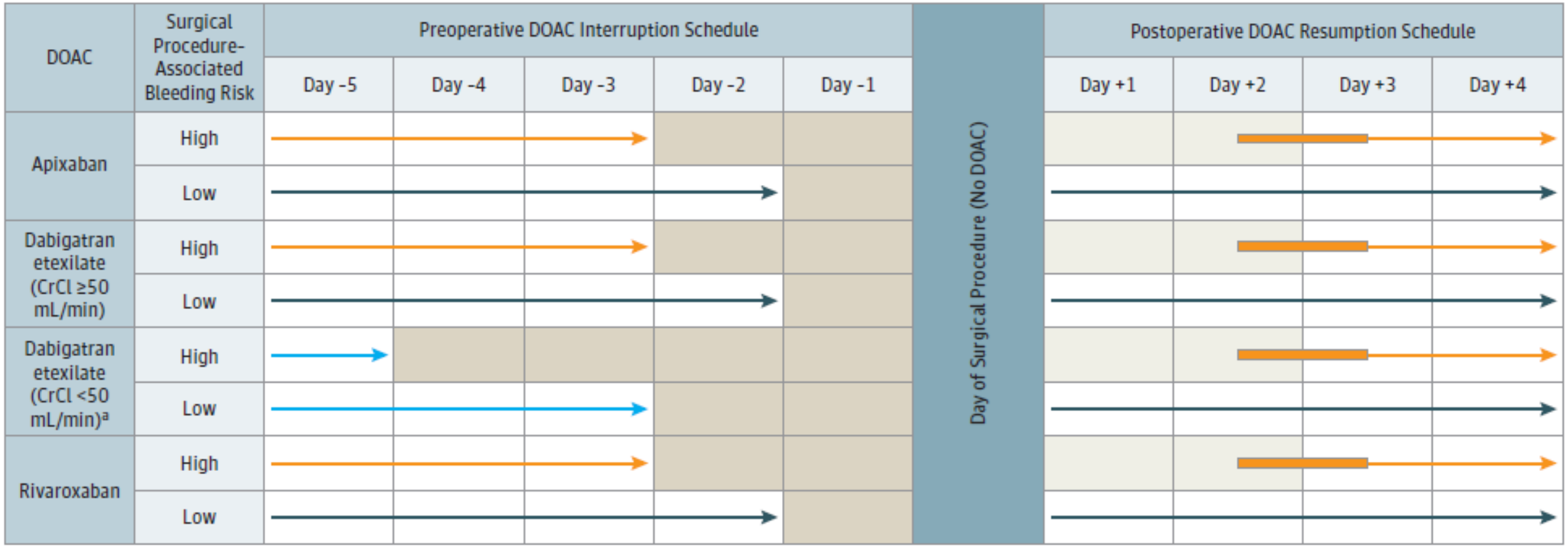
Research

JAMA Internal Medicine | Original Investigation

Perioperative Management of Patients With Atrial Fibrillation Receiving a Direct Oral Anticoagulant

James D. Douketis, MD; Alex C. Spyropoulos, MD; Joanne Duncan, BSc; Marc Carrier, MD, MSc; Gregoire Le Gal, MD; Alfonso J. Tafur, MD; Thomas Vanassche, MD; Peter Verhamme, MD; Sudeep Shivakumar, MD; Peter L. Gross, MD, MSc; Agnes Y. Y. Lee, MD, MSc; Erik Yeo, MD; Susan Solymoss, MD; Jeannine Kassis, MD; Geneviève Le Templier, MD; Stephen Kowalski, MD; Mark Blostein, MD; Vinay Shah, MD; Elizabeth MacKay, MD; Cynthia Wu, MD; Nathan P. Clark, PharmD; Shannon M. Bates, MDCM, MSc; Frederick A. Spencer, MD; Eleni Arnaoutoglou, MD, PhD; Michiel Coppens, MD, PhD; Donald M. Arnold, MD, MSc; Joseph A. Caprini, MD; Na Li, PhD; Karen A. Moffat, MLT; Summer Syed, MD, MSc; Sam Schulman, MD, PhD

