

MHIF Research Highlights: May 2020

Don't Miss Virtual SCAI 2020 Presentations – Online Now!



20 MHI physicians and MHIF staff participated:

- 28 presentations
- 14 poster presentations
- 14 podium presentations and moderated sessions

A special congratulations to **Dr. Brilakis** who was the 2020 Scientific Sessions Program Chair!

Find his welcome talk as part of Day 1 presentations <http://www.scai.org/SCAI2020>

*Interested in MHIF Updates During COVID-19?
Visit mplsheart.org/coronavirus/*

MHIF FEATURE:

HemoLung Emergency Use of ECCO2R
Dr. Saavedra-Romero

CONTACT:

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Carina Benson - carina.benson@allina.com

Thanks to our MHI physician partners who are helping us complete tasks to get patients enrolled in research studies as appropriate during COVID-19!

We appreciate our partnership with you!

HOPE
DISCOVERED HERE™

Minneapolis Heart Institute Foundation
Creating a world without heart and vascular disease

Anticoagulation in Patients Who Also Need Antiplatelet Therapy: How Low Can We Go?!

JoEllyn Carol Moore, MD, FACC, FHRS

Cardiac Electrophysiology, Minneapolis Heart Institute
Abbott Northwestern Hospital, part of Allina Health

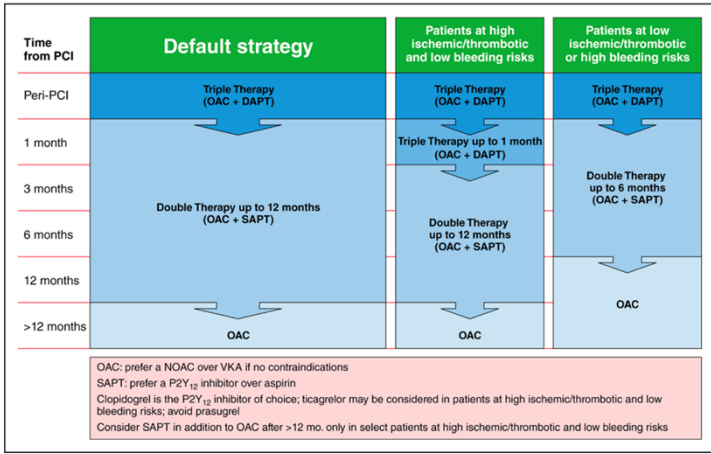
May 18, 2020
MHIF Grand Rounds



Overview

- Most recent guidelines for oral anticoagulant (OAC) use in atrial fibrillation (AF)
- Brief history of anticoagulants and antiplatelet agents
- AF management guideline update
- Pharmacology of antiplatelet agents and anticoagulants
- Bleeding risk
- Managing “dual” and “triple” therapy

2018 North American Guidelines



Angiolillo et al. (2018) *Circulation*

2018 European Guidelines

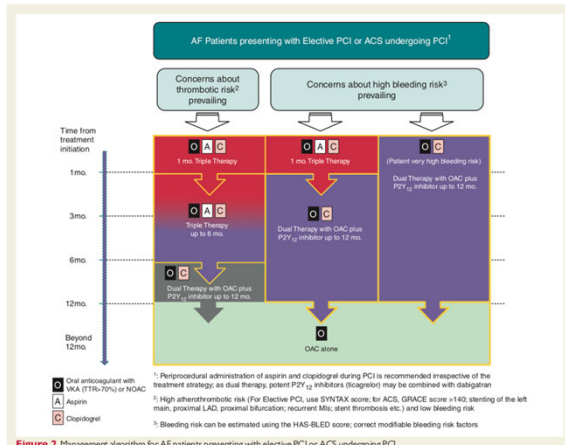


Figure 2. Management algorithm for AF patients presenting with elective PCI or ACS undergoing PCI.

Lip et al. (2019) *Europace*

Scope of the Problem

- 1-4% of the adult population in Australia, Europe and the USA have AF
 - 0.90% in patients 18-64 years old (7% undiagnosed)
 - 9.9% in patients > 65 years old (10% undiagnosed)
 - > 13% in octogenarians
- 20-40% of patients with AF also have CAD
- 20% of patients with AF will go on to need PCI or have ACS
- 5-10% of patients referred for LHC +/- PCI have an indication for an anticoagulant for AF

Rahman et al. (2014) *Nat Rev Card*; Turakhia et al. (2015) *AJC*; Capodanno et al. (2019) *JACC*

Did you know?

Aspirin was first distributed:

- a) As a powder in 1899
- b) As a tablet in 1934
- c) As a liquid in 1849
- d) As a powder in 1921

Did you know?

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- b) As a tablet in 1934
- c) As a liquid in 1849
- d) As a powder in 1921

History of Oral Antiplatelet Agents

- 1899: acetylsalicylic acid is distributed as a powder (called Aspirin by Bayer)
- 1991: ticlopidine FDA approved
- 1997: clopidogrel FDA approved
- 2009: prasugrel FDA approved
- 2011: ticagrelor FDA approved
- 2014: vorapaxar FDA approved

Did you know?

Warfarin was first distributed:

- a) As an insect repellent in 1944
- b) As a household cleaner in 1952
- c) As a rodenticide in 1952
- d) As a sleep aid in 1954

Did you know?

Warfarin was first distributed:

- a) As an insect repellent in 1944
- b) As a household cleaner in 1952
- c) **As a rodenticide in 1952**
- d) As a sleep aid in 1954

History of Oral Anticoagulants

- 1954: warfarin approved for human use (approved as rodenticide in 1952)
- [digoxin also FDA approved in 1954]
- 2010: dabigatran FDA approved
- 2011: rivaroxaban FDA approved
- 2012: apixaban FDA approved
- 2015: edoxaban FDA approved
- 2017: betrixaban FDA approved

New AF

Mr. Smith is a 50 year old male with past medical history of HL who presents in clinic to discuss management of a new diagnosis of PAF with a recent cardioversion in the ED. He is otherwise healthy with a structurally normal heart by echo. You recommend:

- a) No anticoagulation required
- b) ASA 81 mg daily
- c) Rivaroxaban 15 mg daily X 1 month (take with food)
- d) Rivaroxaban 20 mg daily X 1 month (take on an empty stomach)

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- d) Rivaroxaban 20 mg daily X 1 month (take on an empty stomach)

Stroke Risk in Atrial Fibrillation (*NOT including MS or Mechanical Valve*)

- CHA2DS2-VASc score of **0 in men or 1 in women**: reasonable to **omit anticoagulant therapy** (IIa, B)
- CHA2DS2-VASc score of **1 in men and 2 in women**: oral anticoagulant **may be considered** (IIb, C)
- CHA2DS2-VASc score of **2 or greater in men or 3 or greater in women**: oral anticoagulants are **recommended** (I, A-B)

“CHA2DS2-VA score”

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

Risk of Stroke or Death in the WHI Women with Atrial Fibrillation

Table 2 Annualized Rates of Stroke/TIA by CHADS₂ and CHA₂DS₂-VASc Scores

Construct, Level	Stroke/TIA		
	n	Events	Annual %
CHADS₂ score			
0	1760	71	0.36
1	2879	219	0.72
2	922	106	1.27
3	299	38	1.45
4+	121	23	2.43
CHA₂DS₂-VASc score			
1	951	22	0.20
2	1794	96	0.48
3	1799	152	0.82
4	911	108	1.30
5	343	51	1.71
6+	183	28	2.02

TIA = transient ischemic attack.
Does not include hemorrhagic stroke.

