2022 Hospital Medicine Update
May 11-14

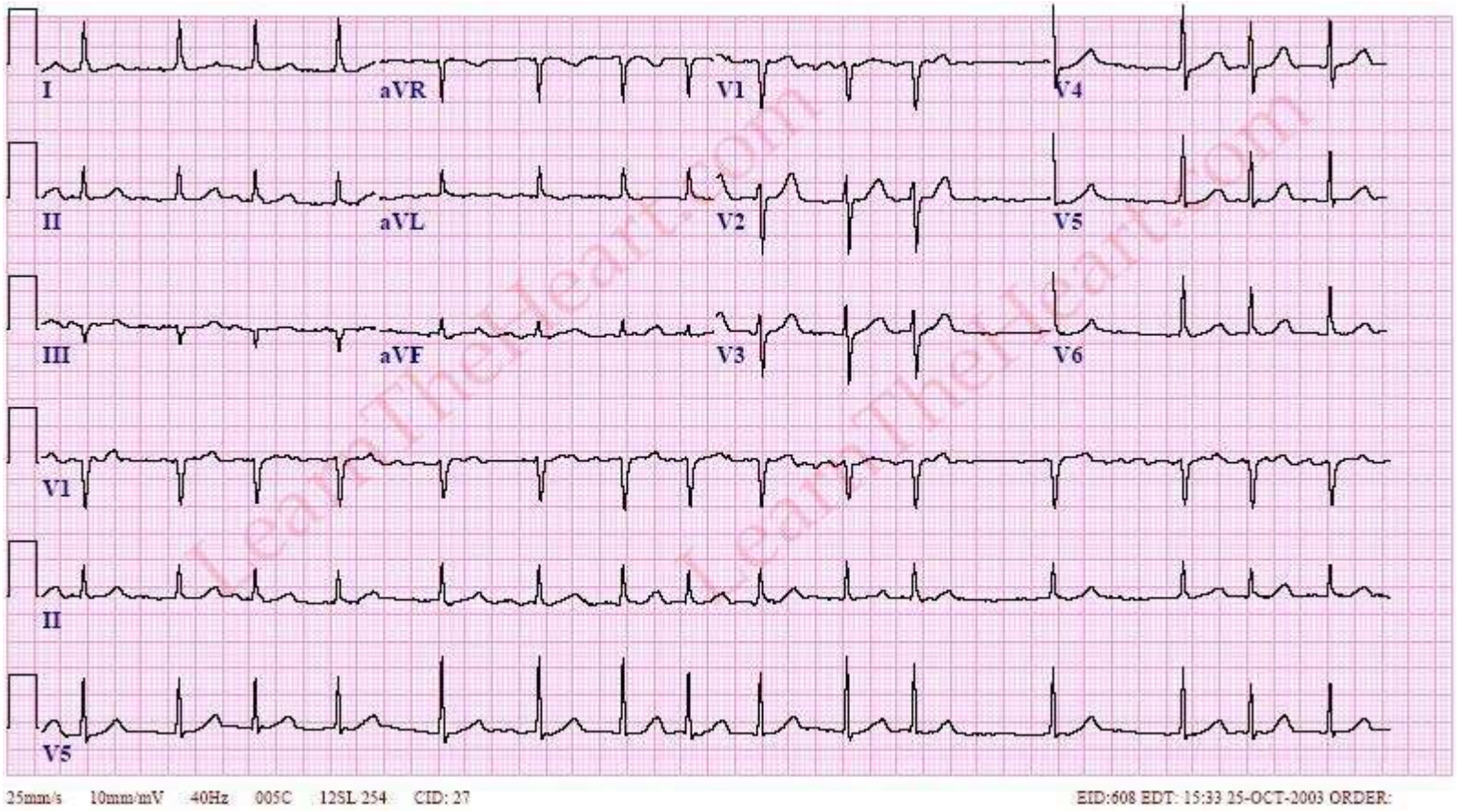
Updated AHA/ACC/HRS Guidelines For the Management of Atrial Fibrillation 2022

Chad Link, DO, FACC, FACOI
Cardiologist
Chairman Cardiology Department
Sparrow TCI-Lansing, MI

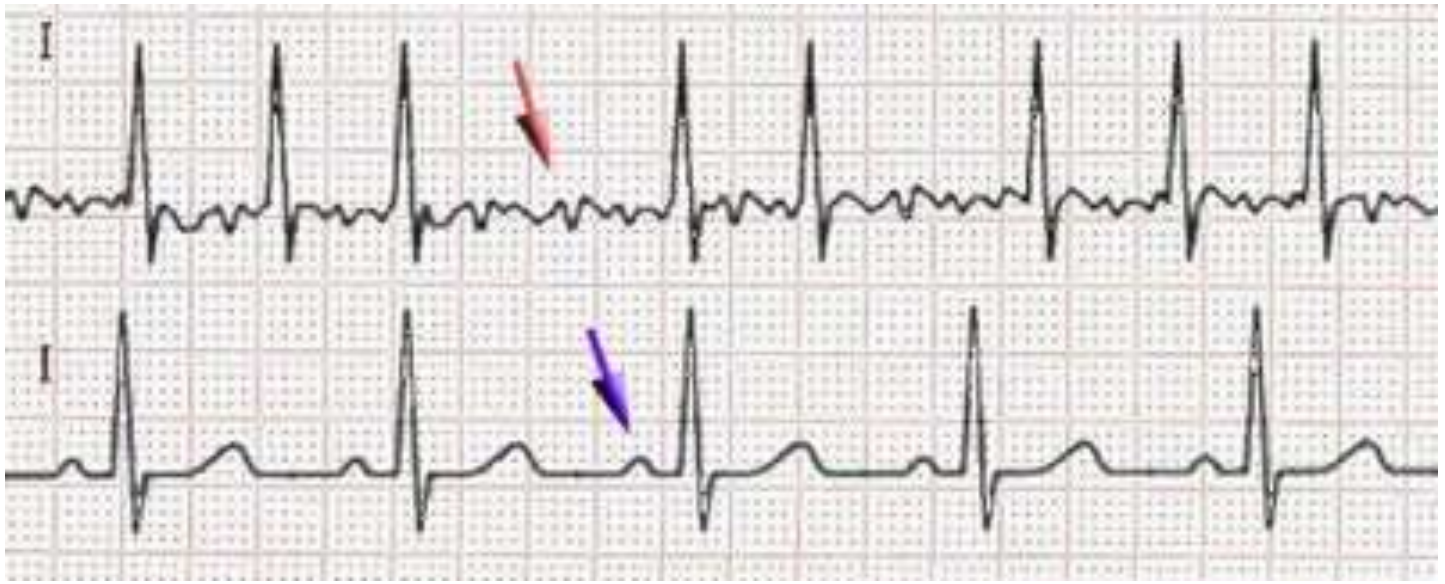
Disclosures

Speakers Bureau – Actelion Pharmaceuticals, J & &, BI, Astra Zeneca, Pfizer and BMS

Atrial Fibrillation



Atrial Fibrillation



Atrial Fibrillation Background

- Atrial fibrillation is the most common sustained arrhythmia
- Affects 2 million Americans-- AF is 0.4% to 1% in the general population
- Expensive- 16 billion
- 6% over the age of 65 experience it
- Responsible for 15% strokes
- Unfortunately, warfarin is received by only 30-60% of appropriate patients
- In the FHS, the lifetime risk of atrial fibrillation (AFib) for adults is 26% for men and 23% for women.
- The 2014 ACC/AHA/HRS Atrial Fibrillation guideline defines Non Valvular Atrial Fibrillation as **AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic valve or mitral valve repair**

- January CT et al. Journal of the American College of Cardiology 2014 doi 10/1016 JACC 2014 0.3.022)

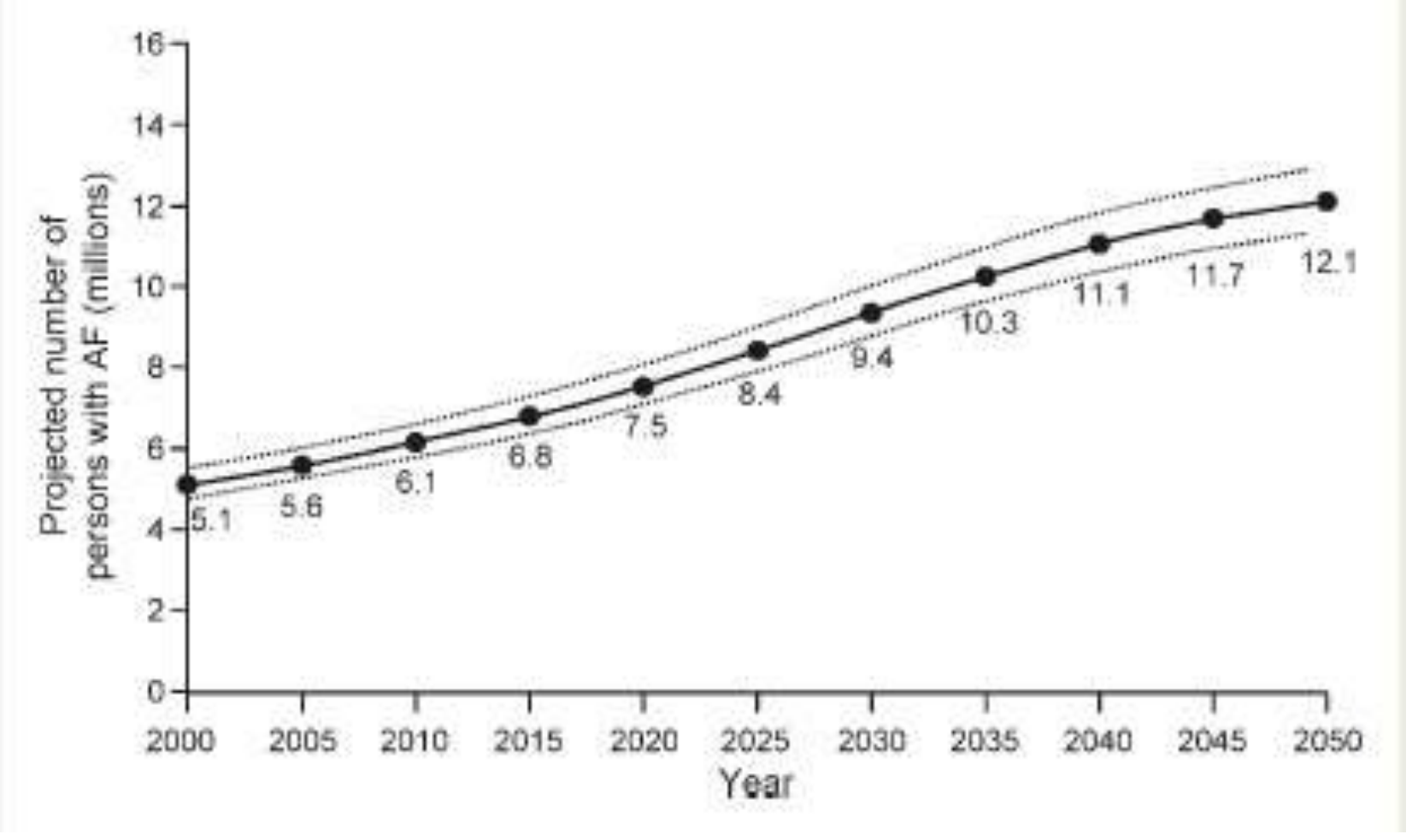
Classification of Atrial Fibrillation Subtypes

- Paroxysmal
- Spontaneous termination usually < 7 days and most often < 48 hours