Figure. Perioperative Direct Oral Anticoagulant (DOAC) Management Protocol



ONE DAY HOLD-(36- to 42-hour interval =~3 DOAC half-lives)
TWO DAY HOLD (60- to 68-hour interval=~ 5DOAC half-lives

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PAUSE-Results

Table 3. Primary Study Outcomes

Outcome	DOAC Cohort		
	Apixaban (n = 1257)	Dabigatran Etexilate (n = 668)	Rivaroxaban (n = 1082)
Primary			
Major bleeding[a]			
No. (%)	17 (1.35)	6 (0.90)	20 (1.85)
1-Sided 95% CI	0-2.00	0-1.73	0-2.65
P value	.051	.02	.36
Arterial thromboembolism[b,c]			
No. (%)	2 (0.16)	4 (0.60)	4 (0.37)
1-Sided 95% CI	0-0.48	0-1.33	0-0.82
P value	<.001	.03	.001

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PAUSE-Results

Table 4. Incidence of Major Bleeding by Elective Surgery or Procedure–Associated Bleeding Risk

Procedure-Associated Bleeding Risk	Apixaban Cohort (n = 1257)	Dabigatran Etexilate Cohort (n = 668)	Rivaroxaban C (n = 1082)
Low bleeding risk			
No. (%)	851 (67.7)	440 (65.9)	709 (65.5)
bleeding, % (95% CI)			

30 day major bleeding rate of 2.96, 0.88 and 2.95 with apixaban, dabigatran & rivaroxaban respectively

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PAUSE TRIAL

- CHADS2 SCORE DID NOT PREDICT TE AND WAS NOT USED TO GUIDE MANAGEMENT
- NO BRIDGE THERAPY OFFERED
- PATIENTS COULD RECEIVE VTE PROPHYLAXIS POST OP (30%)