Table 6 Annualized Rates of Death by CHADS₂ and CHA₂DS₂-VASc Scores

Construct, Level	n	Death	
		Events	Annual %
CHADS₂ Score			
0	1760	175	0.87
1	2879	494	1.57
2	922	309	3.53
3	299	97	3.49
4+	121	63	6.13
CHA₂DS₂-VASc Score			
1	951	56	0.50
2	1794	204	1.00
3	1799	345	1.80
4	911	307	3.53
5	343	133	4.18
6+	183	93	6.28

Abraham et al. (2013) *American Journal of Medicine*

Bleeding Risk Scores

TABLE 2 Bleeding risk scores.

	Hepatic or Renal Disease	Alcohol/Drug Abuse	Malignancy	Age	Reduced Platelet Count/Function	Hypertension	Anemia	Genetic Factors	Fall Risk	Prior Stroke	Female Sex	History of Bleeding	Diabetes	Labile INR
HEMORR ₂ HAGES	X	X	X	X*	X	X	X	X	X	X				
Shireman		X		X**	X***		X				X		X	
HAS-BLED	X	X		X****		X				X		X		X
ATRIA	X*****			X*****		X	X					X		

* >75 years

** ≥70 years

*** antiplatelet use

**** >65 years

***** Glomerular filtration rate <30 mL/min or on hemodialysis

***** ≥75 years

Reprinted from *Heart Failure Reviews*, Abraham et al., 2014;19:305-313 with permission from Springer.

Moore et al. (2017) *Journal of MHIF*

Highlights of 2019 AF Guidelines

- “Valvular AF” definition: moderate-severe mitral stenosis or mechanical heart valve
- Class IA recommendation for DOAC use over warfarin
- Annual renal and *hepatic* function for DOAC monitoring
- It might be reasonable to prescribe apixaban for patients with ESRD
- Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term AC
- Implantable loop recorder to evaluate for AF in patients with cryptogenic stroke

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

Watchman

Ms. Roberts is an 85 year old female with past medical history of persistent atrial fibrillation who had recurrent GI bleeding on OAC leading to a Watchman placement > 6 months ago. She has had ongoing diastolic heart failure despite rate-controlled AF on metoprolol and desires a rhythm control strategy if possible. You recommend:

- a) AVN ablation with a MICRA pacemaker
- b) Change her rate-controlling medication to diltiazem
- c) Tell her that her symptoms have no solution
- d) TEE-guided cardioversion

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- c) Tell her that her symptoms have no solution
- d) **TEE-guided cardioversion??**

DCCV with Watchman

Abstract 10866: Cardioversion Outcomes After Left Atrial Appendage Occlusion With the Watchman Device

Simrat Kaur, Erika Hutt, Walid I Saliba, Mohamed H Kanj, Khaldoun Tarkaji, Bryan Baranowski, Daniel J Cantillon, John Rickard, Thomas J Dresing, Thomas D Callahan, Mandeep Bhargava, Oussama M Wazni, Samir R Kapadia, Ayman Hussein

[See fewer authors](#) ^

Originally published 11 Nov 2019 | *Circulation*. 2019;140:A10866



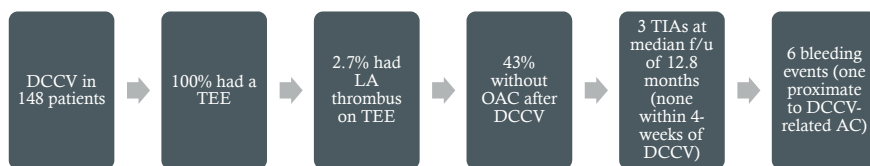
Kaur et al. (2019) Abstract 10866, *Circulation*

DCCV with Watchman

Direct Current Cardioversion of Atrial Fibrillation in Patients With Left Atrial Appendage Occlusion Devices



Sharan Prakash Sharma, MD,^a Mohit K. Turagam, MD,^b Rakesh Gopinathannair, MD,^a Vivek Reddy, MD,^b Saibal Kar, MD,^c Sangamitra Mohanty, MD,^d Jie Cheng, MD,^e David R. Holmes, Jr, MD,^f Lars Sondergaard, MD,^g Andrea Natale, MD,^h Dhanunjaya Lakkireddy, MD^h



Sharma et al. (2019) *JACC*

AC with Watchman

- Warfarin with therapeutic INR at implant
- Warfarin + ASA 325 mg daily → 45 days (TEE at 45 days to evaluate for leak around Watchman) then switch to clopidogrel and ASA
- Clopidogrel 75 mg daily and ASA 325 mg daily → 6 months
- ASA 325 mg daily thereafter

Proposal for DCCV with Watchman

< 6 months post Watchman:

DCCV if therapeutic on warfarin for 3 consecutive weeks

TEE-guided DCCV if sub-therapeutic warfarin or on ASA/Plavix only regimen

Anticoagulation per protocol:

- Warfarin (goal INR 2.5, range 2-3) ± ASA x 45 days
- ASA 325mg plus Plavix 75mg daily day 46 through 6 months

≥ 6 months post Watchman:

TEE-guided DCCV if TEE with no thrombus on device or in left atria AND no significant watchman leak (≤ 5 mm)

Anticoagulation: daily ASA

Revision of draft proposed by Tamara Langeberg and Charles Gornick, MD

What is Next in AC for AF?




- DOACs pre/post Watchman
- DOACs post-TAVR/bioprosthetic AVR
- AC after surgical left atrial appendage ligation
- Watchman with antiplatelet agents only
- DCCV after Watchman without AC
- DCCV with Cardiac CT in place of TEE to exclude LAA thrombus
- Device-detected AF (how much/when??)

Thank you!








Risk and Benefit of Different Antithrombotic Therapies (Focus on AF)

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Associate Professor of Medicine
Section Head, Vascular Medicine
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Medical Director, Vein Practice
Medical Director, Vascular Laboratory
Minneapolis Heart Institute® Abbott Northwestern Hospital

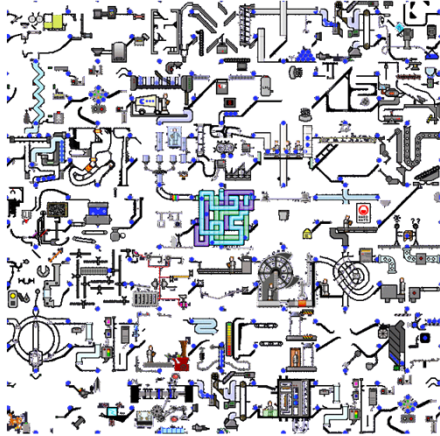
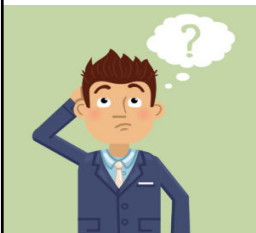


