THE ROLE OF WARFARIN IN THE ERA OF NEW OAC .

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Warfarin

THE GOOD

- Effective
- Reversible
- Inexpensive

THE BAD

- Slow onset of action
- Regular monitoring
- Food interaction
- Medication interaction
- Difficult titration-regular dose adjustments
- Variable response
- Bleeding risks
- "bridging"

Time in Therapeutic Range (TTR)
INR Data

	Warfarin
INR range	Median (25th, 75th)
<1.5	2.7 (0.0 – 9.0)
1.5 to <1.8	7.9 (3.5 – 14.0)
1.8 to <2.0	9.1 (5.3 – 13.6)
2.0 to 3.0	57.8 (43.0 – 70.5)
>3.0 to 3.2	4.0 (1.9 – 6.5)
>3.2 to 5.0	7.9 (3.3 – 13.8)
>5.0	0.0 (0.0 – 0.5)

Based on Rosendaal method with all INR values included
Based on Safety Population
M. Califf, M.D., and the ROCKET AF Steering Committee, for the ROCKET AF Investigators. N Engl J Med2011; 365:883-891September 8, 2011

9th International Winter Arrhythmia School
Collingwood - February 12, 2012

The Role of Warfarin in the Era of New Oral Anticoagulants

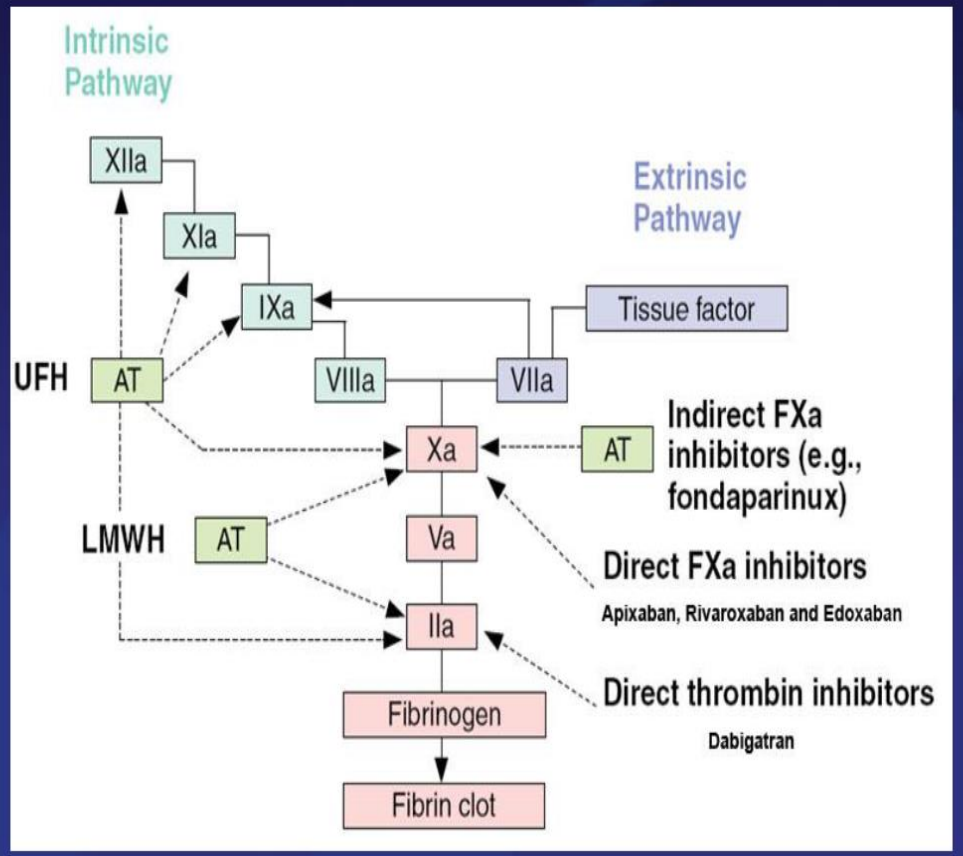
Bill Geerts, MD, FRCPC
Thromboembolism Specialist, Sunnybrook HSC
Professor of Medicine, University of Toronto
National Lead, VTE Prevention, *Safer Healthcare Now!*

Sunnybrook | UofT | safer healthcare now!