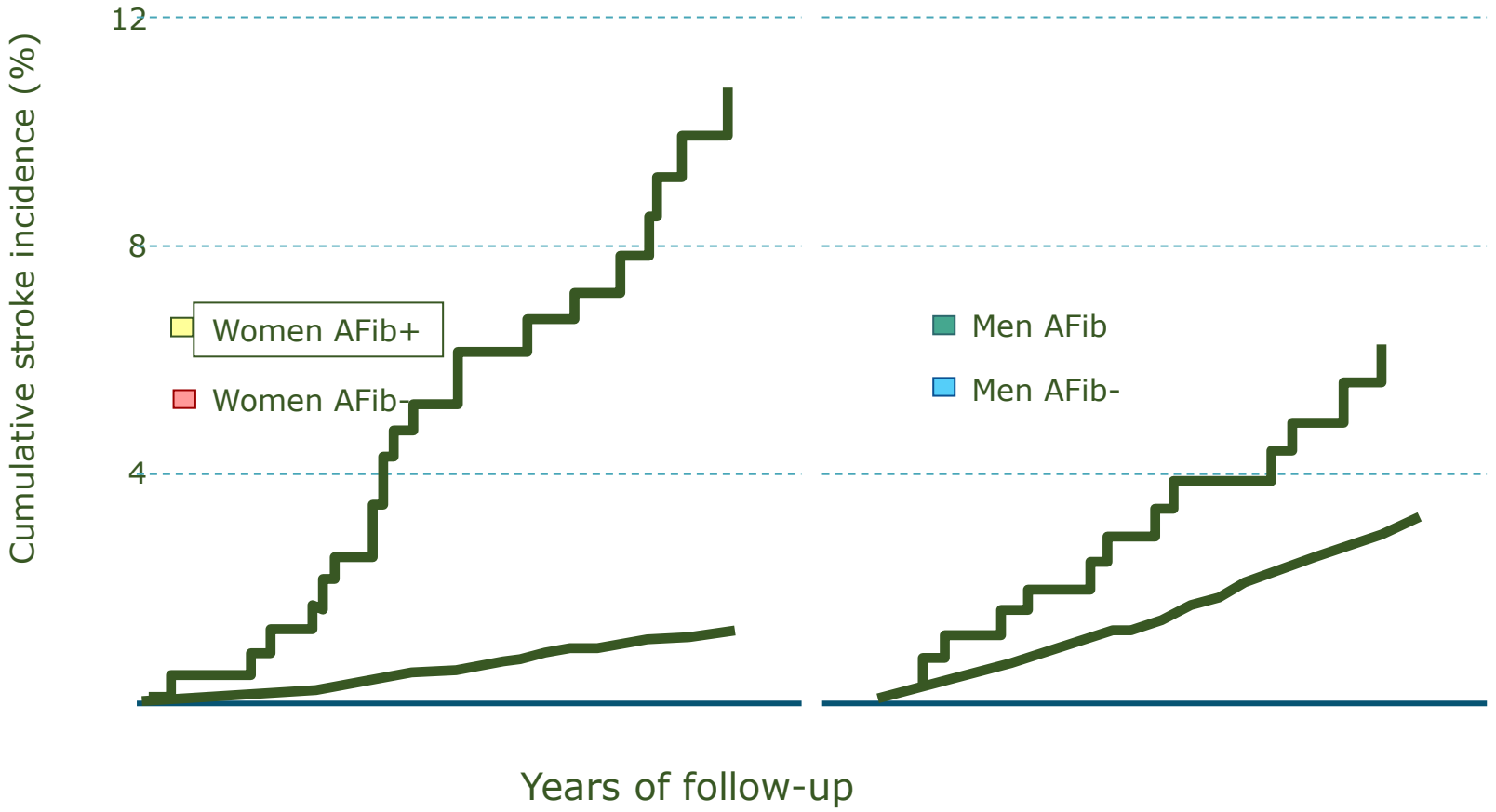
- Persistent
- Does not interrupt spontaneously and needs therapeutic intervention for termination
- (either pharmacological or electrical cardioversion)

- Permanent
- AFib in which cardioversion is attempted but unsuccessful, or successful but immediately relapses, or a form of AFib for which a decision was taken not to attempt cardioversion

Atrial Fibrillation Prevalence Estimates



AFib is Responsible for 15-20% of all Strokes



Wolf PA, et al. Stroke (1991) 22: 983
Go AS, et al. JAMA (2001) 285: 2370
Friberg J, et al. *Am J Cardiol* (2004) 94: 889

Summary

- Background of Atrial Fibrillation
- Anticoagulation
- 2019 ACC Update
- Risks of Bleeding
- Interruption or Discontinuation of Oral Anticoagulation for Surgery/Procedures
- Device Based Solutions
- Management of Bleeding
- Special Populations

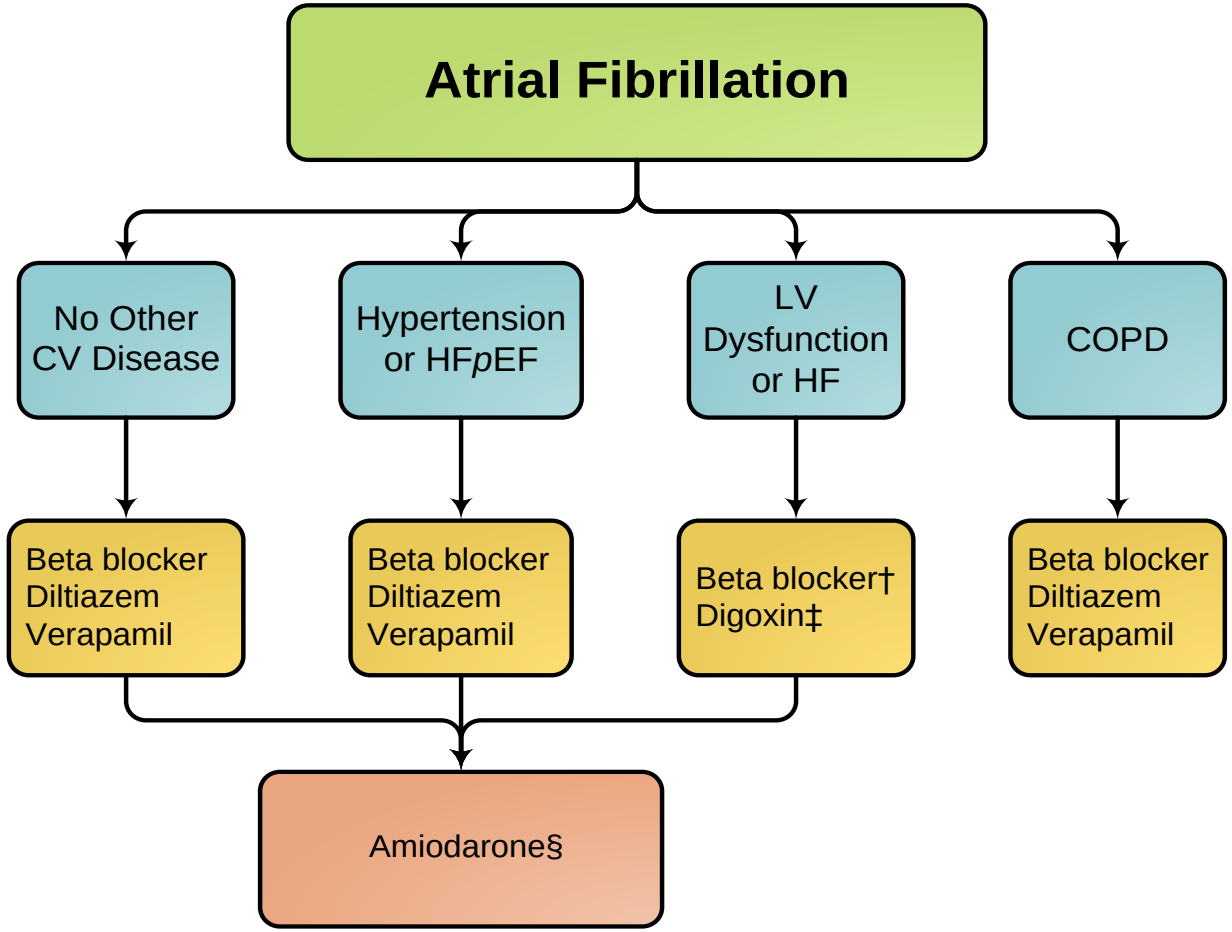
Atrial Fibrillation

Rate Control vs. Rhythm Control
Anticoagulation

Atrial Fibrillation

Rate Control vs. Rhythm Control
Anticoagulation

Atrial Fibrillation- Approach to Selecting Drug Therapy for Ventricular Rate Control



Rate Control Options

- Beta blocker
  - Recommend metoprolol, Avoid carvedilol (Coreg) -less effective in AV node blockade
- Calcium channel blocker
    - Diltiazem, Verapamil

Rate Control Options

- Digoxin
    - Not as the sole agent- May be harmful
- **Digoxin-associated mortality: a systematic review and meta-analysis of the literature. Vamos M, Erath JW, Hohnloser SH.**
  Eur Heart J. May 4 2015. DOI: http://dx.doi.org/10.1093/eurheartj/ehv143

Conclusion

- This meta-analysis on the effects of digoxin on all-cause mortality indicates that digoxin is associated with increased mortality risk in patients with AF or congestive HF. The effect was strongest in AF patients. These observations call for randomised trials evaluating dose-adjusted digoxin therapy. Until those have been completed, digoxin should be used with great caution, especially when used for rate control in AF.

How do we determine stroke risk ?

How do we determine stroke risk ?

CHEST

Original Research

THROMBOEMBOLISM

Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach

The Euro Heart Survey on Atrial Fibrillation

Gregory Y. H. Lip, MD; Robby Nieuwlaat, PhD; Ron Pisters, MD; Deirdre A. Lane, PhD; and Harry J. G. M. Crijns, MD

Atrial Fibrillation

$CHADS_2$

Risk Factor	Score
Cardiac failure	1
HTN	1
Age ≥75 y	1
Diabetes	1
Stroke	2

Total Score	Annual Risk of Stroke (%)
0	1.9
1	2.8
2	4.0
3	5.9
4	8.5
5	12.5
6	18.2

CHA_2DS_2-VASc

Risk Factor	Score
Cardiac failure	1
HTN	1
Age ≥75 y	2
Diabetes	1
Stroke	2
Vasc dz (MI, PAD, aortic ath)	**1**
Age 65-74 y	**1**
Sex **c**ategory (female)	**1**

Atrial Fibrillation

CHA_2DS_2-VASc

Risk Factor	Score
Cardiac failure	1
HTN	1
Age ≥75 y	2
Diabetes	1
Stroke	2
Vasc dz (MI, PAD, aortic ath)	**1**
Age 65-74 y	**1**
Sex **c**ategory (female)	**1**

Summary- Non Valvular AF

Risk Category	CHADs-2-VASC Score	Recommended Therapy American College of Cardiology (ACC) / European Society of Cardiology (ESC)
Two or more Risk Factors	2	ACC- Oral Anticoagulation ESC- Oral Anticoagulation
One Risk Factor	1	ACC- Aspirin 81 mg or Oral Anticoagulation (Exception Female Gender only) ESC- Oral Anticoagulation
No Risk Factors	0	ACC- Aspirin 81 mg daily ESC- No Therapy

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. © American College of Cardiology Foundation and American Heart Association

Atrial Fibrillation

- Anticoagulation Strategies
  - Aspirin
  - Warfarin
  - Dabigatran (Direct Thrombin Inhibitor)
  - Rivaroxaban (Factor Xa Inhibitor)
  - Apixaban (Factor Xa Inhibitor)
  - Endoxiban (Factor Xa Inhibitor)

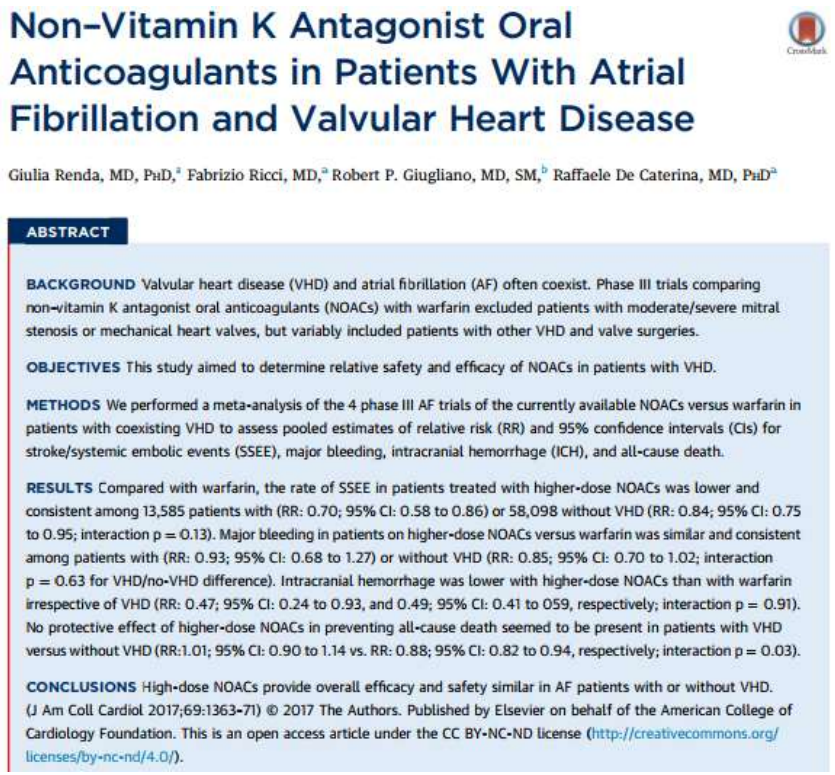
Atrial Fibrillation

- As of 2019, Non-vitamin K oral anticoagulants (NOACs), are now recommended as the preferred alternative to warfarin for reducing the risk of stroke associated with atrial fibrillation (AFib).

- The new recommendation comes from the 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation released Jan. 28 by the ACC, American Heart Association and Heart Rhythm Society and simultaneously published in the Journal of the American College of Cardiology.

Atrial Fibrillation

- In patients with AF and VHD (other than moderate/ severe mitral stenosis or mechanical heart valves) NOACs are attractive alternatives to VKAs because the coexistence of VHD does not affect the overall relative efficacy or safety of NOACs in terms of prevention of SSEE and major bleeding. Current definitions of "valvular" and "nonvalvular" AF are misleading, and the use of NOACs should be permitted in most patients with VHD.
- The recently proposed term "MARM-AF," standing for "Mechanical And Rheumatic Mitral valvular AF" could be useful to identify the true high risk AF patients for whom VKAs are the anticoagulants of choice



Non–Vitamin K Antagonist Oral Anticoagulants in Patients With Atrial Fibrillation and Valvular Heart Disease

Giulia Renda, MD, PhD,[a] Fabrizio Ricci, MD,[a] Robert P. Giugliano, MD, SM,[b] Raffaele De Caterina, MD, PhD[a]

ABSTRACT

BACKGROUND Valvular heart disease (VHD) and atrial fibrillation (AF) often coexist. Phase III trials comparing non-vitamin K antagonist oral anticoagulants (NOACs) with warfarin excluded patients with moderate/severe mitral stenosis or mechanical heart valves, but variably included patients with other VHD and valve surgeries.