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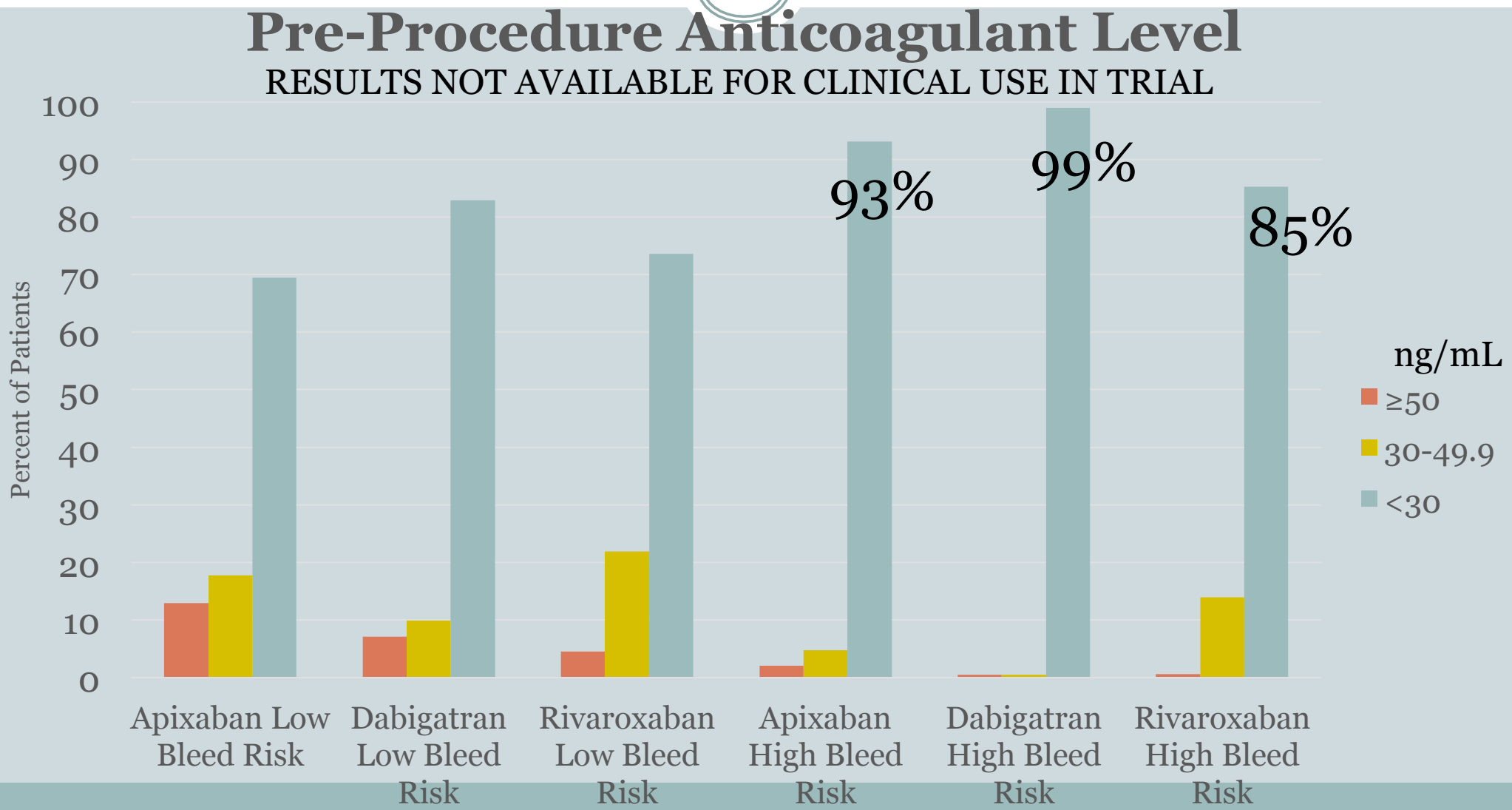
PAUSE-Results