Disclosures

-  Consulting and speaking for Pfizer, BMS, J&J, B.I. and BSC
-  No financial conflict related to this talk
-  Slides were shared prior to the presentation



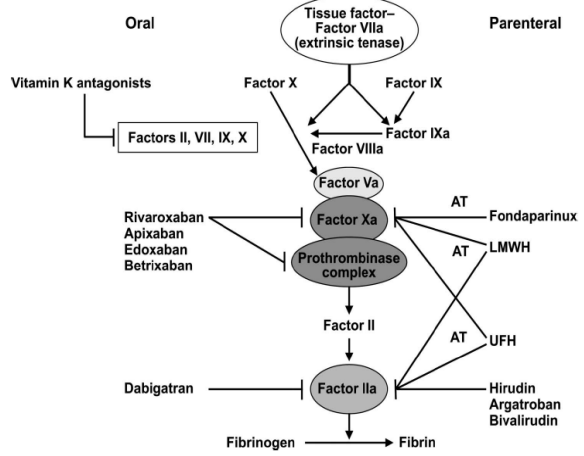
Decision Making is More Complicated



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Targets for Anticoagulation



The Drug Monit. 2010 Dec;32(6):673-9
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Dabigatran (Pradaxa) Only Oral Direct Thrombin Inhibitor

Approved Indications:

1. **NVAF**
 - The only DOAC superior to warfarin to reduce *ischemic* stroke risk
 - More major bleed (extra cranial) in patients ≥ 75 years of age
 - More GI side effects and bleeding
2. **Treatment for DVT and or PE:**
 - Requires 5-10 days of parenteral anticoagulation
3. **Risk reduction of VTE after initial therapy**
4. **DVT prophylaxis in patient going for hip replacement**
 - Not approved for patients needing knee replacement

Circulation. 2011 Apr 5;123(13):1436-50

Hematol. 2008;37:259-65



Factor Xa Inhibitors

- Rivaroxaban (J&J) Xarelto
- Apixaban [Bristol-Myers Squibb, Pfizer] Eliquis
- Edoxaban (Daiichi) Savaysa
- Betrixaban (Portola pharma) Bevyxxa

- YM150 (Astellas)
- LY517717 (Lilly)
- TAK-442 (Takeda)
- PD0348292 (Pfizer)



Apixaban (Eliquis)

Approved Indications:

1. **NVAF**
 - Superior to warfarin, stroke and SE, major bleeding and all-cause mortality
 - Only DOAC studied vs. ASA (AVEROS Trial):
 - ❖ Superior for stroke/SE and no significant difference in major bleeding
2. **Treatment of DVT and or PE**
 - Superior to enoxaparin/warfarin for major bleed
3. **Risk reduction of recurrent VTE after initial therapy**
 - Not significantly different from placebo for major bleed
4. **DVT prophylaxis following hip or knee replacement**

Arterioscler Thromb Vasc Biol. 2007 Jun;27(6):1238-47
N Engl J Med. 2011 Mar 3;364(9):806-17



Rivaroxaban (Xarelto)

Approved indications:

1. **NVAF (ROCKET-AF, mean CHADS2: 3.5)**
 - Can be given once daily *with food* for the NVAF indication
 - More GI bleeding and need for transfusion versus warfarin
2. **Treatment of DVT and or PE**
 - Superior to enoxaparin/warfarin for major bleed
3. **Risk reduction of recurrent VTE after initial therapy**
 - 10mg dose has similar major bleeding risk to ASA (EINSTEIN CHOICE Trial, only DOAC compared to ASA for this indication)
4. **DVT prophylaxis following hip or knee replacement**
5. **DVT prophylaxis in medically ill patients (not at high bleeding risk!)**
6. **MACE risk reduction in patients with chronic CAD/PAD in addition to ASA 81 mg daily**

Pharmacotherapy. 2009 Feb;29(2):167-81
Weitz J.I. et al. N Engl J Med 2017; 376:1211-1222



Edoxaban (Savaysa)

Approved Indications:

1. **NVAF**
 - Superior to warfarin for major bleeding
 - Once daily dosage
 - Lower GI bleed with 30 mg dosage vs. warfarin
 2. **Treatment of DVT and or PE**
 - Requires 5-10 days of parenteral anticoagulation
 - Superior to warfarin for major and CRNM bleed
- Not indicated for secondary VTE prevention after initial therapy
 - Not indicated for DVT prophylaxis after THR or TKR

Skeik N. *Vasc Med.* 2014 May 30;19(3):205-214
Roskob G.E. et al. *N Engl J Med* 2018; 378:615-624



Betrixaban (Bevyxxa)

Approved Indications:

1. **VTE prophylaxis in adults hospitalized for an acute medical illness** who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE.
 - Superior to enoxaparin with similar major but more CRNM bleedings




N Engl J Med. 2016;375(6):534.



Antiplatelet Agents

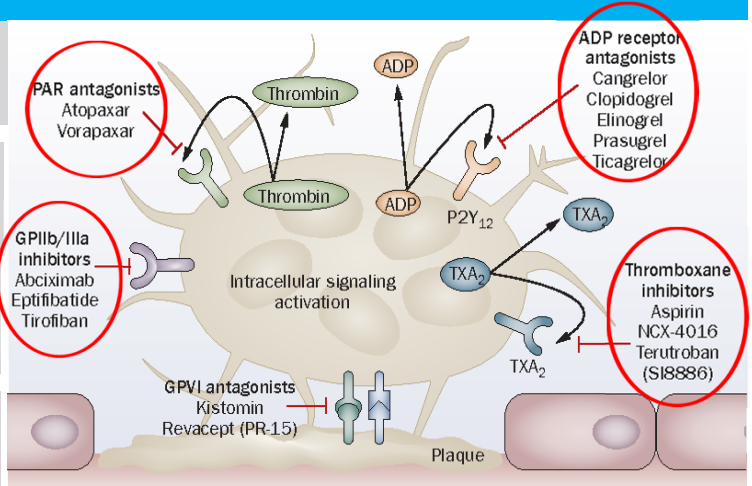
- **Aspirin (NSAID and sulfinpyrazone):** blocks cyclooxygenase, thereby inhibits the biosynthesis of PGs and TXs from arachidonic acid. TXA₂ is a potent stimulator of PLT aggregation.
- **The platelet P2Y₁₂ inhibitors** (clopidogrel, ticlopidine, ticagrelor, prasugrel, and cangrelor): block the binding of ADP to P2Y₁₂ receptor, thereby inhibiting PLT activation and aggregation.
- **Vorapaxar:** antagonist of the protease-activated receptor-1 expressed on PLT. It inhibits thrombin-induced PLT aggregation.
- **Glycoprotein IIb/IIIa inhibitors:** bind GP IIb/IIIa receptor inhibiting PLT aggregation.