OBJECTIVES This study aimed to determine relative safety and efficacy of NOACs in patients with VHD.

METHODS We performed a meta-analysis of the 4 phase III AF trials of the currently available NOACs versus warfarin in patients with coexisting VHD to assess pooled estimates of relative risk (RR) and 95% confidence intervals (CIs) for stroke/systemic embolic events (SSEE), major bleeding, intracranial hemorrhage (ICH), and all-cause death.

RESULTS Compared with warfarin, the rate of SSEE in patients treated with higher-dose NOACs was lower and consistent among 13,585 patients with (RR: 0.70; 95% CI: 0.58 to 0.86) or 58,098 without VHD (RR: 0.84; 95% CI: 0.75 to 0.95; interaction p = 0.13). Major bleeding in patients on higher-dose NOACs versus warfarin was similar and consistent among patients with (RR: 0.93; 95% CI: 0.68 to 1.27) or without VHD (RR: 0.85; 95% CI: 0.70 to 1.02; interaction p = 0.63 for VHD/no-VHD difference). Intracranial hemorrhage was lower with higher-dose NOACs than with warfarin irrespective of VHD (RR: 0.47; 95% CI: 0.24 to 0.93, and 0.49; 95% CI: 0.41 to 059, respectively; interaction p = 0.91). No protective effect of higher-dose NOACs in preventing all-cause death seemed to be present in patients with VHD versus without VHD (RR:1.01; 95% CI: 0.90 to 1.14 vs. RR: 0.88; 95% CI: 0.82 to 0.94, respectively; interaction p = 0.03).

CONCLUSIONS High-dose NOACs provide overall efficacy and safety similar in AF patients with or without VHD.

Atrial Fibrillation

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

Developed in Collaboration With the Society of Thoracic Surgeons

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**B**	**In patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve), the CHA_2DS_2-VASc score is recommended for assessment of stroke risk.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. Patients with AF with bioprosthetic heart valves are addressed in the supportive text. (Section 4.1. in the 2014 AF guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	A	**For patients with AF and an elevated CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended.** **Options include:** • **Warfarin (LOE: A)** • **Dabigatran (LOE: B)** • **Rivaroxaban (LOE: B)** • **Apixaban (LOE: B) or** • **Edoxaban (LOE: B-R)** **MODIFIED**: This recommendation has been updated in response to the approval of edoxaban, a new factor Xa inhibitor. More precision in the use of CHA_2DS_2-VASc scores is specified in subsequent recommendations. The LOEs for warfarin, dabigatran, rivaroxaban, and apixaban have not been updated for greater granularity as per the new LOE system. (Section 4.1. in the 2014 AF Guideline) The original text can be found in Section 4.1 of the 2014 AF guideline. Additional information about the comparative effectiveness and bleeding risk of NOACs can be found in Section 4.2.2.2.
	B	
	B	
	B	
	B-R	

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
IIa	**B**	**For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a CHA_2DS_2-VASc score of 0 in men or 1 in women, it is reasonable to omit anticoagulant therapy.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. (Section 4.1. in the 2014 AF Guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation

Journal of the American College of Cardiology

Volume 65, Issue 3, January 2015
DOI: 10.1016/j.jacc.2014.10.052

PDF Article

Benefit of Anticoagulation Unlikely in Patients With Atrial Fibrillation and a CHA_2DS_2-VASc Score of 1

Leif Friberg, Mika Skeppholm, Andreas Terént

⊞ Author + information

Abstract

Background Patients with atrial fibrillation (AF) and ≥1 point on the stroke risk scheme CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, age 65–74 years, sex category) are considered at increased risk for future stroke, but the risk associated with a score of 1 differs markedly between studies.

Objectives The goal of this study was to assess AF-related stroke risk among patients with a score of 1 on the CHA_2DS_2-VASc.

Methods We conducted this retrospective study of 140,420 patients with AF in Swedish nationwide health registries on the basis of varying definitions of "stroke events."

Results Using a wide "stroke" diagnosis (including hospital discharge diagnoses of ischemic stroke as well as unspecified stroke, transient ischemic attack, and pulmonary embolism) yielded a 44% higher annual risk than if only ischemic strokes were counted. Including stroke events in conjunction with the index hospitalization for AF doubled the long-term risk beyond the first 4 weeks. For women, annual stroke rates varied between 0.1% and 0.2% depending on which event definition was used; for men, the corresponding rates were 0.5% and 0.7%.

Conclusions The risk of ischemic stroke in patients with AF and a CHA_2DS_2-VASc score of 1 seems to be lower than previously reported.

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**A**	**NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve).** **NEW**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. When the NOAC trials are considered as a group, the direct thrombin inhibitor and factor Xa inhibitors were at least noninferior and, in some trials, superior to warfarin for preventing stroke and systemic embolism and were associated with lower risks of serious bleeding.

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation

	Rivaroxaban	Warfarin		
	Event Rate	Event Rate	HR (95% CI)	P-value
Vascular Death, Stroke, Embolism	3.11	3.63	0.86 (0.74, 0.99)	0.034
Stroke Type				
Hemorrhagic	0.26	0.44	0.59 (0.37, 0.93)	0.024
Ischemic	1.34	1.42	0.94 (0.75, 1.17)	0.581
Unknown Type	0.06	0.10	0.65 (0.25, 1.67)	0.366
Non-CNS Embolism	0.04	0.19	0.23 (0.09, 0.61)	0.003
Myocardial Infarction	0.91	1.12	0.81 (0.63, 1.06)	0.121
All Cause Mortality	1.87	2.21	0.85 (0.70, 1.02)	0.073
Vascular	1.53	1.71	0.89 (0.73, 1.10)	0.289
Non-vascular	0.19	0.30	0.63 (0.36, 1.08)	0.094
Unknown Cause	0.15	0.20	0.75 (0.40, 1.41)	0.370

Atrial Fibrillation

	Rivaroxaban	Warfarin		
	Event Rate or N (Rate)	Event Rate or N (Rate)	HR (95% CI)	P-value
Major	3.60	3.45	1.04 (0.90, 1.20)	0.576
≥2 g/dL Hgb drop	2.77	2.26	1.22 (1.03, 1.44)	0.019
Transfusion (> 2 units)	1.65	1.32	1.25 (1.01, 1.55)	0.044
Critical organ bleeding	0.82	1.18	0.69 (0.53, 0.91)	0.007
Bleeding causing death	0.24	0.48	0.50 (0.31, 0.79)	0.003
Intracranial Hemorrhage	55 (0.49)	84 (0.74)	0.67 (0.47, 0.94)	0.019
Intraparenchymal	37 (0.33)	56 (0.49)	0.67 (0.44, 1.02)	0.060
Intraventricular	2 (0.02)	4 (0.04)		
Subdural	14 (0.13)	27 (0.27)	0.53 (0.28, 1.00)	0.051
Subarachnoid	4 (0.04)	1 (0.01)		

Atrial Fibrillation

Outcome	Apixaban (N=9120) Event Rate (%/yr)	Warfarin (N=9081) Event Rate (%/yr)	HR (95% CI)	P Value
Stroke or systemic embolism*	1.27	1.60	0.79 (0.66, 0.95)	0.011
Stroke	1.19	1.51	0.79 (0.65, 0.95)	0.012
Ischemic or uncertain	0.97	1.05	0.92 (0.74, 1.13)	0.42
Hemorrhagic	0.24	0.47	0.51 (0.35, 0.75)	<0.001
Systemic embolism (SE)	0.09	0.10	0.87 (0.44, 1.75)	0.70
All-cause death*	3.52	3.94	0.89 (0.80, 0.998)	0.047
Stroke, SE, or all-cause death	4.49	5.04	0.89 (0.81, 0.98)	0.019
Myocardial infarction	0.53	0.61	0.88 (0.66, 1.17)	0.37

* Part of sequential testing sequence preserving the overall type I error

Atrial Fibrillation

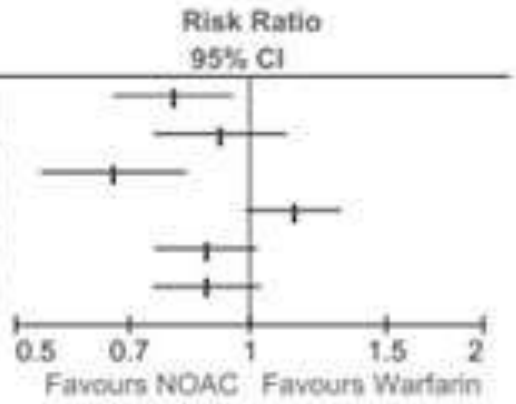
Outcome	Apixaban (N=9088) Event Rate (%/yr)	Warfarin (N=9052) Event Rate (%/yr)	HR (95% CI)	P Value
Primary safety outcome: ISTH major bleeding*	2.13	3.09	0.69 (0.60, 0.80)	<0.001
Intracranial	0.33	0.80	0.42 (0.30, 0.58)	<0.001
Gastrointestinal	0.76	0.86	0.89 (0.70, 1.15)	0.37
Major or clinically relevant non-major bleeding	4.07	6.01	0.68 (0.61, 0.75)	<0.001
GUSTO severe bleeding	0.52	1.13	0.46 (0.35, 0.60)	<0.001
TIMI major bleeding	0.96	1.69	0.57 (0.46, 0.70)	<0.001
Any bleeding	18.1	25.8	0.71 (0.68, 0.75)	<0.001

* Part of sequential testing sequence preserving the overall type

Atrial Fibrillation- DOAC Events Summary

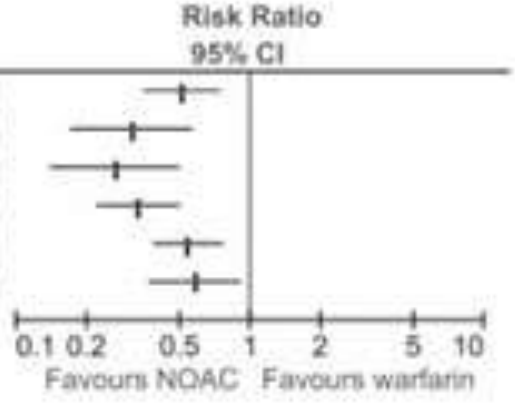
A. Primary Efficacy Outcome

Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	212	9120	265	9081	0.80 [0.67, 0.95]
Dabigatran 110mg bid	182	6015	199	6022	0.92 [0.75, 1.12]
Dabigatran 150mg bid	134	6076	199	6022	0.67 [0.54, 0.83]
Edoxaban 30mg daily	383	7034	337	7036	1.14 [0.99, 1.31]
Edoxaban 60mg daily	296	7035	337	7036	0.88 [0.75, 1.02]
Rivaroxaban 20mg daily	269	7081	306	7090	0.88 [0.75, 1.03]



B. Haemorrhagic stroke

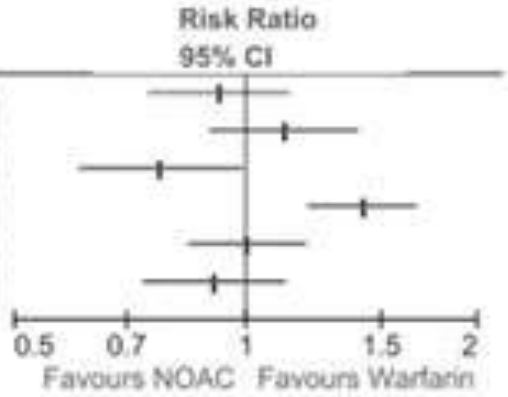
Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	40	9120	78	9081	0.51 [0.35, 0.75]
Dabigatran 110mg bid	14	6015	45	6022	0.31 [0.17, 0.57]
Dabigatran 150mg bid	12	6076	45	6022	0.26 [0.14, 0.50]
Edoxaban 30mg daily	30	7034	90	7036	0.33 [0.22, 0.50]
Edoxaban 60mg daily	49	7035	90	7036	0.54 [0.39, 0.77]
Rivaroxaban 20mg daily	29	7061	50	7082	0.58 [0.37, 0.92]



Atrial Fibrillation- DOAC Events Summary

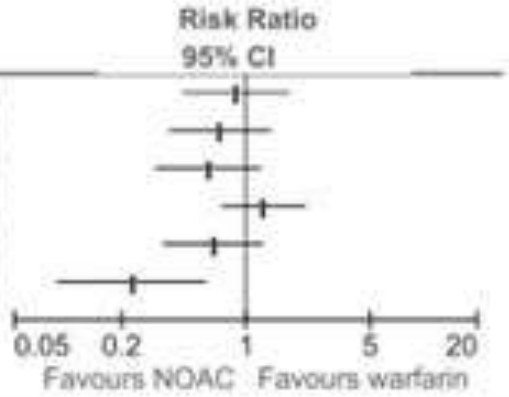
C. Non-haemorrhagic stroke

Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	162	9120	175	9081	0.92 [0.75, 1.14]
Dabigatran 110mg bid	159	6015	142	6022	1.12 [0.90, 1.40]
Dabigatran 150mg bid	111	6076	142	6022	0.77 [0.61, 0.99]
Edoxaban 30mg daily	333	7034	235	7036	1.42 [1.20, 1.67]
Edoxaban 60mg daily	236	7035	235	7036	1.00 [0.84, 1.20]
Rivaroxaban 20mg daily	156	7061	172	7082	0.91 [0.73, 1.13]