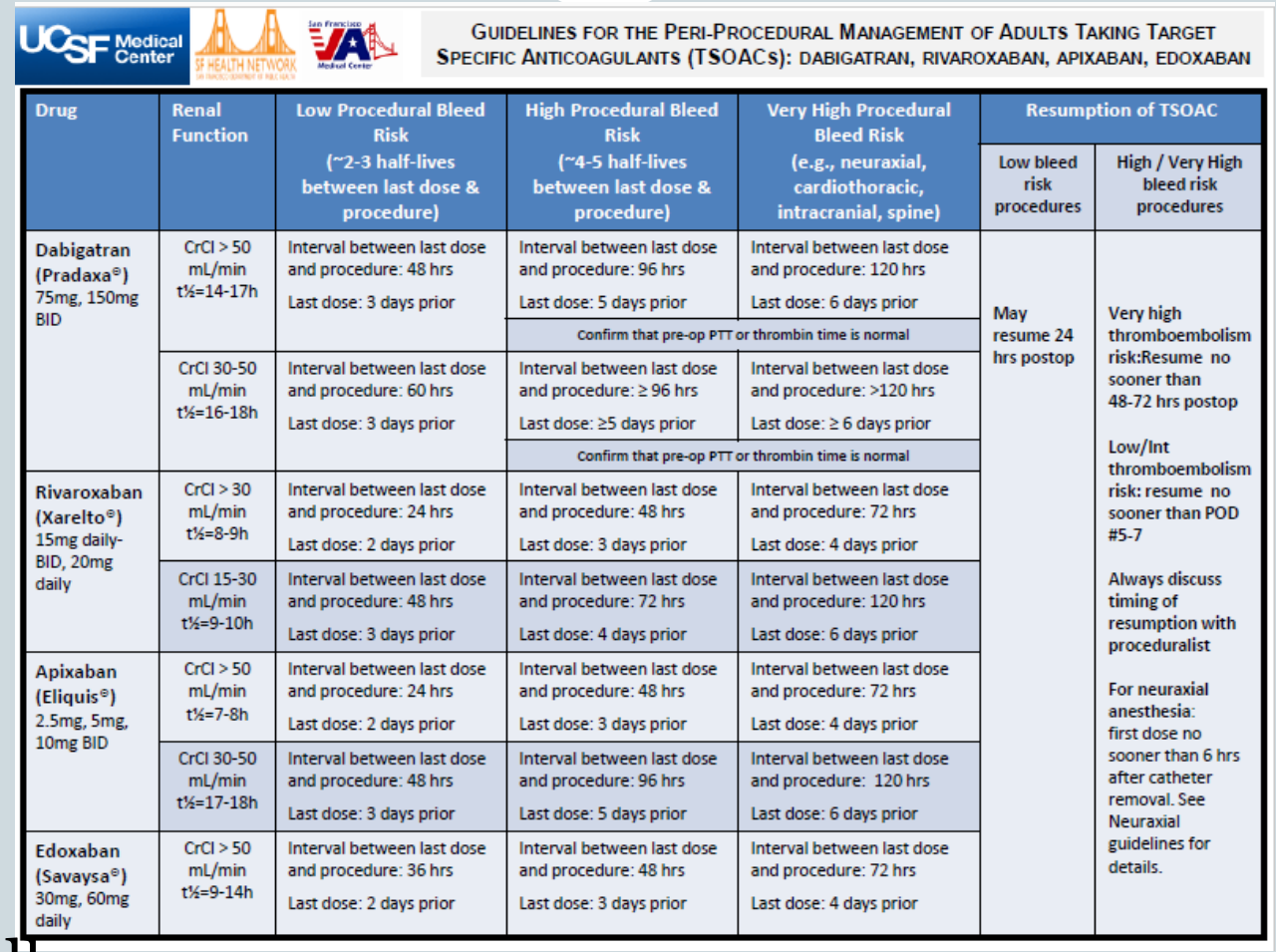


Conclusion

- Standard perioperative strategy
- No heparin bridging
- No laboratory testing
- Questions remaining:
  - WHAT ABOUT PATIENTS WITH LOW CRCL < 30 ML/MIN OR ON DIALYSIS
  - WHAT ABOUT PATIENTS ON LOW DOSE RIVAROXABAN 2. 5 MG BID
  - WHAT ABOUT VERY VERY HIGH BLEED RISK PROCEDURES-CRANIOTOMY, NEURAXIAL ANETHESIA
  - PRE OP RIVAROXABAN LEVELS HIGHER