Updated AHA/ACC/HRS Guidelines For the Management of Atrial Fibrillation 2017

Chad Link, DO, FACC
Cardiologist
Chairman Cardiology Section
Sparrow TCI

Emerging Therapies



Modified from the Am J Health-Syst Pharm;65:1520

The Ideal Anticoagulant

- Oral
- Once daily dosing
- Quick onset
- Limited monitoring
- Limited or no drug interactions
- Available and effective antidote
- Wide therapeutic index
- Low cost

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 17, 2009 VOL. 361 NO. 12

Dabigatran versus Warfarin in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., Michael D. Ezekowitz, M.B., Ch.B., D.Phil., Salim Yusuf, F.R.C.P.C., D.Phil., John Eikelboom, M.D., Jonas Oldgren, M.D., Ph.D., Amit Parekh, M.D., Janice Pogue, M.Sc., Paul A. Reilly, Ph.D., Ellison Themeles, B.A., Jeanne Varrone, M.D., Susan Wang, Ph.D., Marco Alings, M.D., Ph.D., Denis Xavier, M.D., Jun Zhu, M.D., Rafael Diaz, M.D., Basil S. Lewis, M.D., Harald Darius, M.D., Hans-Christoph Diener, M.D., Ph.D., Campbell D. Joyner, M.D., Lars Wallentin, M.D., Ph.D., and the RE-LY Steering Committee and Investigators*

ABSTRACT

BACKGROUND

Warfarin reduces the risk of stroke in patients with atrial fibrillation but increases the risk of hemorrhage and is difficult to use. Dabigatran is a new oral direct thrombin inhibitor.

METHODS

In this noninferiority trial, we randomly assigned 18,113 patients who had atrial fibrillation and a risk of stroke to receive, in a blinded fashion, fixed doses of dabigatran — 110 mg or 150 mg twice daily — or, in an unblinded fashion, adjusted-dose warfarin. The median duration of the follow-up period was 2.0 years. The primary outcome was stroke or systemic embolism.

RESULTS

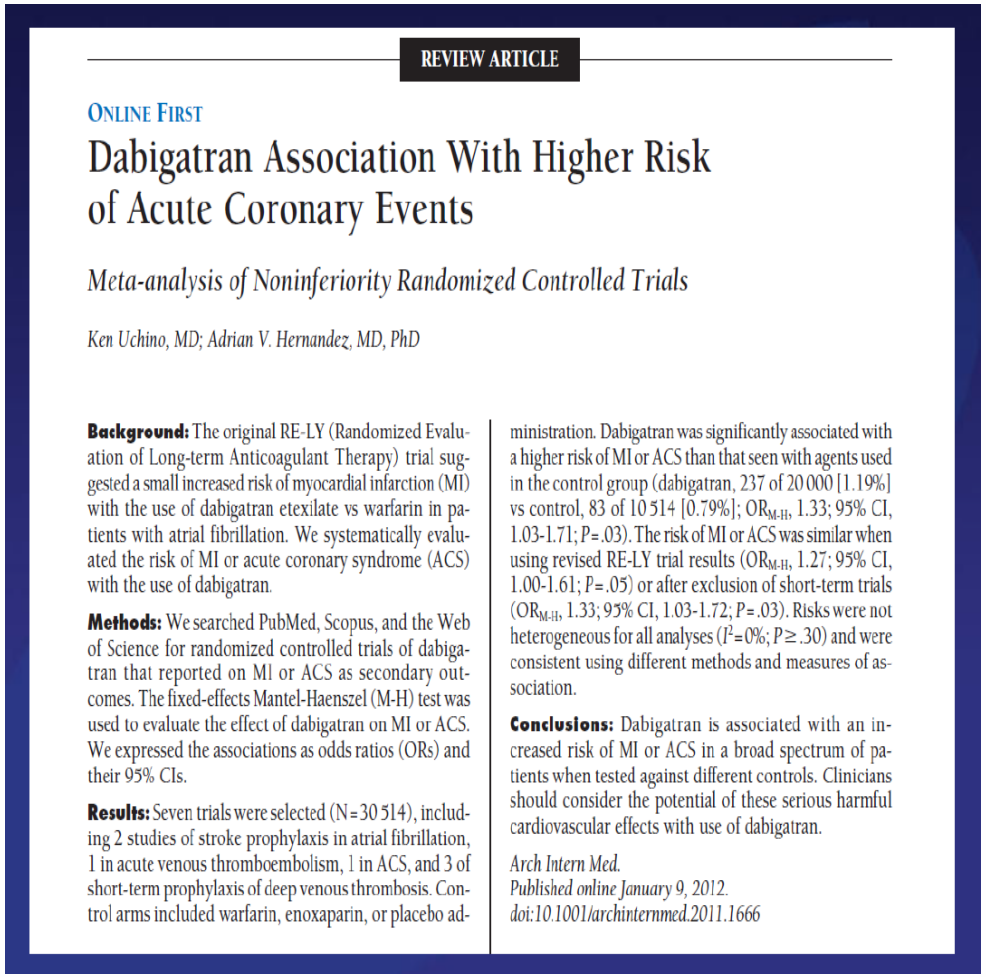
From the Population Health Research Institute, McMaster University and Hamilton Health Sciences, Hamilton, ON, Canada (S.J.C., S.Y., J.E., J.P., E.T.); Lankenau Institute for Medical Research and the Heart Center, Wynnewood, PA (M.D.E., A.P.); Uppsala Clinical Research Center, Uppsala, Sweden (J.O., L.W.); Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT (P.A.R., J.V., S.W.); Working Group on Cardiovascular Research the Netherlands, Utrecht, the Netherlands (M.A.); St. John's National Academy of Health Sciences, Bangalore, India (D.X.); FuWai Hospital, Beijing (J.Z.); Estudios Clínicos Latinoamérica, Rosario, Argentina (R.D.); Lady