D. Systemic Embolism

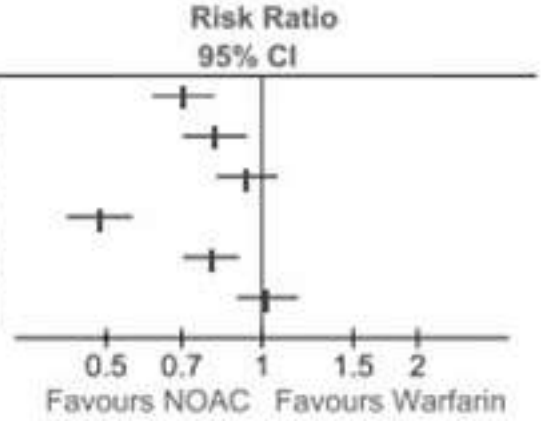
Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	15	9120	17	9081	0.88 [0.44, 1.76]
Dabigatran 110mg bid	15	6015	21	6022	0.72 [0.37, 1.39]
Dabigatran 150mg bid	13	6076	21	6022	0.61 [0.31, 1.22]
Edoxaban 30mg daily	29	7034	23	7036	1.26 [0.73, 2.18]
Edoxaban 60mg daily	15	7035	23	7036	0.65 [0.34, 1.25]
Rivaroxaban 20mg daily	5	7061	22	7082	0.23 [0.09, 0.60]



Atrial Fibrillation- DOAC Events Summary

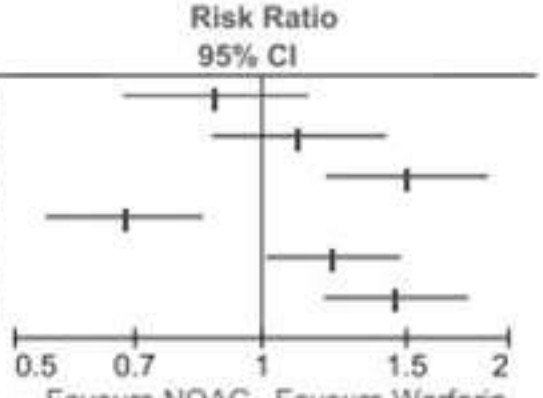
A. Major bleeding

Study or Subgroup	NOAC Events	NOAC Total	Control Events	Control Total	Risk Ratio 95% CI
Apixaban 5mg bid	327	9088	462	9052	0.70 [0.61, 0.81]
Dabigatran 110mg bid	322	6015	397	6022	0.81 [0.70, 0.94]
Dabigatran 150mg bid	375	6076	397	6022	0.94 [0.82, 1.07]
Edoxaban 30mg daily	254	7002	524	7012	0.49 [0.42, 0.56]
Edoxaban 60mg daily	418	7012	524	7012	0.80 [0.70, 0.90]
Rivaroxaban 20mg daily	395	7111	386	7125	1.03 [0.89, 1.18]



B. Major gastrointestinal bleeding

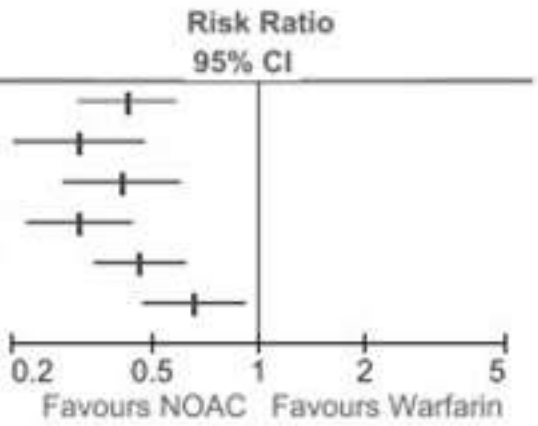
Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	105	9088	119	9052	0.88 [0.68, 1.14]
Dabigatran 110mg bid	133	6015	120	6022	1.11 [0.87, 1.42]
Dabigatran 150mg bid	182	6076	120	6022	1.50 [1.20, 1.89]
Edoxaban 30mg daily	129	7002	190	7012	0.68 [0.55, 0.85]
Edoxaban 60mg daily	232	7012	190	7012	1.22 [1.01, 1.47]
Rivaroxaban 20mg daily	224	7111	154	7125	1.46 [1.19, 1.78]



Atrial Fibrillation- DOAC Events Summary

C. Intracranial bleeding

Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	52	9088	122	9052	0.42 [0.31, 0.59]
Dabigatran 110mg bid	27	6015	87	6022	0.31 [0.20, 0.48]
Dabigatran 150mg bid	36	6076	87	6022	0.41 [0.28, 0.60]
Edoxaban 30mg daily	41	7002	132	7012	0.31 [0.22, 0.44]
Edoxaban 60mg daily	61	7012	132	7012	0.46 [0.34, 0.62]
Rivaroxaban 20mg daily	55	7111	84	7125	0.66 [0.47, 0.92]



Atrial Fibrillation

Gastroenterology 2017;152:1014–1022

Gastrointestinal Safety of Direct Oral Anticoagulants: A Large Population-Based Study

Neena S. Abraham,[1,2,3] Peter A. Noseworthy,[2,4] Xiaoxi Yao,[2] Lindsey R. Sangaralingham,[2] and Nilay D. Shah[2,3,5]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Mayo Clinic, Scottsdale, Arizona; [2]Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Mayo Clinic, Rochester, Minnesota; [3]Division of Health Care Policy and Research, Mayo Clinic, Rochester, Minnesota; [4]Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota; and [5]Optum Labs, Cambridge, Massachusetts

CONCLUSIONS: In a population-based study of patients receiving DOAC agents, we found apixaban had the most favorable GI safety profile and rivaroxaban the least favorable profile. GI bleeding events among patient aged 75 years or older taking DOACs increased with age; the risk was greatest among persons 75 years. Apixaban had the most favorable GI safety profile among all age groups.

Atrial Fibrillation

CURRENT MEDICAL RESEARCH AND OPINION, 2016
VOL. 32, NO. 12, 2047–2053
http://dx.doi.org/10.1080/03007995.2016.1237937
Article FT-0400.R2/1237937

Taylor & Francis
Taylor & Francis Group

BRIEF REPORT

Real-world evidence of stroke prevention in patients with nonvalvular atrial fibrillation in the United States: the REVISIT-US study

Craig I. Coleman[a], Matthias Antz[b], Kevin Bowrin[c], Thomas Evers[d], Edgar P. Simard[e], Hendrik Bonnemeier[f] and Riccardo Cappato[g]

[a]University of Connecticut School of Pharmacy, Storrs, CT, USA; [b]Hospital Oldenburg, Department of Cardiology, Oldenburg, Germany; [c]Bayer Pharma AG, Berlin, Germany; [d]Bayer Pharma AG, Wuppertal, Germany; [e]Aetion Inc., New York, NY, USA; [f]University Medical Center of Schleswig-Holstein, Department of Electrophysiology and Rhythmology, Kiel, Germany; [g]Arrhythmia and Electrophysiology Research Center, Humanitas Clinical and Research Center, Rozzano, MI, Italy

ABSTRACT

Background: Little data exists regarding the effectiveness and safety of rivaroxaban or apixaban versus warfarin in nonvalvular atrial fibrillation (NVAF) patients treated outside of clinical trials.

Methods: This was a retrospective study using MarketScan claims from January 2012 to October 2014. We included adults, newly initiated on rivaroxaban, apixaban or warfarin, with a baseline CHA_2DS_2-VASc score ≥2, ≥2 diagnosis codes for NVAF and ≥180 days of continuous medical and prescription benefits. Patients with a prior stroke, systemic embolism or intracranial hemorrhage (ICH) were excluded. Eligible rivaroxaban or apixaban users were 1:1 propensity-score matched individually to warfarin users. Cox regression was performed to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for rivaroxaban and apixaban versus warfarin for the combined endpoint of ischemic stroke or ICH and each endpoint individually.

Results: Upon matching 11,411 rivaroxaban to 11,411 warfarin users, rivaroxaban was associated with a significant reduction of the combined endpoint of ischemic stroke or ICH versus warfarin (HR = 0.61, 95% CI = 0.45–0.82). ICH was significantly (HR = 0.53, 95% CI = 0.35–0.79) and ischemic stroke nonsignificantly reduced (HR = 0.71, 95% CI = 0.47–1.07) by rivaroxaban versus warfarin. After matching 4083 apixaban and 4083 warfarin users, apixaban was found to nonsignificantly reduce the combined endpoint of ischemic stroke or ICH versus warfarin (HR = 0.63, 95% CI = 0.35–1.12) and to reduce ICH risk (HR = 0.38, 95% CI = 0.17–0.88). Ischemic stroke risk was nonsignificantly increased with apixaban (HR = 1.13, 95% CI = 0.49–2.63) versus warfarin.

Limitations: Sample size and number of combined events observed were relatively small. Residual confounding could not be ruled out.

Conclusions: Rivaroxaban and apixaban were associated with less ICH than warfarin and both are likely associated with reductions in the combined endpoint. Further investigation to validate the numerically higher rate of ischemic stroke with apixaban versus warfarin is required.

ARTICLE HISTORY
Received 10 August 2016
Revised 13 September 2016
Accepted 13 September 2016
Published online 20 September 2016

KEYWORDS
Anticoagulants; Apixaban; Nonvalvular atrial fibrillation; Rivaroxaban; Stroke prevention; Warfarin

Atrial Fibrillation- Aristophanes ACC 2018

COMPARISON OF EFFECTIVENESS, SAFETY, AND THE NET CLINICAL OUTCOME BETWEEN DIFFERENT DIRECT ORAL ANTICOAGULANTS IN 162,707 NON-VALVULAR ATRIAL FIBRILLATION PATIENTS TREATED IN US CLINICAL PRACTICE

Oral Contributions
Room 314 A
Sunday, March 11, 2018, 8:51 a.m.-9:01 a.m.

Session Title: Highlighted Original Research: Arrhythmias and Clinical EP and the Year in Review
Abstract Category: 06. Arrhythmias and Clinical EP: Other
Presentation Number: 900-10

Authors: *Steve Deitelzweig, Allison Keshishian, Xiaoyan Li, Melissa Hamilton, Cristina Masseria, Kiran Gupta, Xuemei Luo, Jack Mardekian, Keith Friend, Anagha Nadkarni, Xianying Pan, Onur Baser, Gregory Y. H. Lip, Bristol-Myers Squibb Company, Lawrenceville, NJ, USA, Pfizer, Inc., New York, NY, USA*

Background: Most observational studies on direct oral anticoagulants (DOACs) used single data sources with limited generalizability. This ARISTOPHANES (Anticoagulants for Reduction In STroke: Observational Pooled analysis on Health outcomes ANd Experience of patientS) study aimed to use multiple data sources to compare stroke/systemic embolism (S/SE), major bleeding (MB), and net clinical outcome (composite of S/SE and MB) among a large number of non-valvular atrial fibrillation (NVAF) patients on different DOACs.

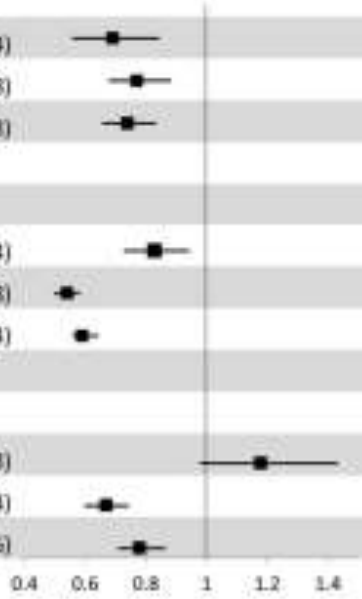
Methods: A retrospective observational study of NVAF patients initiating apixaban, dabigatran, or rivaroxaban from 01/01/2013-09/30/2015 was conducted pooling CMS Medicare data and 4 US commercial claims databases - which covers >180 million beneficiaries annually (~56% of the US population). After 1:1 DOAC-DOAC propensity score matching in each database, the resulting patient records were pooled. Cox models were used to evaluate the risk of S/SE, MB, and the net clinical outcome (identified using inpatient claims) across DOACs within 1 year of therapy initiation.

Results: The study included 162,707 patients followed for a mean of 6 months. Results are shown in Figure 1.

Conclusion: In this largest observational study to date on DOAC-DOAC comparisons, apixaban was associated with a lower risk of S/SE, MB, and net clinical outcome compared to dabigatran and rivaroxaban; dabigatran was associated with a lower risk of MB and net clinical outcome compared to rivaroxaban.