J Clin Invest. 2001;107(12):1591

Antiplatelet Therapies

- **Aspirin (NSAID and sulfinpyrazone):**
 - PLT aggregation
- **The platelet P2Y₁₂ inhibitors:**
 - PLT activation and aggregation
- **Vorapaxar, PAR 1 antagonist:**
 - PLT aggregation
- **Glycoprotein IIb/IIIa inhibitors:**
 - PLT aggregation



2019 ACC/AHA/HRS Treatment Guidelines Update to Prevent Thromboembolism in Patients with AF

Assess stroke risk with CHA₂DS₂-VASc score

- Score 1 in men & 2 in women: Annual stroke risk 1%-2%, oral anticoagulants or aspirin may be considered
- Score ≥2 in men & ≥3 in women: Annual stroke risk 2%-15%, oral anticoagulants are recommended

&

Balance stroke risk reduction benefit vs. bleeding risk

CHA ₂ DS ₂ -VASc Score in Men	CHA ₂ DS ₂ -VASc Score In Women	Recommendation
0	0	No anticoagulant
1	2	Aspirin (81-325 mg daily) or oral anticoagulants may be considered
≥ 2	≥ 3	Oral anticoagulants are recommended*

*DOACS (dabigatran, rivaroxaban, apixaban, and edoxaban) recommended over warfarin in DOAC-eligible patients

January, CT, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. JACC. 2019; doi: 10.1161/CIR.0000000000000665



2019 ACC/AHA/HRS Focused Update on Atrial Fibrillation

4.4. Nonpharmacological Stroke Prevention

4.4.1. Percutaneous Approaches to Occlude the LAA

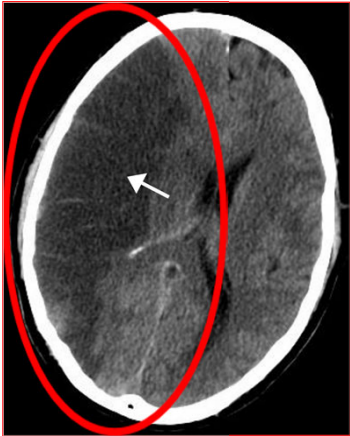
Recommendation for Percutaneous Approaches to Occlude the LAA		
Referenced studies that support the new recommendation are summarized in Online Data Supplement 4 .		
COR	LOE	Recommendation
IIb	B-NR	1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation (S4.4.1-1–S4.4.1-5). NEW: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.

“Oral anticoagulation remains the preferred therapy for stroke prevention for most patients with AF and elevated stroke risk. However, for patients who are poor candidates for long-term oral anticoagulation (because of the propensity for bleeding or poor drug tolerance or adherence), the Watchman device provides an alternative.”

January, CT, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. JACC. 2019; doi: 10.1161/CIR.0000000000000665



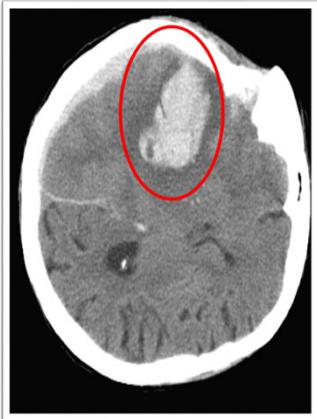
AF Related Major Ischemic Stroke



Courtesy to BSC



Anticoagulant Therapy Carries Risk of Intracerebral Hemorrhage or Death



Courtesy to BSC



CHA₂DS₂-VASc: Scoring Systems to Assess Stroke Risks

Condition	Points
C Congestive Heart Failure/LV Dysfunction	1
H Hypertension (SBP > 160)	1
A ₂ Age ≥ 75 years	2
D Diabetes Mellitus	1
S ₂ Prior Stroke, TIA, or Thromboembolism	2
V Vascular Disease (PAD, MI)	1
A Age 65-74 Years	1
Sc Sec Category (Female)	1

CHA ₂ DS ₂ -VASc Score	Annual % Stroke Risk		
	No Warfarin	With Aspirin ²	With Warfarin ²
0	0	0	0
1	1.3	1.0	0.5
2	2.2	1.7	0.8
3	3.2	2.5	1.2
4	4.0	3.1	1.4
5	6.7	5.2	2.4
6	9.8	7.6	3.5

January, CT. et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. JACC. 2019; doi: 10.1161/CIR.0000000000000665



HAS-BLED: Scoring Systems to Assess Bleeding Risks

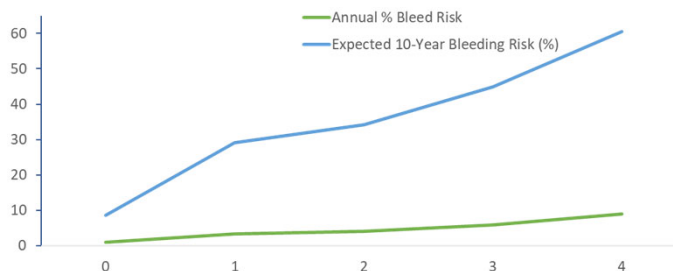
Condition	Points
H Hypertension	1
A Abnormal Renal/Liver Function (1 pt each)	1 or 2
S Stroke	1
B Bleeding History or Disposition	1
L Labile INRs	1
E Elderly	1
D Current Drugs (Medication) or Alcohol Use (1 pt each)	1 or 2
TOTAL POINTS	9

HAS-BLED Score	Annual % Major Bleeding Risk
0	0.9
1	3.4
2	4.1
3	5.8
4	8.9
5	9.1

Lip. JACC . 2011; 57(2): 173-180



Bleeding Risk Compounds Over Patients' Lifetime



Lip. JACC. 2011; 57(2): 173-180



Antithrombotic Options for Atrial Fibrillation

- **Aspirin:**

- Meta-analysis (8 trials, 4876 participants), reduced stroke by 22% (CI, 6% to 35%)
- Major bleeding risk 0.23% / year

- **Warfarin:**

- Meta-analysis (6 trials, 2900 participants), reduced stroke by 64% (95% CI, 49% to 74%)
- Major bleeding risk ~ 1-6%

- **Aspirin and Plavix:**

- Pooled analysis (5 studies involving 24,084 patients) reduced stroke vs. aspirin alone (p<0.05)
- Increased risk of major bleeding (p<0.05)



Ann Intern Med. 2007 Jun 19;146(12):857-67
 JAMA. Published online January 22 2019
 J Manag Care Spec Pharm. 2017 Sep;23(9):968-978



Direct Oral Anticoagulants (DOACs)

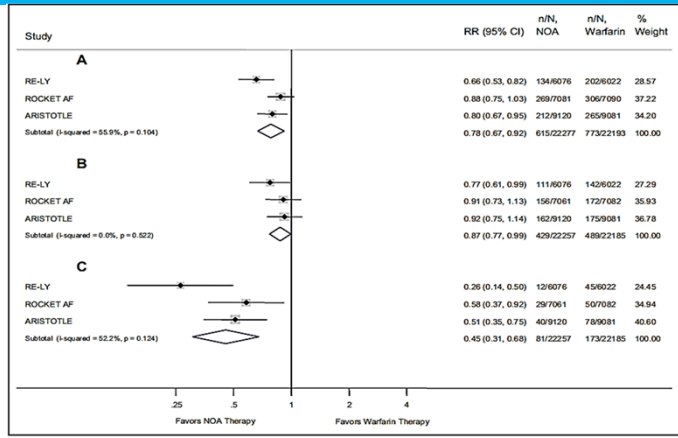
- Compared to warfarin:
 - Dabigatran: lower ischemic stroke
 - Apixaban and edoxaban: lower hemorrhagic stroke and major bleeding
 - All DOACs: lower ICH
- Do not require monitoring
- Less drug to drug and drug to food interactions
- Maximum concentration in plasma within hours
- Short half-life
- Antidotes are now approved (idarucizumab and andexanet alfa)

- Bleeding complications!
- Compliance, adherence and dosing issues!
- Antidote cost !