Wann et al Atrial Fibrillation Focused Update: Dabigatran

Table 2 Recommendation for emerging antithrombotic agents

2011 Focused update recommendation	Comments
Class I	
1. Dabigatran is useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure (creatinine clearance <15 mL/min) or advanced liver disease (impaired baseline clotting function).[3] *(Level of Evidence: B)*	New recommendation

Wann et al. 2011 ACCF/AHA/HRS Focus Update on the Management of Patients with Atrial Fibrillation. March 2011



REVIEW ARTICLE

ONLINE FIRST

Dabigatran Association With Higher Risk of Acute Coronary Events

Meta-analysis of Noninferiority Randomized Controlled Trials

Ken Uchino, MD; Adrian V. Hernandez, MD, PhD

Background: The original RE-LY (Randomized Evaluation of Long-term Anticoagulant Therapy) trial suggested a small increased risk of myocardial infarction (MI) with the use of dabigatran etexilate vs warfarin in patients with atrial fibrillation. We systematically evaluated the risk of MI or acute coronary syndrome (ACS) with the use of dabigatran.

Methods: We searched PubMed, Scopus, and the Web of Science for randomized controlled trials of dabigatran that reported on MI or ACS as secondary outcomes. The fixed-effects Mantel-Haenszel (M-H) test was used to evaluate the effect of dabigatran on MI or ACS. We expressed the associations as odds ratios (ORs) and their 95% CIs.

Results: Seven trials were selected (N = 30 514), including 2 studies of stroke prophylaxis in atrial fibrillation, 1 in acute venous thromboembolism, 1 in ACS, and 3 of short-term prophylaxis of deep venous thrombosis. Control arms included warfarin, enoxaparin, or placebo administration. Dabigatran was significantly associated with a higher risk of MI or ACS than that seen with agents used in the control group (dabigatran, 237 of 20 000 [1.19%] vs control, 83 of 10 514 [0.79%]; OR_{M-H}, 1.33; 95% CI, 1.03-1.71; $P = .03$). The risk of MI or ACS was similar when using revised RE-LY trial results (OR_{M-H}, 1.27; 95% CI, 1.00-1.61; $P = .05$) or after exclusion of short-term trials (OR_{M-H}, 1.33; 95% CI, 1.03-1.72; $P = .03$). Risks were not heterogeneous for all analyses ($I^2 = 0\%$; $P \geq .30$) and were consistent using different methods and measures of association.