Atrial Fibrillation- Aristophanes ACC 2018

	Comparator No. of events (incidence per 100 person-years)	Reference No. of events (incidence per 100 person-years)	Hazard Ratio (95% CI)	P-value
Apixaban vs. Dabigatran (ref.)*				
N= 27,096	**N= 27,096**			
S/SE	153 (1.21)	231 (1.73)	0.69 (0.56-0.84)	<0.001
MB	386 (3.05)	519 (3.90)	0.77 (0.68-0.88)	<0.001
Net Clinical Outcome	507 (4.02)	714 (5.38)	0.74 (0.66-0.83)	<0.001
Apixaban vs. Rivaroxaban (ref.)**				
N= 62,619	**N= 62,619**			
S/SE	412 (1.41)	531 (1.66)	0.83 (0.73-0.94)	0.004
MB	1,062 (3.64)	2,077 (6.54)	0.54 (0.50-0.58)	<0.001
Net Clinical Outcome	1,370 (4.70)	2,439 (7.71)	0.59 (0.56-0.64)	<0.001
Dabigatran vs. Rivaroxaban (ref.)***				
N= 27,538	**N= 27,538**			
S/SE	232 (1.72)	202 (1.43)	1.18 (0.98-1.43)	0.080
MB	523 (3.88)	808 (5.76)	0.67 (0.60-0.74)	<0.001
Net Clinical Outcome	719 (5.35)	943 (6.74)	0.78 (0.71-0.86)	<0.001



* Mean age: 72 years, mean CHA_2DS_2-VASc score: 3.3, mean HAS-BLED score: 2.7;
** Mean age: 73 years, mean CHA_2DS_2-VASc score: 3.5, mean HAS-BLED score: 2.8;
*** Mean age: 71 years, mean CHA_2DS_2-VASc score: 3.3, mean HAS-BLED score: 2.6.
Note: Outcomes for altogether 162,707 unique patients were evaluated in the analysis, including 62,835 apixaban patients, 27,552 dabigatran patients, and 72,320 rivaroxaban patients. For each DOAC, two different subgroups were separately evaluated in two different matched cohorts.

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**A**	**Among patients treated with warfarin, the international normalized ratio (INR) should be determined at least weekly during initiation of anticoagulant therapy and at least monthly when anticoagulation (INR in range) is stable.** **MODIFIED**: **"**Antithrombotic" was changed to "anticoagulant."

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**B**	**For patients with AF who have mechanical heart valves, warfarin is recommended.** **MODIFIED**: New information is included in the supportive text.

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**B**	**Selection of anticoagulant therapy should be based on the risk of thromboembolism, irrespective of whether the AF pattern is paroxysmal, persistent, or permanent.** **MODIFIED**: "Antithrombotic" was changed to "anticoagulant."

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**B-NR**	**Renal function and hepatic function should be evaluated before initiation of a NOAC and should be reevaluated at least annually.** **MODIFIED**: Evaluation of hepatic function was added. LOE was updated from B to B-NR. New evidence was added. (Section 4.1. in the 2014 AF Guideline)

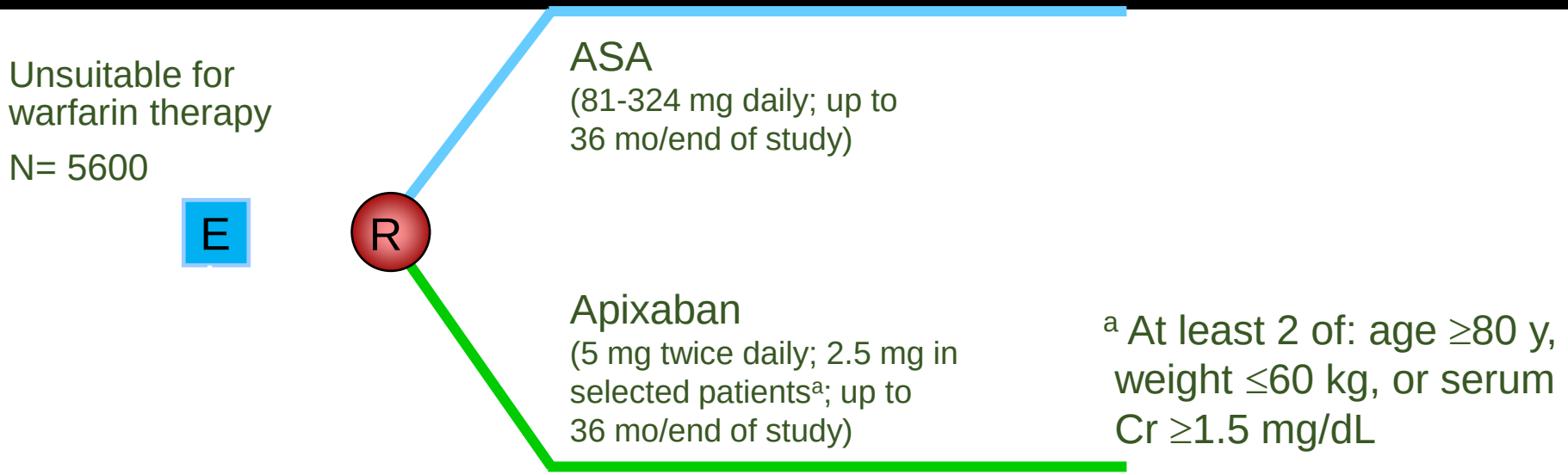
This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**C**	**In patients with AF, anticoagulant therapy should be individualized on the basis of shared decision-making after discussion of the absolute risks and relative risks of stroke and bleeding, as well as the patient's values and preferences.** **MODIFIED**: "Antithrombotic" was changed to "anticoagulant."

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation



- Is apixaban more effective than ASA in preventing stroke and systemic embolism in moderate to high-risk (stroke; at least 1 risk factor) AF patients?
- 1^0 efficacy end point: confirmed ischemic or hemorrhagic stroke or systemic embolism
- 2^0 study end points: as above, including MI or vascular death
- 1^0 safety end point: major bleeding
- Study period: until 226 primary outcome events have been observed
- In June 2010, BMS-Pfizer announced that the study had been stopped early because a predefined interim analysis revealed clear evidence of a clinically important reduction in stroke and systemic embolism. Results presented at ESC 2010, Stockholm, Sweden

Atrial Fibrillation

- Apixaban significantly reduced risk of stroke or systemic embolic events by 54%
- The trial was stopped early when the data and safety monitoring board performed a prespecified interim analysis showing significant benefit with apixaban

---

Primary and secondary end points

Outcomes	Apixaban (n=2809), %	Aspirin (n=2791), %	Relative risk (95% CI)
Primary end point	1.6	3.6	0.46 (0.33–0.64)
Stroke, embolic event, MI, or vascular death	4.1	6.2	0.66 (0.53–0.83)
- MI	0.7	0.8	0.85 (0.48–1.50)
- Vascular death	2.5	2.9	0.86 (0.64–1.16)
CV hospitalization	11.8	14.9	0.79 (0.68–0.91)
Total death	3.4	4.4	0.79 (0.62–1.02)

Atrial Fibrillation

- The risk of major bleeding increased by a statistically nonsignificant 14%
- There was no increased risk of fatal or intracranial hemorrhage, two particular concerns with AF patients who receive anticoagulation therapy

Bleeding events

Outcomes	Apixaban (n=2809), %	Aspirin (n=2791), %	Relative risk (95% CI)
Major bleeding	1.4	1.2	1.14 (0.74–1.75)
Clinical relevant nonmajor bleeding	3.0	2.6	1.18 (0.88–1.58)
Minor bleeding	5.2	4.1	1.27 (1.01–1.61)
Fatal bleeding	0.1	0.1	0.84 (0.26–2.75)
Intracranial	0.4	0.3	1.09 (0.50–2.39)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**C**	**For patients with atrial flutter, anticoagulant therapy is recommended according to the same risk profile used for AF.** **MODIFIED**: "Antithrombotic" was changed to "anticoagulant."

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**C**	**Reevaluation of the need for and choice of anticoagulant therapy at periodic intervals is recommended to reassess stroke and bleeding risks.** **MODIFIED**: "Antithrombotic" was changed to "anticoagulant."

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**C-EO**	**For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) who are unable to maintain a therapeutic INR level with warfarin, use of a NOAC is recommended.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and this recommendation has been changed in response to the approval of edoxaban. (Section 4.1. in the 2014 AF Guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
IIb	**B-NR**	**For patients with AF who have a CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women and who have end-stage chronic kidney disease (CKD; creatinine clearance [CrCl] <15 mL/min) or are on dialysis, it might be reasonable to prescribe warfarin (INR 2.0 to 3.0) or apixaban for oral anticoagulation.** **MODIFIED**: New evidence has been added. LOE was updated from B to B-NR. (Section 4.1. in the 2014 AF Guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation and ESRD

Circulation. 2018 Oct 9;138(15):1519-1529. doi: 10.1161/CIRCULATIONAHA.118.035418.

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

Siontis KC[1,2], Zhang X[3], Eckard A[4], Bhave N[1], Schaubel DE[5], He K[4], Tilea A[3], Stack AG[6], Balkrishnan R[7], Yao X[8,9], Noseworthy PA[8,10], Shah ND[8,9], Saran R[3,4], Nallamothu BK[1,11].

Author information

Erratum in

Correction to: Outcomes Associated with Apixaban Use in End-Stage Kidney Disease Patients with Atrial Fibrillation in the United States. [Circulation. 2018]

Correction to: Genetic Lineage Tracing of Sca-1^{+} Cells Reveals Endothelial but Not Myogenic Contribution to the Murine Heart. [Circulation. 2018]

Abstract

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 dabigatran and rivaroxaban, but apixaban has not been evaluated despite current labeling supporting its use in this population. The goal of this study was to determine patterns of apixaban use and its associated outcomes in dialysis-dependent patients with ESKD and AF.

METHODS: We performed a retrospective cohort study of Medicare beneficiaries included in the United States Renal Data System (October 2010 to December 2015). Eligible patients were those with ESKD and AF undergoing dialysis who initiated treatment with an oral anticoagulant. Because of the small number of dabigatran and rivaroxaban users, outcomes were only assessed in patients treated with apixaban or warfarin. Apixaban and warfarin patients were matched (1:3) based on prognostic score. Differences between groups in survival free of stroke or systemic embolism, major bleeding, gastrointestinal bleeding, intracranial bleeding, and death were assessed using Kaplan-Meier analyses. Hazard ratios (HRs) and 95% CIs were derived from Cox regression analyses.

RESULTS: The study population consisted of 25 523 patients (45.7% women; 68.2±11.9 years of age), including 2351 patients on apixaban and 23 172 patients on warfarin. An annual increase in apixaban prescriptions was observed after its marketing approval at the end of 2012, such that 26.6% of new anticoagulant prescriptions in 2015 were for apixaban. In matched cohorts, there was no difference in the risks of stroke/systemic embolism between apixaban and warfarin (HR, 0.88; 95% CI, 0.69-1.12; P=0.29), but apixaban was associated with a significantly lower risk of major bleeding (HR, 0.72; 95% CI, 0.59-0.87; P<0.001). In sensitivity analyses, standard-dose apixaban (5 mg twice a day; n=1034) was associated with significantly lower risks of stroke/systemic embolism and death as compared with either reduced-dose apixaban (2.5 mg twice a day; n=1317; HR, 0.61; 95% CI, 0.37-0.98; P=0.04 for stroke/systemic embolism; HR, 0.64; 95% CI, 0.45-0.92; P=0.01 for death) or warfarin (HR, 0.64; 95% CI, 0.42-0.97; P=0.04 for stroke/systemic embolism; HR, 0.63; 95% CI, 0.46-0.85; P=0.003 for death).

CONCLUSIONS: Among patients with ESKD and AF on dialysis, apixaban use may be associated with a lower risk of major bleeding compared with warfarin, with a standard 5 mg twice a day dose also associated with reductions in thromboembolic and mortality risk.

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
IIb	**B-R**	**For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and moderate-to-severe CKD (serum creatinine ≥1.5 mg/dL [apixaban], CrCl 15 to 30 mL/min [dabigatran], CrCl ≤50 mL/min [rivaroxaban], or CrCl 15 to 50 mL/min [edoxaban]) with an elevated CHA_2DS_2-VASc score, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (e.g., dabigatran, rivaroxaban, apixaban, or edoxaban).** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and this recommendation has been changed in response to the approval of edoxaban. LOE was updated from C to B-R. (Section 4.1. in the 2014 AF Guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
III: No Benefit	**C-EO**	**In patients with AF and end-stage CKD or on dialysis, the direct thrombin inhibitor dabigatran or the factor Xa inhibitors rivaroxaban or edoxaban are not recommended because of the lack of evidence from clinical trials that benefit exceeds risk.** **MODIFIED**: New data have been included. Edoxaban received FDA approval and has been added to the recommendation. LOE was updated from C to C-EO. (Section 4.1. in the 2014 AF Guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
III: Harm	**B-R**	**The direct thrombin inhibitor dabigatran should not be used in patients with AF and a mechanical heart valve.** **MODIFIED**: Evidence was added. LOE was updated from B to B-R. Other NOACs are addressed in the supportive text. (Section 4.1. in the 2014 AF Guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation

ORIGINAL ARTICLE

Dabigatran versus Warfarin in Patients with Mechanical Heart Valves

John W. Eikelboom, M.D., Stuart J. Connolly, M.D., Martina Brueckmann, M.D., Christopher B. Granger, M.D., Arie P. Kappetein, M.D., Ph.D., Michael J. Mack, M.D., Jon Blatchford, C.Stat., Kevin Devenny, B.Sc., Jeffrey Friedman, M.D., Kelly Guiver, M.Sc., Ruth Harper, Ph.D., Yasser Khder, M.D., et al., for the RE-ALIGN Investigators*

September 26, 2013
N Engl J Med 2013; 369:1206-1214
DOI: 10.1056/NEJMoa1300615

25 References 529 Citing Articles

Abstract

BACKGROUND

Dabigatran is an oral direct thrombin inhibitor that has been shown to be an effective alternative to warfarin in patients with atrial fibrillation. We evaluated the use of dabigatran in patients with mechanical heart valves.