Example of Guideline

Suggested management of DOACs & VKAs before an invasive procedure



UCSF Medical Center · SF Health Network · San Francisco VA Medical Center

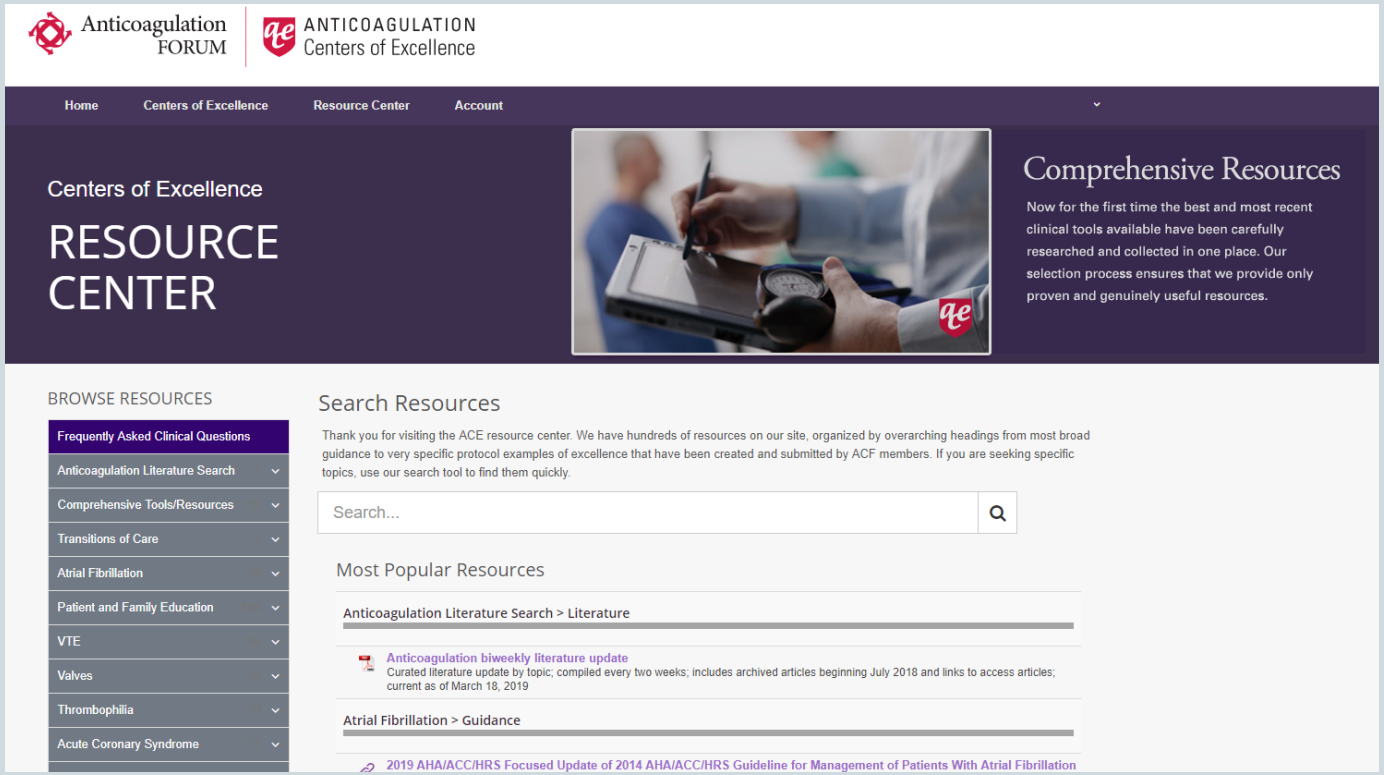
Guidelines for the Peri-Procedural Management of Adults Taking Target Specific Anticoagulants (TSOACs): dabigatran, rivaroxaban, apixaban, edoxaban