Conclusions: Dabigatran is associated with an increased risk of MI or ACS in a broad spectrum of patients when tested against different controls. Clinicians should consider the potential of these serious harmful cardiovascular effects with use of dabigatran.

Arch Intern Med.
Published online January 9, 2012.
doi:10.1001/archinternmed.2011.1666

theheart.org Medscape

News > News Alerts > Heartwire

FDA Review Finds No Increased Risk of MI With Dabigatran (Pradaxa)

Shelley Wood

DISCLOSURES | May 13, 2014

Increased risk of myocardial infarction with dabigatran: fact or fiction?

Giglio, Ada F.; Basile, Eloisa; Santangeli, Pasquale; Di Biase, Luigi; Trotta, Francesco; Natale, Andrea

Journal of Cardiovascular Medicine: January 2014 - Volume 15 - Issue 1 - p 19–26
doi: 10.2459/JCM.0b013e328364beb8
Reviews: Antithrombotic treatment

Journal of the American College of Cardiology
Volume 72, Issue 1, 3 July 2018, Pages 17-26

Original Investigation

Risk of Myocardial Infarction in Anticoagulated Patients With Atrial Fibrillation

Christina Ji-Young Lee MD [a, b] … Christian Torp-Pedersen MD, DMSc [a]

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https://doi.org/10.1016/j.jacc.2018.04.036

Referred to by Stefan H. Hohnloser, John W. Eikelboom
Direct Oral Anticoagulants and Myoc…
Journal of the American College of Cardiology, Volume 72, Issue 1, 3 July 2018, Pages 27-28

Risk of Myocardial Infarction in Anticoagulated Patients With Atrial Fibrillation.

Lee CJ, et al. J Am Coll Cardiol. 2018.
Show full citation

Abstract

BACKGROUND: Evidence is conflicting as to the efficacy of direct oral anticoagulation (DOAC) and vitamin K antagonist (VKA) for prevention of myocardial infarction (MI).

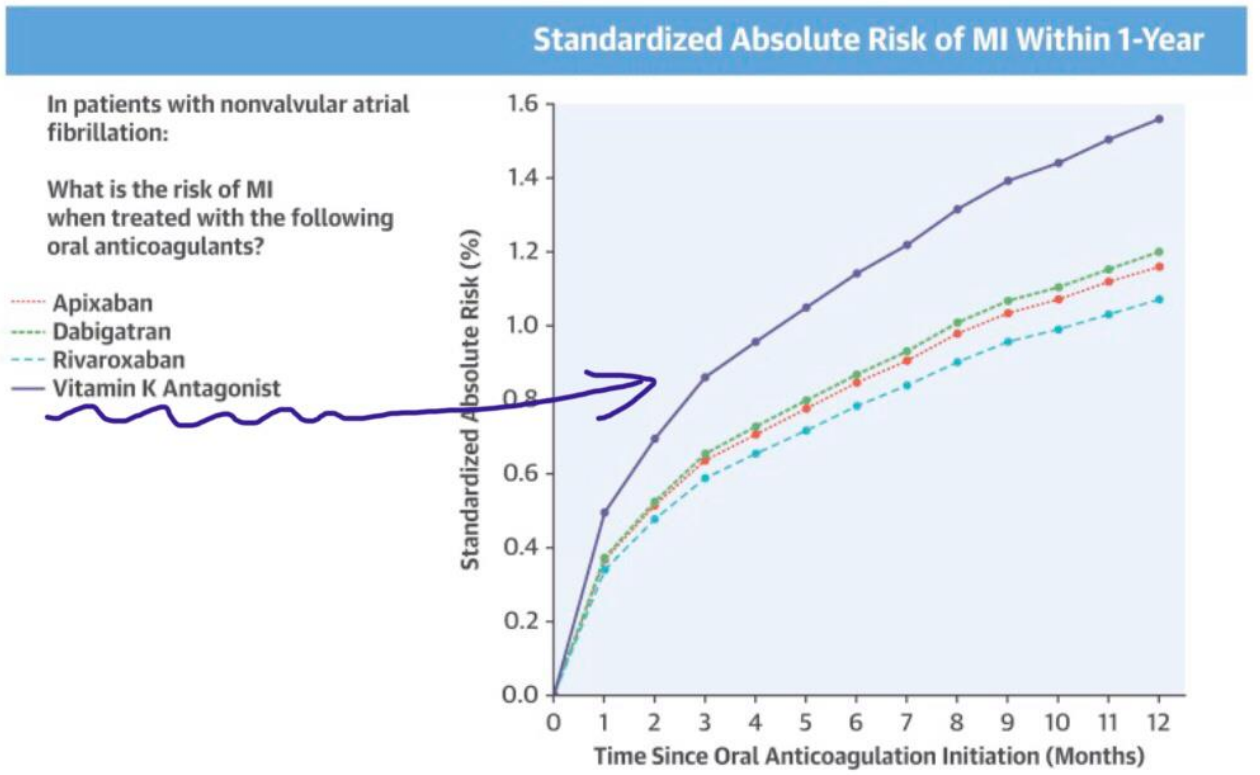
OBJECTIVES: This study aimed to investigate the risk of MI associated with the use of apixaban, dabigatran, rivaroxaban, and VKA in patients with atrial fibrillation.