Ruff CT et al. Lancet 2014; 383: 955-962



Meta-Analysis of Efficacy and Safety of DOACs (Dabigatran, Rivaroxaban, Apixaban) vs. Warfarin in Patients with AF

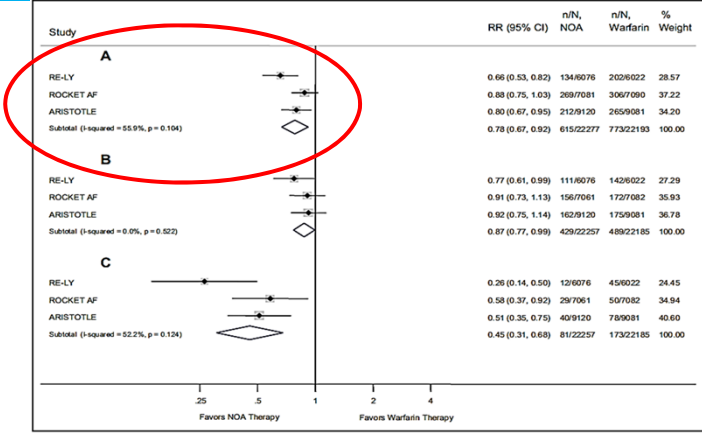


Forest plot for (A) all-cause stroke and SE, (B) ischemic and unspecified stroke, and (C) hemorrhagic stroke, DOAC vs. warfarin in patients with AF

Ruff CT et al. Lancet 2014; 383: 955-962



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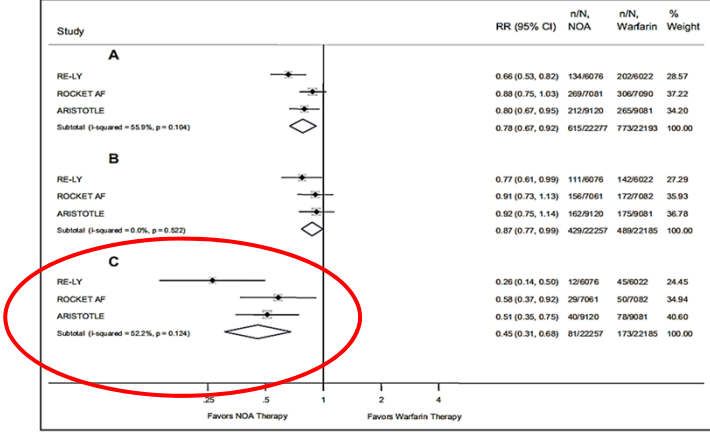


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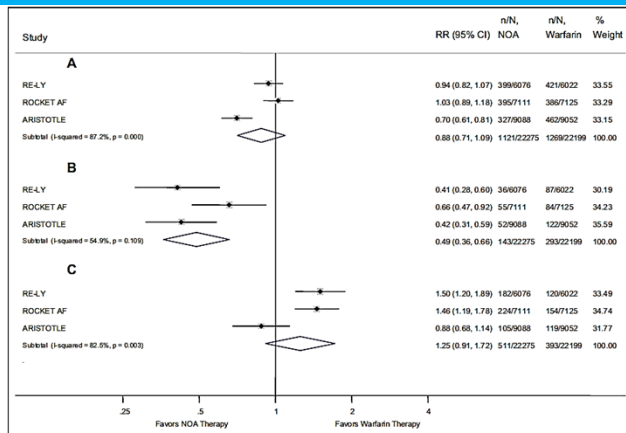


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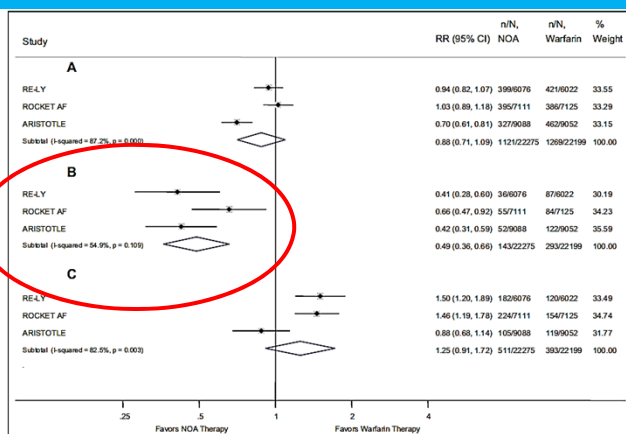


Forest plot for (A) major bleeding, (B) intracranial bleeding, and (C) GI bleeding, DOAC vs. warfarin in patients with AF.

Ruff CT et al. Lancet 2014; 383: 955-962



Meta-Analysis of Efficacy and Safety of DOACs (Dabigatran, Rivaroxaban, Apixaban) vs. Warfarin in Patients with AF

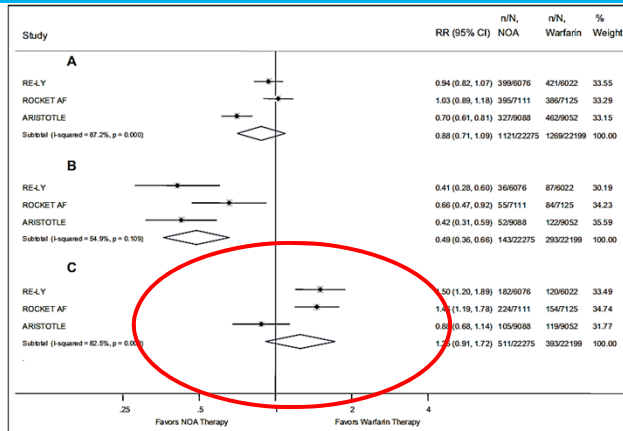


Forest plot for (A) major bleeding, (B) intracranial bleeding, and (C) GI bleeding, DOAC vs. warfarin in patients with AF.