CONCLUSIONS

The use of dabigatran in patients with mechanical heart valves was associated with increased rates of thromboembolic and bleeding complications, as compared with warfarin, thus showing no benefit and an excess risk. (Funded by Boehringer Ingelheim; ClinicalTrials.gov numbers, NCT01452347 and NCT01505881.)

Related Articles

EDITORIAL SEP 26, 2013

Dabigatran and Mechanical Heart Valves — Not as Easy as We Hoped

E.M. Hylek

Interruption and Bridging Anticoagulation

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

2019 Focused Update on Atrial Fibrillation

Recommendations for Interruption and Bridging Anticoagulation		
COR	**LOE**	**Recommendations**
I	C	**Bridging therapy with unfractionated heparin or low-molecular-weight heparin is recommended for patients with AF and a mechanical heart valve undergoing procedures that require interruption of warfarin. Decisions on bridging therapy should balance the risks of stroke and bleeding.**
I	B-R	**For patients with AF without mechanical heart valves who require interruption of warfarin for procedures, decisions about bridging therapy (unfractionated heparin or low-molecular-weight heparin) should balance the risks of stroke and bleeding and the duration of time a patient will not be anticoagulated.** **MODIFIED**: LOE was updated from C to B-R because of new evidence. (Section 4.1. in the 2014 AF Guideline)

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation**. Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation and Bridging

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation

James D. Douketis, M.D., Alex C. Spyropoulos, M.D., Scott Kaatz, D.O., Richard C. Becker, M.D., Joseph A. Caprini, M.D., Andrew S. Dunn, M.D., David A. Garcia, M.D., Alan Jacobson, M.D., Amir K. Jaffer, M.D., M.B.A., David F. Kong, M.D., Sam Schulman, M.D., Ph.D., Alexander G.G. Turpie, M.B., Vic Hasselblad, Ph.D., and Thomas L. Ortel, M.D., Ph.D., for the BRIDGE Investigators*

ABSTRACT

BACKGROUND

It is uncertain whether bridging anticoagulation is necessary for patients with atrial fibrillation who need an interruption in warfarin treatment for an elective operation or other elective invasive procedure. We hypothesized that forgoing bridging anticoagulation would be noninferior to bridging with low-molecular-weight heparin for the prevention of perioperative arterial thromboembolism and would be superior to bridging with respect to major bleeding.

METHODS

We performed a randomized, double-blind, placebo-controlled trial in which, after perioperative interruption of warfarin therapy, patients were randomly assigned to receive bridging anticoagulation therapy with low-molecular-weight heparin (100 IU of dalteparin per kilogram of body weight) or matching placebo administered subcutaneously twice daily, from 3 days before the procedure until 24 hours before the procedure and then for 5 to 10 days after the procedure. Warfarin treatment was stopped 5 days before the procedure and was resumed within 24 hours after the procedure. Follow-up of patients continued for 30 days after the procedure. The primary outcomes were arterial thromboembolism (stroke, systemic embolism, or transient ischemic attack) and major bleeding.

RESULTS

In total, 1884 patients were enrolled, with 950 assigned to receive no bridging therapy and 934 assigned to receive bridging therapy. The incidence of arterial thromboembolism was 0.4% in the no-bridging group and 0.3% in the bridging group (risk difference, 0.1 percentage points; 95% confidence interval [CI], −0.6 to 0.8, $P=0.01$ for noninferiority). The incidence of major bleeding was 1.3% in the no-bridging group and 3.2% in the bridging group (relative risk, 0.41; 95% CI, 0.20 to 0.78; $P=0.005$ for superiority).

CONCLUSIONS

In patients with atrial fibrillation who had warfarin treatment interrupted for an elective operation or other elective invasive procedure, forgoing bridging anticoagulation was noninferior to perioperative bridging with low-molecular-weight heparin for the prevention of arterial thromboembolism and decreased the risk of major bleeding. (Funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health; BRIDGE ClinicalTrials.gov number, NCT00786474.)

From St. Joseph's Healthcare Hamilton (J.D.D.) and the Department of Medicine (J.D.D.) and Hamilton Health Sciences Center (S.S., A.G.G.T.), McMaster University, Hamilton, ON, Canada; Hofstra North Shore–Long Island Jewish School of Medicine, Manhasset (A.C.S.), and Mount Sinai Medical Center, New York (A.S.D.) — both in New York; Hurley Medical Center, Flint, MI (S.K.); University of Cincinnati College of Medicine, Cincinnati (R.C.B.); NorthShore University HealthSystem, Evanston (J.A.C.), and Rush University Medical Center, Chicago (A.K.J.) — both in Illinois; University of Washington Medical Center, Seattle (D.A.G.); Veterans Affairs Loma Linda Healthcare System, Loma Linda, CA (A.J.); and Duke Clinical Research Institute (J.I.W., V.H.) and Department of Medicine (T.L.O.), Duke University Medical Center, Durham, NC. Address reprint requests to Dr. Ortel at Duke University Medical Center, Box 3422, Durham, NC, 27710, or at thomas.ortel@duke.edu.

*A complete list of investigators in the Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery (BRIDGE) study is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on June 22, 2015, at NEJM.org.

N Engl J Med 2015;373:823-33.
DOI: 10.1056/NEJMoa1501035

https://www.nejm.org/doi/pdf/10.1056/NEJMoa1501035

Atrial Fibrillation- Current Practice

In high-risk patients (particularly those with mechanical valves, prior stroke, TIA, or systemic embolism), or when a series of procedures requires interruption of oral anticoagulant therapy for longer than a 10 day period, low-molecular-weight heparin may be administered subcutaneously.

Atrial Fibrillation

Temporary interruption of NOAC prior to endoscopic procedure		
Drug (Creatinine Clearance)	**Last dose prior to low–risk endoscopic procedure ***	**Last dose prior to high–risk endoscopic procedure ****
Dabigatran (>50 mL/min)	**1 day**	**2 days**
Dabigatran (31- 50 mL/min)	**2 days**	**4 days**
Dabigatran (<30 mL/min)	**4 days**	**6 days**
Rivaroxaban/Apixaban/ Edoxaban (>50 mL/min)	**1 days**	**2 days**
Rivaroxaban/Apixaban/ Edoxaban (31 to 50 mL/min)	**1-2 days**	**3-4 days**
Rivaroxaban/Apixaban/ Edoxaban (< 30 mL/min)	**2 days**	**4 days**

2019 Focused Update on Atrial Fibrillation

Recommendations for Interruption and Bridging Anticoagulation		
COR	**LOE**	**Recommendations**
I	**B-NR**	**Idarucizumab is recommended for the reversal of dabigatran in the event of life-threatening bleeding or an urgent procedure.** **NEW**: New evidence has been published about idarucizumab to support LOE B-NR.
IIa	**B-NR**	**Andexanet alfa can be useful for the reversal of rivaroxaban and apixaban in the event of life-threatening or uncontrolled bleeding.** **NEW**: New evidence has been published about andexanet alfa to support LOE B-NR.

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation

- Reversal Agents

REVERSE-AD: Trial Design

300 patients total

- 90 patients analyzed for this cohort snapshot

Groups

- A (n = 51)
  - Overt, uncontrollable, or life-threatening bleeding
- B (n = 39)
  - Emergent procedure or surgery required within 8 hours

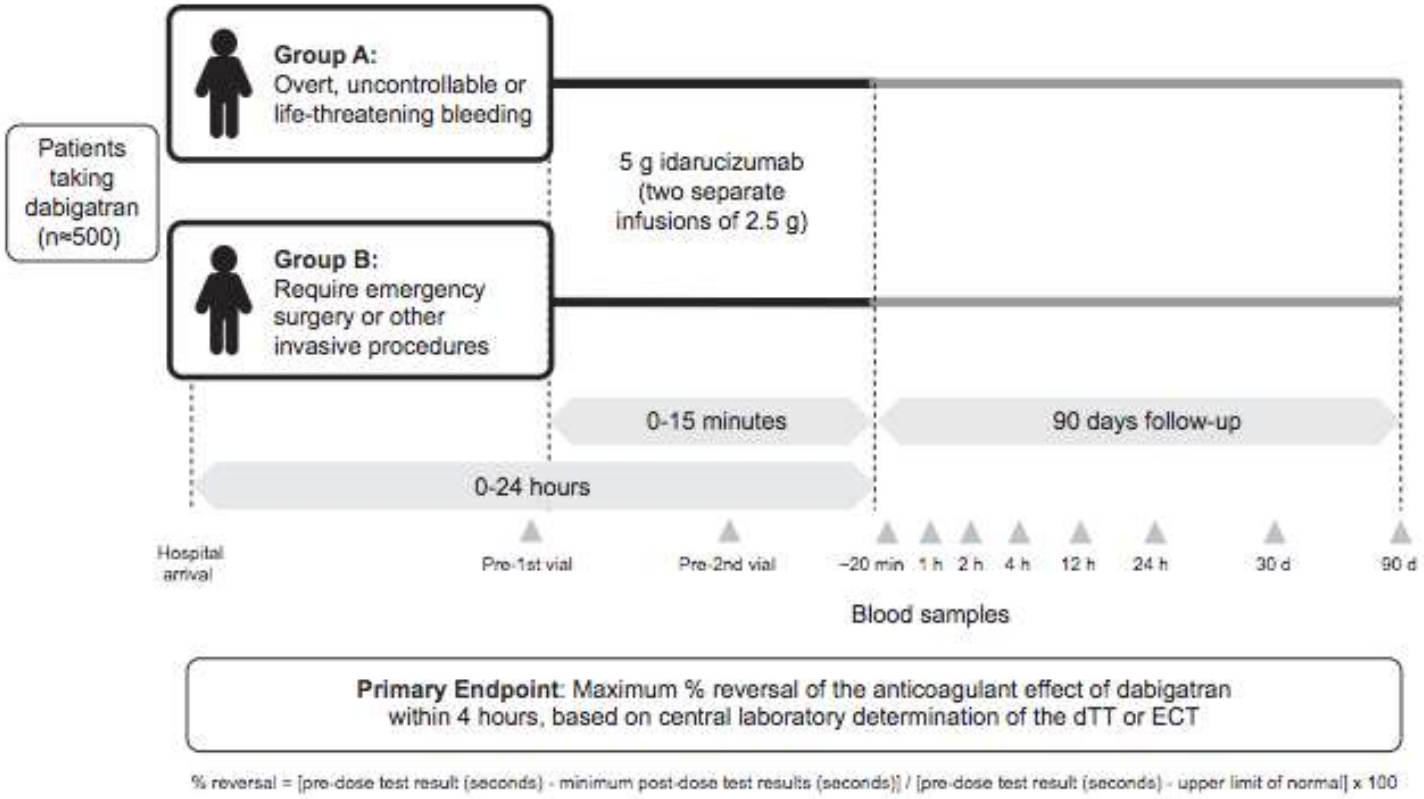
Idarucizumab

- Administered as 2- 2.5g boluses (5g total dose, 50 mL each)
- Boluses administered within 15 minutes of one another

Demonstrate the <u>efficacy</u> and <u>safety</u> of *idarucizumab/ PRAXBIND* for the reversal of the anticoagulant effects of dabigatran in patients who presented with **serious bleeding** or who **require urgent surgery or intervention**

N Engl J Med, 2015, 373: 511-520

REVERSE-AD: Trial Design



N Engl J Med, 2015, 373: 511-520

REVERSE-AD: Author's Conclusions

Idarucizumab is safe and effective for reversing the anticoagulant effects of dabigatran for patients presenting with overt, uncontrollable, life-threatening bleeding or needing urgent surgery or procedure within 8 hours

Atrial Fibrillation Reversal Agents

Factor Xa (FXa) inhibitors reduce thrombotic events, but can precipitate major bleeding

- >100,000 bleeding hospitalizations per year in the US
- Fatality rate of 15-20%

Andexanet alfa was developed as a specific reversal agent for all direct and indirect FXa inhibitors

It rapidly and safely reversed anti-FXa activity in healthy volunteers

Atrial Fibrillation Reversal Agents

As Presented at the ACC Scientific Sessions, 12 March 2018

Andexanet alfa in Factor Xa Inhibitor-Associated Acute Major Bleeding

- Stuart J. Connolly, M.D., Truman J. Milling, Jr., M.D., John W. Eikelboom, M.D., C. Michael Gibson, M.D., John T. Curnutte, M.D., Ph.D., Michele D. Bronson, Ph.D., Patrick Yue, M.D., Genmin Lu, Ph.D., Pamela B. Conley, Ph.D., Peter Verhamme, M.D., Ph.D., Jeannot Schmidt, M.D., Saskia Middeldorp, M.D., Alexander T. Cohen, M.D., Jan Beyer-Westendorf, M.D., Pierre Albaladejo, M.D., Jose Lopez-Sendon, M.D., Andrew Demchuk, M.D., Shelly Goodman, B.S.N., Janet Leeds, Ph.D., Deborah M. Siegal, M.D., Elena Zotova, Ph.D., Brandi Meeks, M.Sc., Juliet Nakamya, Ph.D., Balakumar Swaminathan, M.Sc., Mark Crowther, M.D.
- on behalf of the ANNEXA-4 investigators