Drug	Renal Function	Low Procedural Bleed Risk (~2-3 half-lives between last dose & procedure)	High Procedural Bleed Risk (~4-5 half-lives between last dose & procedure)	Very High Procedural Bleed Risk (e.g., neuraxial, cardiothoracic, intracranial, spine)	Resumption of TSOAC	
					Low bleed risk procedures	High / Very High bleed risk procedures
Dabigatran (Pradaxa®) 75mg, 150mg BID	CrCl > 50 mL/min t½=14-17h	Interval between last dose and procedure: 48 hrs Last dose: 3 days prior	Interval between last dose and procedure: 96 hrs Last dose: 5 days prior	Interval between last dose and procedure: 120 hrs Last dose: 6 days prior	May resume 24 hrs postop	Very high thromboembolism risk:Resume no sooner than 48-72 hrs postop Low/Int thromboembolism risk: resume no sooner than POD #5-7 Always discuss timing of resumption with proceduralist For neuraxial anesthesia: first dose no sooner than 6 hrs after catheter removal. See Neuraxial guidelines for details.
			Confirm that pre-op PTT or thrombin time is normal			
	CrCl 30-50 mL/min t½=16-18h	Interval between last dose and procedure: 60 hrs Last dose: 3 days prior	Interval between last dose and procedure: ≥ 96 hrs Last dose: ≥5 days prior	Interval between last dose and procedure: >120 hrs Last dose: ≥ 6 days prior		
			Confirm that pre-op PTT or thrombin time is normal			
Rivaroxaban (Xarelto®) 15mg daily-BID, 20mg daily	CrCl > 30 mL/min t½=8-9h	Interval between last dose and procedure: 24 hrs Last dose: 2 days prior	Interval between last dose and procedure: 48 hrs Last dose: 3 days prior	Interval between last dose and procedure: 72 hrs Last dose: 4 days prior		
	CrCl 15-30 mL/min t½=9-10h	Interval between last dose and procedure: 48 hrs Last dose: 3 days prior	Interval between last dose and procedure: 72 hrs Last dose: 4 days prior	Interval between last dose and procedure: 120 hrs Last dose: 6 days prior		
Apixaban (Eliquis®) 2.5mg, 5mg, 10mg BID	CrCl > 50 mL/min t½=7-8h	Interval between last dose and procedure: 24 hrs Last dose: 2 days prior	Interval between last dose and procedure: 48 hrs Last dose: 3 days prior	Interval between last dose and procedure: 72 hrs Last dose: 4 days prior		
	CrCl 30-50 mL/min t½=17-18h	Interval between last dose and procedure: 48 hrs Last dose: 3 days prior	Interval between last dose and procedure: 96 hrs Last dose: 5 days prior	Interval between last dose and procedure: 120 hrs Last dose: 6 days prior		
Edoxaban (Savaysa®) 30mg, 60mg daily	CrCl > 50 mL/min t½=9-14h	Interval between last dose and procedure: 36 hrs Last dose: 2 days prior	Interval between last dose and procedure: 48 hrs Last dose: 3 days prior	Interval between last dose and procedure: 72 hrs Last dose: 4 days prior		

ACF Centers of Excellence:
https://acforum-excellence.org/Resource-Center/resource_files/-2017-04-07-132011.pptx