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Meta-Analysis of Efficacy and Safety of DOACs (Dabigatran, Rivaroxaban, Apixaban) vs. Warfarin in Patients with AF



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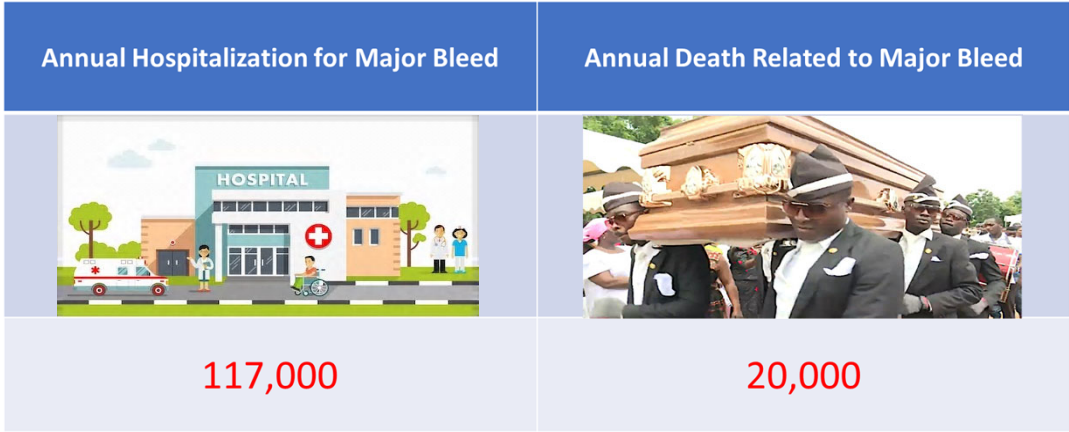
Rates of Bleeding with DOACs

	Major Bleed (% / year)	ICH (% / year)	GI Bleed (% / year)
Dabigatran (RE-LY)	3.11	0.30	1.51
Apixaban (ARISTOTLE)	2.13	0.33	0.76
Rivaroxaban (ROCKET-AF)	3.6	0.50	3.2
Edoxaban (ENGAGE AF-TIMI 48)	2.75	0.39	1.51

N Engl J Med. 2011;365(10):883-991.
N Engl J Med. 2011;365(11):981-992.



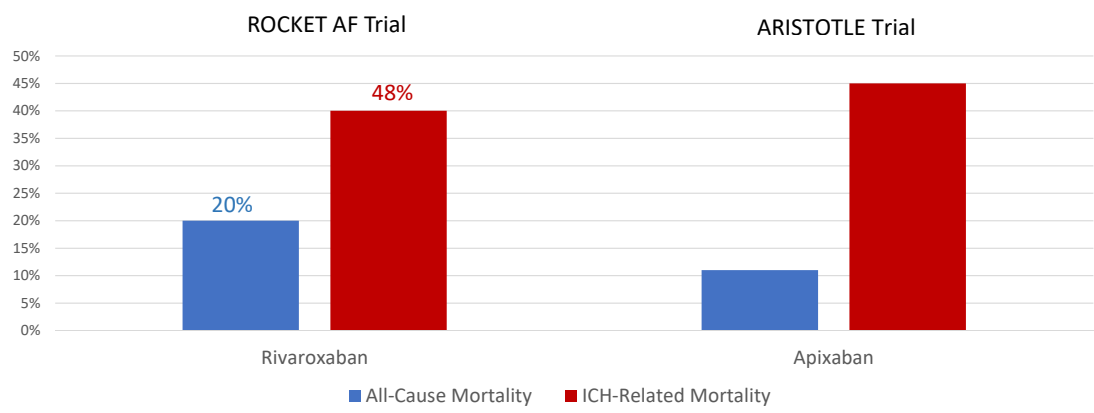
Hospitalization and Life Threatening Bleed Related to Anti-Xa Inhibitors



Truven Health Analytics, 12 months ending December 31, 2016 for Commercial, Medicare and Medicaid pts.
Skaistis J, et al. *PLoS One*. 2015;10(9):e0137444.



All Cause and ICH Mortality



N Engl J Med. 2011;365(10):883-991.
N Engl J Med. 2011;365(11):981-992.



ACS and AF

- DAPT (aspirin plus P2Y12 inhibitor) prevents MACE after PCI for ACS or stable disease.
- Current debate regarding optimal duration of DAPT!
- Approximately 5-10% of patients undergoing PCI have AF.
- The CV benefits gained by using triple therapy could be offset by higher risk for bleeding.
- Withdrawal of aspirin might lead to higher rates of stent thrombosis and ischemic events.

Ann Intern Med. 2020. PMID: 32176890



Bleeding Complications Dual (DOAC+P2Y12i) vs Triple (warfarin+P2Y12i+ASA)

	Dual %	Triple %
REDUA-PCI (Dabigatran)		
CRNM or Major	20.2	26.9
Major bleeding	5.6	8.4
PIONEER-AF-PCI (Rivaroxaban)		
CRNM or Major	16.8	26.7
Major	2.1	3.3
AGUSTUS (Apixaban)		
CRNM or Major	10.5	14.7
Major	3	4.6
ENTRUST-AF-PCI (Edoxaban)		
CRNM or Major	17	20
Major	6.7	7.2


Ann Intern Med. 2020. PMID: 32176890







Decision Making!











Summary

-  Antithrombotic therapies have different indications and bleeding risk
-  DOACs have lower bleeding complications than warfarin in general
-  Combinations of antithrombotic therapies carry higher bleeding risk
-  Bleeding Complications: DOAC+P2Y12i < warfarin+P2Y12i+ASA

Skeik N et al. *Ann Vasc Surg.* 2019 Oct;60:128-146





Sunset, Gaza City






   

Thank You!

Nedaa Skeik

Questions at the End?



Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention

Mario Goessl, MD PhD
Interventional Cardiology

Circulation

WHITE PAPER

Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention

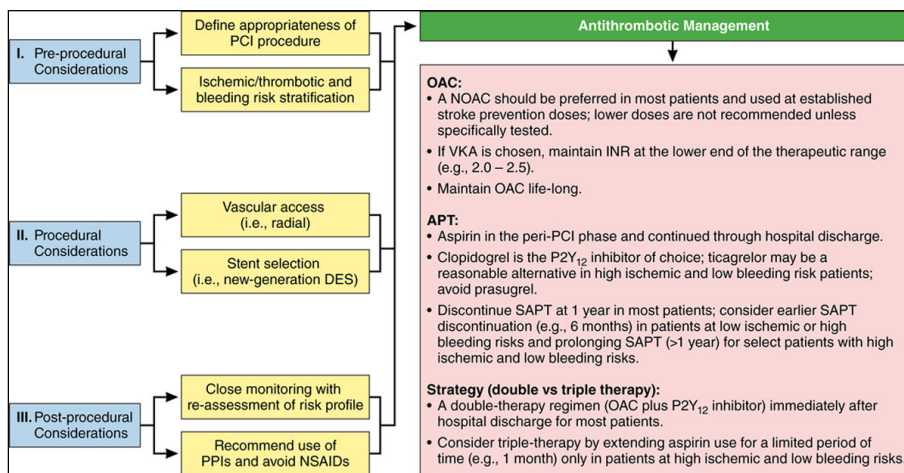
A North American Perspective–2018 Update