PORTOLA PHARMACEUTICALS

McMaster University

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Reversal Agents Dose Selection

Acute major bleeding ≤ 18 hours of last dose of apixaban, edoxaban, rivaroxaban, or enoxaparin

Andexanet IV bolus and 2 hour infusion

Pts on apixaban or >7 h from last rivaroxaban dose	Pts on enoxaparin, edoxaban or ≤7 h from last rivaroxaban dose
Bolus 400 mg + Infusion 480 mg @ 4 mg/min	**Bolus 800 mg + Infusion 960 mg @ 8 mg/min**

Atrial Fibrillation Reversal Agents

Effective Hemostasis at 12 hours Post Andexanet

Number of Major Bleeds Adjudicated	Number of Patients who Achieved Excellent or Good Hemostasis	Percent of Patients who Achieved Excellent or Good Hemostasis	95% Confidence Interval
132	109	83%	76% - 89%

Nonpharmacological Stroke Prevention

2019 Focused Update on Atrial Fibrillation

Recommendation for Percutaneous Approaches to Occlude the LAA		
COR	**LOE**	**Recommendation**
IIb	**B-NR**	**Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation.** **NEW**: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

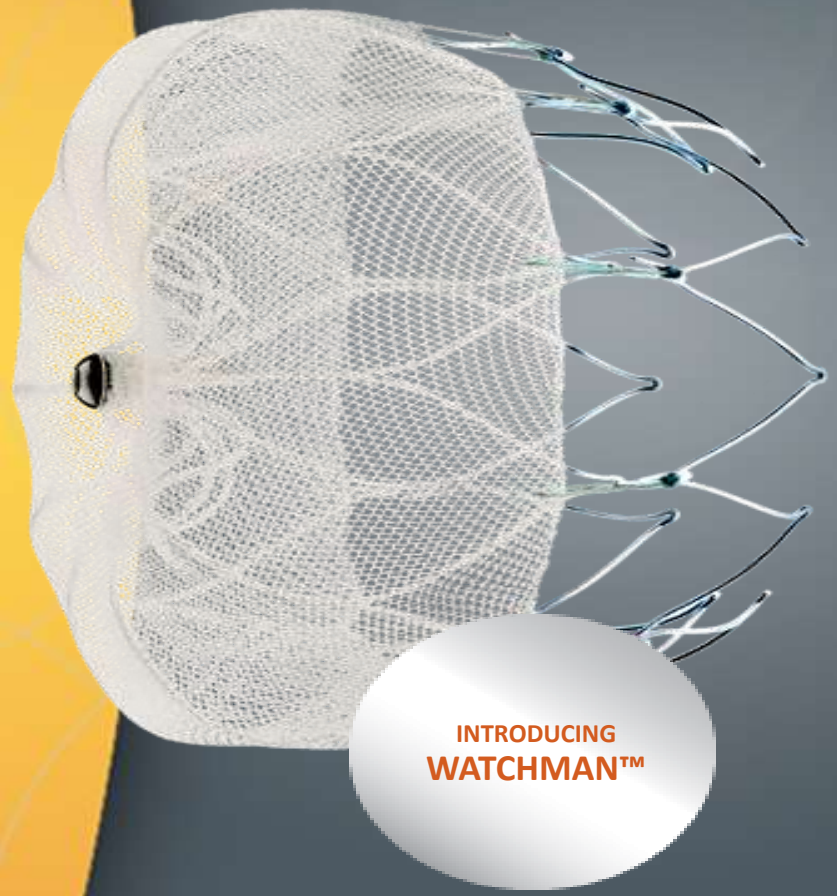
Introducing the WATCHMAN™ LAAC Device

Boston Scientific

A **first-of-its-kind, proven alternative** to long-term warfarin therapy for stroke risk reduction in patients with non-valvular AF

Most studied LAAC therapy, only one proven with long-term data from randomized trials or multi-center registries

Comparable stroke risk reduction, **and statistically superior reductions in hemorrhagic stroke, disabling stroke and cardiovascular death** compared to warfarin over long-term follow-up[1,2]



1. Reddy, V et al. JAMA 2014; Vol. 312, No. 19.
2. Reddy, V et al. Watchman I: First Report of the 5-Year PROTECT-AF and Extended PREVAIL Results. TCT 2014.
3. Boston Scientific WATCHMAN™ Left Atrial Appendage Closure Device. Advancing Science for Life ppt presentation SH230-609-AD June 2015

WATCHMAN Therapy
Indications for

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

The WATCHMAN™ Device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

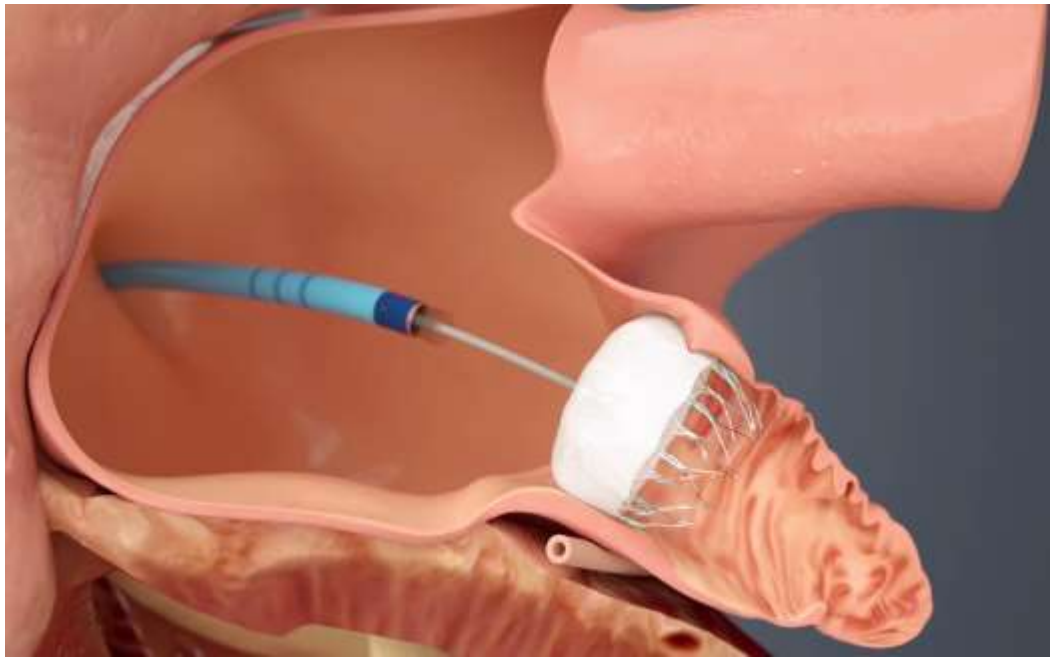
- Are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores and are recommended for anticoagulation therapy;
- Are deemed by their physicians to be suitable for warfarin; and
- Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

WATCHMAN™ Left Atrial Appendage Closure (LAAC) Device Procedure

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

- One-time implant that does not need to be replaced
- Performed in a cardiac cath lab/EP suite, does not need hybrid OR
- Performed by a Heart Team
  - IC/EP or IC&EP, TEE, General Anesthesia, Surgical Back- up, WATCHMAN Clinical Specialist
- Transfemoral Access: Catheter advanced to the LAA via the femoral vein
  (Does not require open heart surgery)

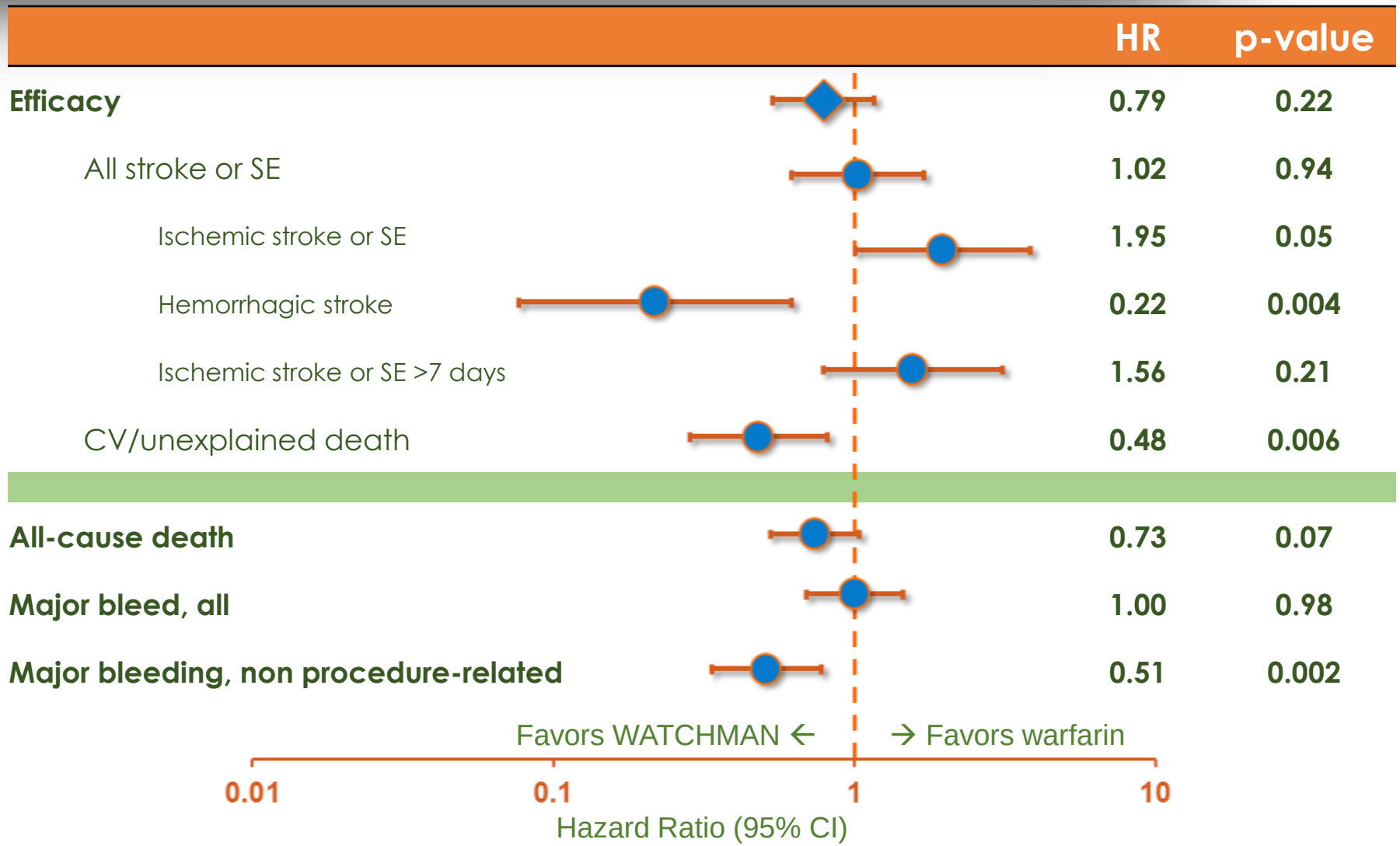
- General anesthesia*
- 1 hour procedure*
- 1-2 day hospital stay*



* Typical to patient treatment in U.S. clinical trials

Meta-Analysis Shows Comparable Primary Efficacy Results to Warfarin

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE



Source: Holmes DR, et al. Holmes, DR et al. *JACC* 2015; In Press. Combined data set of all PROTECT AF and PREVAIL WATCHMAN patients versus chronic warfarin patients

AF Catheter Ablation to Maintain Sinus Rhythm

2019 Focused Update on Atrial Fibrillation

Recommendation for Catheter Ablation in HF		
COR	**LOE**	**Recommendation**
IIb	**B-R**	**AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF.** **NEW**: New evidence, including data on improved mortality rate, has been published for AF catheter ablation compared with medical therapy in patients with HF.