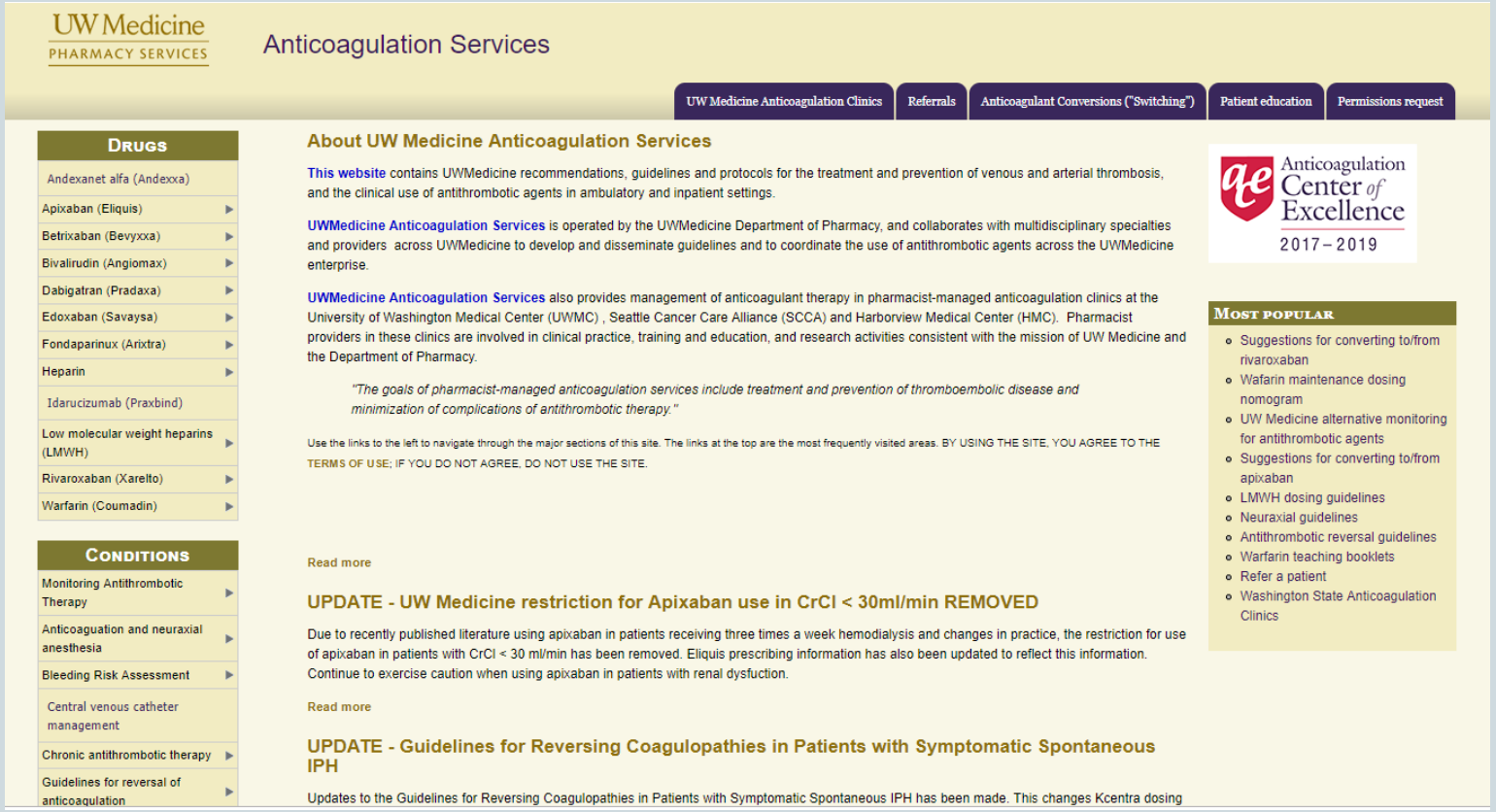
Where Do I Find Them?

Sample resources can be found at the Anticoagulation Centers of Excellence: https://acforum-excellence.org/



Where Do I Find Them?

University of Washington Medicine Pharmacy Services:
https://depts.washington.edu/anticoag/home/



Case

A 75 year old man with HTN, PAD, DM and AFIB on rivaroxaban is admitted with recurrent osteomyelitis of the foot. Given his poor perfusion he will need a TMA. How long should you hold his rivaroxaban before going to the OR?

1) 5-7 days, seemed to work for warfarin

2) Last dose 2 days prior to OR

3) Last dose 3 day prior to OR

4) no hold required

5) I have absolutely no idea but I do know I need more coffee

Thromboembolism & Anticoagulation Workshop

- Approach to subsegmental PE, calf vein DVT and superficial vein thrombosis
- Determine duration of anticoagulation for VTE
- Review options for secondary prevention of VTE
- Manage anticoagulation in recurrent VTE
- Choose appropriate DOAC for VTE
- Role of thrombophilia work up

Questions?

Reversal Agents for DOACs

Agent	Type	FDA approval	Other
Idarucizumab (PRAXBIND)	Specific for dabigatran	Bleeding, peri-procedural	
Andexanet (ANDEXXA)	Specific for FXa inhibitors	Bleeding w/ apixaban and rivaroxaban only	Off-label for other FXa inhibitors, procedures
4F-PCC (KCentra)	Nonspecific	Warfarin reversal	Off-label for DOACs
aPCC (FEIBA)	Nonspecific	Hemophilia A, B	Off-label for DOACs

Periprocedural Bridging in Patients With Venous Thromboembolism: A Systematic Review

Study Results

Number of procedures	Major bleeding pooled analysis	Thrombosis pooled analysis
With bridging (3448)	1.8%	0.7%
Without bridging (3459)	0.4%	0.5%

Baumgartner Amer J Med 2019