Table 1. Summary of the PIONEER AF-PCI and RE-DUAL PCI Trials

Trial	Patient Population	Indication for PCI	Primary Safety End Point	Secondary Efficacy End Point	End Points	Treatment Arms and Outcomes			
RE-DUAL PCI	AF with PCI and stent (DES, 82.6%) CrCl>30 mL/min No major bleed within 1 mo No stroke within 1 mo n=2725	ACS, 50.5%	ISTH major or clinically relevant nonmajor bleeding	Death, MI, stroke, SE, or unplanned revascularization		Warfarin with ASA* and P2Y ₁₂ inhibitor†	Dabigatran 110 mg twice daily and P2Y ₁₂ inhibitor†	Dabigatran 150 mg± twice daily and P2Y ₁₂ inhibitor†	
					Safety	26.9%	15.4%	20.2%	P<0.001 for D110 vs W P=0.002 for D150 vs W
					Efficacy	13.4%	15.2%	11.8%	P=0.005 (NI) for D combined vs W P=0.30 for D110 vs W P=0.44 for D150 vs W
PIONEER AF-PCI	AF with PCI and stent (DES, 66.1%) CrCl>30 mL/min No major bleed within 1 mo No GI bleed within 12 mo No prior stroke or TIA n=2124	ACS, 51.6%	Any clinically significant bleeding	CV death, MI, stroke		Warfarin with ASA and P2Y ₁₂ inhibitor†	Rivaroxaban 2.5 mg twice daily with ASA and P2Y ₁₂ inhibitor†	Rivaroxaban 15 mg daily† and P2Y ₁₂ inhibitor†	P<0.001 for R2.5 vs W P<0.001 for R15 vs W
					Safety	26.7%	18.0%	16.8%	P<0.001 for R2.5 vs W P<0.001 for R15 vs W
					Efficacy	6.0%	5.6%	6.5%	P=0.75 for R15 vs W P=0.76 for R2.5 vs W

Circulation. 2018;138:527–536. DOI: 10.1161/CIRCULATIONAHA.118.034722

A North American Perspective—2018 Update



Dominick J. Angiolillo. Circulation. Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention, Volume: 138, Issue: 5, Pages: 527-536, DOI: (10.1161/CIRCULATIONAHA.118.034722)

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What is high ischemic risk?

Any Acute Coronary Syndrome

PCI with

- ≥ 3 stents implanted
- ≥ 3 lesions treated, and/or
- 3 coronary vessels treated; and/or
- bifurcation with 2 stents implanted
- total stent length >60 mm, and/or
- treatment of a chronic total occlusion (CTO)

What is high bleeding risk?

Precise DAPT

very low risk: score ≤ 10 ; **low risk:** score 11 to 17;
moderate risk: score 18 to 24; and **high risk:** score ≥ 25)

PRECISEDAPT Home WebCalculator Disclaimer About Contact Us

Haemoglobin unit g/dl mmol/L

Age (years)

White blood cells unit u/mcL $10^9/L$

Creatinine Clearance (mL/min)

Prior Bleeding

CALCULATE

RESET

RESULT:

Cluster of risk: **Moderate**

Score Calculated: **22**

12 months risk of TIMI major or minor Bleeding: **1.5%**

12 months risk of TIMI Major Bleeding: **0.8%**

Copy to clipboard

1 year bleeding risk (%)

PRECISE DAPT score

Result: TIMI Major Bleeding, TIMI Major or Minor Bleeding

Non-High PRECISE-DAPT Score (score ≥ 25) Long DAPT (12-24 months) vs. Short DAPT (3-6 months)

ISCHAEMIA \downarrow **ARD -1.53%** $P=0.02$

BLEEDING \uparrow **ARD +0.14%** $P=0.23$

Myocardial infarction, definite/possible thrombosis, stroke or target vessel revascularization

TIMI Major or Minor Bleeding

DAPT Duration: 12-24 months 3-6 months

Cumulative incidence (%)

In patients without high PRECISE-DAPT score (Score ≥ 25) a long DAPT (12-24 months) as compared with a short DAPT (3-6 months) was associated with a lower

Costa F. et al. Lancet 2017, 389

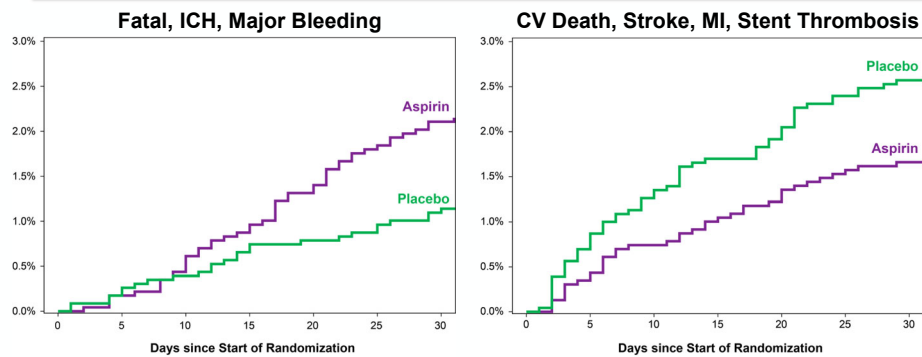
Circulation

The Risk / Benefit Tradeoff of Antithrombotic Therapy in Patients with Atrial Fibrillation Early and Late After an Acute Coronary Syndrome or Percutaneous Coronary Intervention: Insights from AUGUSTUS

ACC.20
TOGETHER WITH
WORLD CONGRESS
OF CARDIOLOGY

Severe Bleeding and Ischemic Outcomes

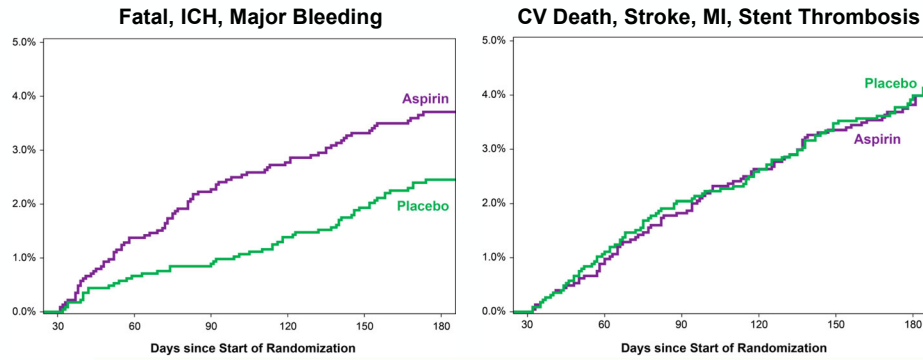
Randomization to 30 Days



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Severe Bleeding and Ischemic Outcomes

30 Days to 6 Months



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Time from PCI	Default strategy	Patients at high ischemic/thrombotic and low bleeding risks	Patients at low ischemic/thrombotic or high bleeding risks
Peri-PCI	Triple Therapy (OAC + DAPT)	Triple Therapy (OAC + DAPT)	Triple Therapy (OAC + DAPT)
1 month	Double Therapy up to 12 months (OAC + SAPT)	Triple Therapy up to 1 month (OAC + DAPT)	Double Therapy up to 6 months (OAC + SAPT)
3 months		Double Therapy up to 12 months (OAC + SAPT)	
6 months			OAC
12 months	OAC	OAC	OAC
>12 months			

OAC; prefer a NOAC over VKA if no contraindications
 SAPT; prefer a P2Y₁₂ inhibitor over aspirin
 Clopidogrel is the P2Y₁₂ inhibitor of choice; ticagrelor may be considered in patients at high ischemic/thrombotic and low bleeding risks; avoid prasugrel
 Consider SAPT in addition to OAC after >12 mo. only in select patients at high ischemic/thrombotic and low bleeding risks