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Specific Patient Groups and AF

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

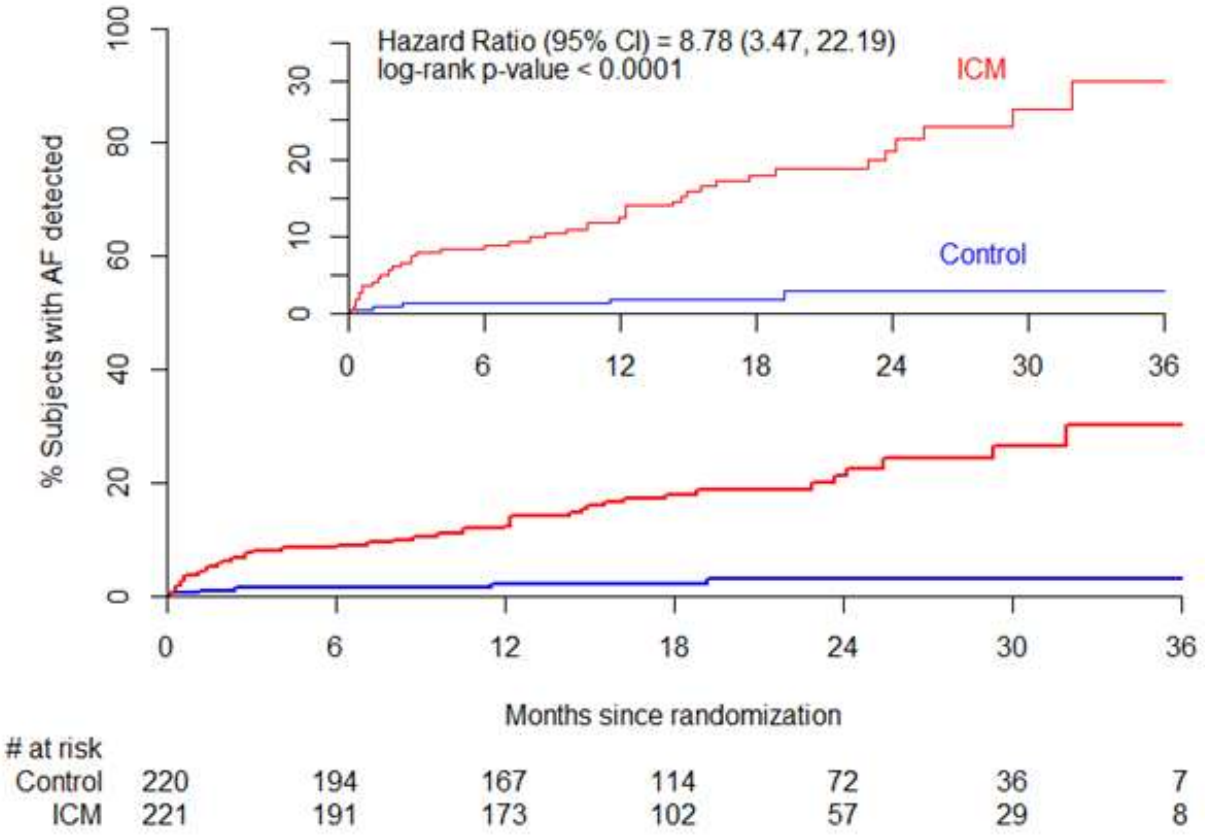
2019 Focused Update on Atrial Fibrillation

Recommendations for Device Detection of AF and Atrial Flutter		
COR	**LOE**	**Recommendations**
I	B-NR	In patients with cardiac implantable electronic devices (pacemakers or implanted cardioverter-defibrillators), the presence of recorded atrial high-rate episodes (AHREs) should prompt further evaluation to document clinically relevant AF to guide treatment decisions.
IIa	B-R	In patients with cryptogenic stroke (i.e., stroke of unknown cause) in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize detection of silent AF.

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

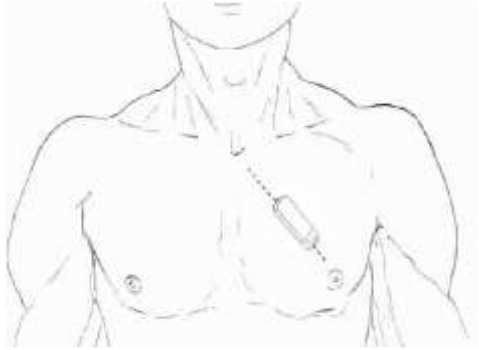
Atrial Fibrillation Detection at 3 years

Rate of detection in ICM arm was 30.0% vs 3.0% in control



CRYptogenic STroke and underlying AtriaL Fibrillation (CRYSTAL AF), *Richard Bernstein, MD, Ph.D., et al.* NEJM June 26, 2014

Comparison of Monitoring Strategies



Continuous Monitoring Arm: Implantation of REVEAL® XT

Minimally invasive outpatient procedure

Local anesthetic and no leads or fluoroscopy

15-30 minute procedure

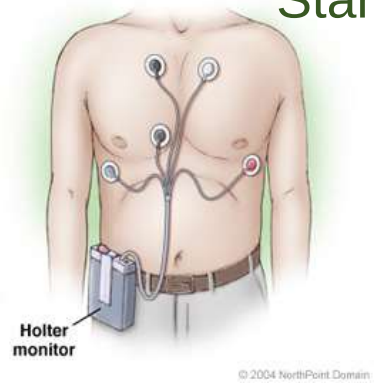
Device can be followed remotely

MRI conditional

3 year device longevity

Automatic AF detection algorithm

Standard Monitoring Arm



Cardiac monitoring performed according to local standards, after mandated testing completed

Symptoms consistent with AF were evaluated by study physicians

2019 Focused Update on Atrial Fibrillation

Recommendation for Weight Loss in Patients with AF		
COR	**LOE**	**Recommendation**
I	**B-R**	**For overweight and obese patients with AF, weight loss, combined with risk factor modification, is recommended.** **NEW**: New data demonstrate the beneficial effects of weight loss and risk factor modification on controlling AF.

This slide set is adapted from the **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation.** Published on January 28, 2019, available at: *Journal of the American College of Cardiology* [(insert full link)] and *Circulation* [(insert full link)] The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

Atrial Fibrillation

Use of the Direct Oral Anticoagulants in Obese Patients

Atrial Fibrillation

VIA MEDICA

REVIEW ARTICLE

Cardiology Journal
2016, Vol. 23, No. 1, 12–16
DOI: 10.5603/CJ.a2015.0054

ISSN 1897–5593

The use of anticoagulants in morbidly obese patients

Justyna Domienik-Karłowicz, Piotr Pruszczyk

Department of Internal Medicine and Cardiology with the Center for Diagnosis and Treatment of Venous Thromboembolism, Medical University of Warsaw, Poland

Abstract

Due to its constantly growing incidence, obesity is an increasingly serious social and medical problem. Available data on the use of novel oral anticoagulants in morbidly obese and obese patients are very limited. However, we tried to summarize the available knowledge on the use of anticoagulants in this subpopulation of patients in everyday clinical practice. Studies on the clinical use of anticoagulants provide a poor basis for any adjustment of doses in obese patients as compared to patients with normal body weight. In our opinion, further studies are required in this particular population. (Cardiol J 2016; 23, 1: 12–16)

Accessing Fall Risk in Patients with AF

Atrial Fibrillation

ORIGINAL INVESTIGATION

Choosing Antithrombotic Therapy for Elderly Patients With Atrial Fibrillation Who Are at Risk for Falls

Malcolm Man-Son-Hing, MD, MSc, FRCPC; Graham Nichol, MD, MPH, FRCPC; Anita Lau; Andreas Laupacis, MD, MSc, FRCPC

Objective: To determine whether the risk of falling (with a possible increased chance of subdural hematoma) should influence the choice of antithrombotic therapy in elderly patients with atrial fibrillation.

Design: A Markov decision analytic model was used to determine the preferred treatment strategy (no antithrombotic therapy, long-term aspirin use, or long-term warfarin use) for patients with atrial fibrillation who are 65 years of age and older, are at risk for falling, and have no other contraindications to antithrombotic therapy. Input data were obtained by systematic review of MEDLINE. Outcomes were expressed as quality-adjusted life-years.

Results: For patients with average risks of stroke and falling, warfarin therapy was associated with 12.90 quality-adjusted life-years per patient; aspirin therapy, 11.17 quality-adjusted life-years; and no antithrombotic therapy, 10.15 quality-adjusted life-years. Sensitivity analysis demonstrated that, regardless of the patients' age or baseline risk of stroke, the risk of falling was not an important factor in determining their optimal antithrombotic therapy.

Conclusions: For elderly patients with atrial fibrillation, the choice of optimal therapy to prevent stroke depends on many clinical factors, especially their baseline risk of stroke. However, patients' propensity to fall is not an important factor in this decision.

Arch Intern Med. 1999;159:677-685

Atrial Fibrillation

Choosing Antithrombotic Therapy for Elderly Patients with AF Who are at Risk for Falls

- Persons taking Warfarin must fall about **295 times in 1 year** for warfarin to not be the optimal therapy

- Since approximately 1 in 10 falls cause major injury, including fractures, persons who fall are much more likely to suffer other serious morbidity before developing brain hemorrhage

(Arch Intern Med. 1999; 159, 677-685)

Atrial Fibrillation

Validation of a Modified CHA_2DS_2-VASc Score for Stroke Risk Stratification in Asian Patients With Atrial Fibrillation

A Nationwide Cohort Study

Tze-Fan Chao, MD*; Gregory Y.H. Lip, MD*; Chia-Jen Liu, MD; Ta-Chuan Tuan, MD; Su-Jung Chen, MD; Kang-Ling Wang, MD; Yenn-Jiang Lin, MD; Shih-Lin Chang, MD; Li-Wei Lo, MD; Yu-Feng Hu, MD; Tzeng-Ji Chen, MD; Chern-En Chiang, MD, PhD; Shih-Ann Chen, MD

***Background and Purpose*—**The age threshold for an increased stroke risk for patients with atrial fibrillation may be different for Asians and non-Asians. We hypothesized that a modified CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65–74 years, female) scheme, $mCHA_2DS_2$-VASc, which assigned one point for patients aged 50 to 74 years, may perform better than CHA_2DS_2-VASc score for stroke risk stratification in Asians.

***Methods*—**This study used the Taiwan National Health Insurance Research Database, which included 224 866 newly diagnosed atrial fibrillation patients. The predictive accuracies of ischemic stroke of CHA_2DS_2-VASc and $mCHA_2DS_2$-VASc scores were compared among 124 271 patients without antithrombotic therapies. From the whole cohort, 15 948 patients had a CHA_2DS_2-VASc score 0 (males) or 1 (females), and 8654 patients had an $mCHA_2DS_2$-VASc score 1 (males) or 2 (females). The latter were categorized into 3 groups, that is, no treatment, antiplatelet therapy, and warfarin, and the risks of ischemic stroke and intracranial hemorrhage (ICH) were compared.

***Results*—**During a follow-up of 538 653 person-years, 21 008 patients experienced ischemic stroke. The $mCHA_2DS_2$-VASc performed better than CHA_2DS_2-VASc score in predicting ischemic stroke assessed by C indexes and net reclassification index. For 8654 patients having an $mCHA_2DS_2$-VASc score of 1 (males) or 2 (females) because of the resetting of the age threshold, use of warfarin was associated with a 30% lower risk of ischemic stroke and a similar risk of ICH compared with nontreatment. Net clinical benefit analyses also favored the use of warfarin in different weighted models.

Conclusions*—**In this Asian atrial fibrillation cohort, the $mCHA_2DS_2$-VASc score performed better than the CHA_2DS_2-VASc and would further identify atrial fibrillation patients who may derive a positive net clinical benefit from oral anticoagulation. (Stroke*. 2016;47:00-00. DOI: 10.1161/STROKEAHA.116.013880.)

Conclusions

- Atrial Fibrillation is significantly underestimated
- CHADS-2 VASC scoring system allows for a more accurate method of assessing risk and appropriate treatment
- DOACs provide opportunity to minimize growing burden of potentially preventable thromboembolism (especially AF)
- Reductions in both stroke and bleeding translate into important benefits for patients
- Most bleeding can be managed without specific antidotes
- Specific antidotes in development will provide reassurance to physicians
- Device based approaches to detecting the incidence of AF and reducing the risk of thromboembolism are readily available.

Use of Direct Oral Anticoagulants in Patients with Bioprosethic Valves

Atrial Fibrillation

Non–Vitamin K Antagonist Oral Anticoagulants in Patients With Atrial Fibrillation and Valvular Heart Disease

Giulia Renda, MD, PhD,[a] Fabrizio Ricci, MD,[a] Robert P. Giugliano, MD, SM,[b] Raffaele De Caterina, MD, PhD[a]

ABSTRACT

BACKGROUND Valvular heart disease (VHD) and atrial fibrillation (AF) often coexist. Phase III trials comparing non-vitamin K antagonist oral anticoagulants (NOACs) with warfarin excluded patients with moderate/severe mitral stenosis or mechanical heart valves, but variably included patients with other VHD and valve surgeries.

OBJECTIVES This study aimed to determine relative safety and efficacy of NOACs in patients with VHD.

METHODS We performed a meta-analysis of the 4 phase III AF trials of the currently available NOACs versus warfarin in patients with coexisting VHD to assess pooled estimates of relative risk (RR) and 95% confidence intervals (CIs) for stroke/systemic embolic events (SSEE), major bleeding, intracranial hemorrhage (ICH), and all-cause death.

RESULTS Compared with warfarin, the rate of SSEE in patients treated with higher-dose NOACs was lower and consistent among 13,585 patients with (RR: 0.70; 95% CI: 0.58 to 0.86) or 58,098 without VHD (RR: 0.84; 95% CI: 0.75 to 0.95; interaction p = 0.13). Major bleeding in patients on higher-dose NOACs versus warfarin was similar and consistent among patients with (RR: 0.93; 95% CI: 0.68 to 1.27) or without VHD (RR: 0.85; 95% CI: 0.70 to 1.02; interaction p = 0.63 for VHD/no-VHD difference). Intracranial hemorrhage was lower with higher-dose NOACs than with warfarin irrespective of VHD (RR: 0.47; 95% CI: 0.24 to 0.93, and 0.49; 95% CI: 0.41 to 059, respectively; interaction p = 0.91). No protective effect of higher-dose NOACs in preventing all-cause death seemed to be present in patients with VHD versus without VHD (RR:1.01; 95% CI: 0.90 to 1.14 vs. RR: 0.88; 95% CI: 0.82 to 0.94, respectively; interaction p = 0.03).

CONCLUSIONS High-dose NOACs provide overall efficacy and safety similar in AF patients with or without VHD.

Thank You For Your Attention!