Dominick J. Angiolillo. Circulation. Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention, Volume: 138, Issue: 5, Pages: 527-536, DOI: (10.1161/CIRCULATIONAHA.118.034722)

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

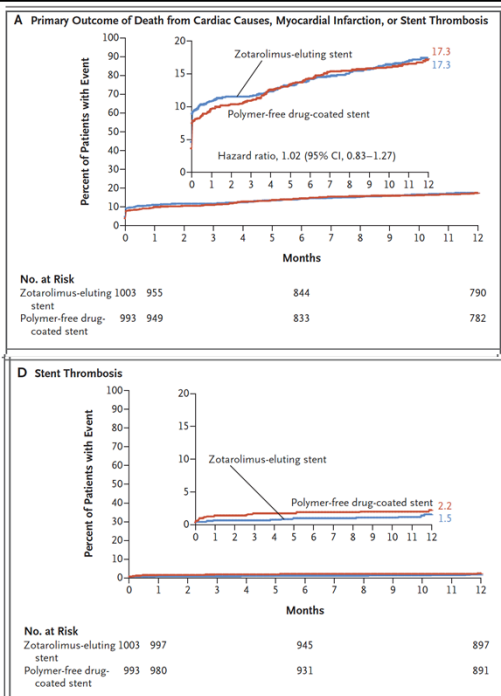
Polymer-based or Polymer-free Stents in Patients at High Bleeding Risk

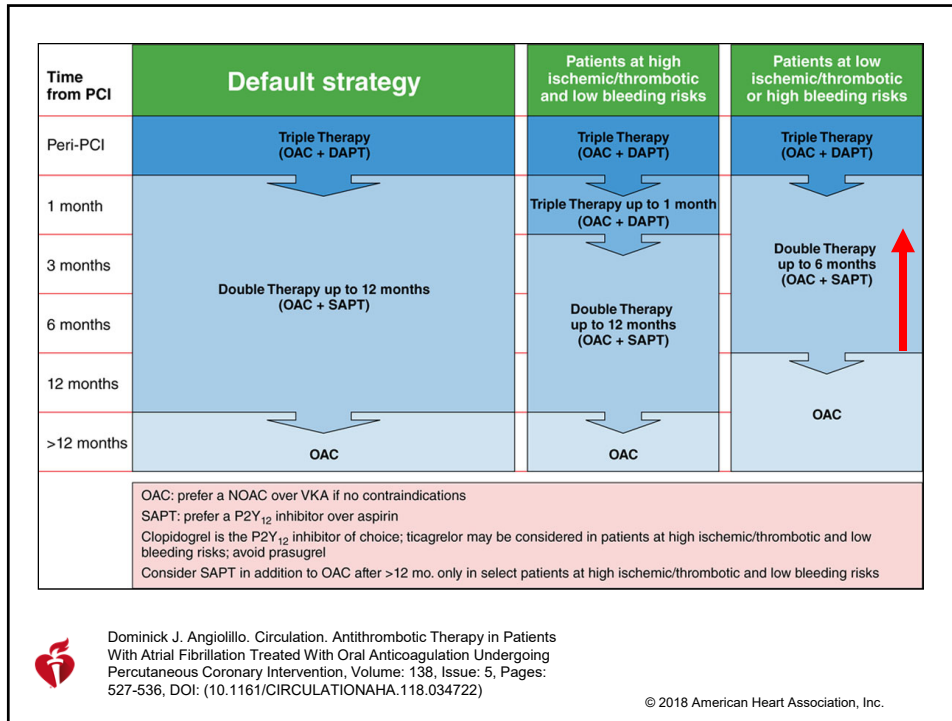
S. Windecker, A. Latib, E. Kedhi, A.J. Kirtane, D.E. Kandzari, R. Mehran, M.J. Price, A. Abizaid, D.I. Simon, S.G. Worthley, A. Zaman, M. Hudec, P. Poliacikova, A.K. Abdul Gharar, K. Selvaraj, I. Petrov, D. Mylotte, E. Pinar, R. Moreno, F. Fabbicchi, S. Pasupati, H.-S. Kim, A. Aminian, C. Tie, A. Włodarczak, S.-H. Hur, S.O. Marx, I. Jankovic, S. Brar, L. Bousquette, M. Liu, and G.W. Stone, for the ONYX ONE Investigators*

CONCLUSIONS

Among patients at high bleeding risk who received 1 month of dual antiplatelet therapy after PCI, use of polymer-based zotarolimus-eluting stents was noninferior to use of polymer-free drug-coated stents with regard to safety and effectiveness composite outcomes. (Funded by Medtronic; ONYX ONE ClinicalTrials.gov number, NCT03344653.)

N Engl J Med 382;13 nejm.org March 26, 2020





Summary

- Double vs Triple antithrombotic therapy is an individualized decision but
 - **DON'T** use DAPT + OAC/NOAC >1 mo post PCI
 - **DON'T** use Prasugrel
- ONYX ONE shows that even shorter (1 mo) DAPT may be possible

Thank you

We are happy to take your questions now ...

Table 3. Summary of Randomized Trials of NOACs Compared With Warfarin Therapy in Patients With AF, With Relative Risk Reductions of Major Clinical Events

	Dabigatran		Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct thrombin inhibitor		Anti-factor Xa inhibitor	Anti-factor Xa inhibitor	Anti-factor Xa inhibitor
Clinical trial acronym	RE-LY		ROCKET-AF	ARISTOTLE	ENGAGE-AF
CHADS ₂ score (mean)	2.1		3.5	2.1	2.8
TTR (median), %	67		58	66	68
Approved dose	150 mg twice daily*	110 mg twice daily*	20 mg once daily (15 mg once daily in selected patients†)	5 mg twice daily (2.5 mg twice daily in selected patients†)	60 mg once daily (30 mg once daily in selected patients†‡)
Stroke or SE, HR (95% CI)	0.66 (0.53–0.82)	0.91 (0.74–1.11)	0.88 (0.74–1.03)	0.79 (0.66–0.95)	0.87 (0.73–1.04)
Ischemic stroke, HR (95% CI)	0.76 (0.60–0.98)	1.11 (0.89–1.40)	0.94 (0.75–1.17)	0.92 (0.74–1.13)	1.00 (0.83–1.19)
Hemorrhagic stroke, HR (95% CI)	0.26 (0.14–0.49)	0.31 (0.17–0.56)	0.59 (0.37–0.93)	0.51 (0.35–0.75)	0.54 (0.38–0.77)
All-cause mortality, HR (95% CI)	0.88 (0.77–1.00)	0.91 (0.80–1.03)	0.85 (0.70–1.02)	0.89 (0.80–0.998)	0.92 (0.83–1.01)
Major bleed, HR (95% CI)	0.93 (0.81–1.07)	0.80 (0.69–0.93)	1.04 (0.90–1.20)	0.69 (0.60–0.80)	0.80 (0.71–0.91)
GI bleeding, HR (95% CI)	1.50 (1.19–1.89)	1.10 (0.86–1.41)	1.39 (1.19–1.61)	0.89 (0.70–1.15)	1.23 (1.02–1.50)

Circulation. 2018;138:527–536. DOI: 10.1161/CIRCULATIONAHA.118.034722