METHODS: Patients with atrial fibrillation were identified using Danish health care registers and stratified by initial oral anticoagulant treatment. Standardized absolute 1-year risks were estimated based on Cox regression for hazard rates of MI hospitalizations and mortality. Reported were absolute risks separately for the oral anticoagulation treatments and standardized to the characteristics of the study population.

RESULTS: Of the 31,739 patients included (median age, 74 years; 47% females), the standardized 1-year risk of MI for VKA was 1.6% (95% confidence interval [CI]: 1.3 to 1.8), apixaban was 1.2% (95% CI: 0.9 to 1.4),

CONCLUSIONS: No significant risk differences of MI were found in the direct comparisons of DOACs, and DOACs were all associated with a significant risk reduction of MI compared with VKA.

CENTRAL ILLUSTRATION: Oral Anticoagulation Therapy and Risk of MI in Patients With Atrial Fibrillation



Lee, C.J.-Y. et al. J Am Coll Cardiol. 2018;72(1):17-26.

DOAC Summary

Table 1: Study characteristics.

Studies		RE-LY (1)	ROCKET AF (2)	ARISTOTLE (3)	ENGAGE AF-TIMI 48 (4)
Trial size (n)		18,113	14,264	18,201	21,105
Patient characteristics	Mean age (years)	71.5	73	70	72
	Male (%)	63.5%	59.3%	64.5%	61.9%
	Mean $CHADS_2$	2.1	3.5	2.1	2.8
Intervention vs Comparator	Intervention	Two intervention arms: 1. Dabigatran 150 mg bid 2. Dabigatran 150 mg bid	Rivaroxaban 20 mg daily	Apixaban 5 mg bid	Two intervention arms: 1. Edoxaban 30 mg daily 2. Edoxaban 60 mg daily
	Dose modification	No	Yes, at randomisation	Yes, at randomisation	Yes, at randomisation and during study
	Criteria for modified dose	N/A	15 mg daily in patients with CrCl 30–49 ml/min	2.5 mg bid in patients who met 2 of the 3 following criteria: • age >80 years, • weight <60 kg, • creatinine >133 µmol/l	Half dose in patients with any of the following criteria: • CrCl 30–50 ml/min, • weight <60 kg, • concomitant use of potent p-glycoprotein inhibitors such as verapamil, quinidine, dronaderone. Standard dose resumed once these medications ceased.
	Comparators	Open label warfarin	Blinded warfarin	Blinded warfarin	Blinded warfarin
Outcomes	Primary efficacy	Stroke or systemic embolism	Stroke or systemic embolism	Stroke or systemic embolism	Stroke or systemic embolism
	Primary safety	Major bleeding	Major bleeding + clinically relevant non major bleeding	Major bleeding	Major bleeding

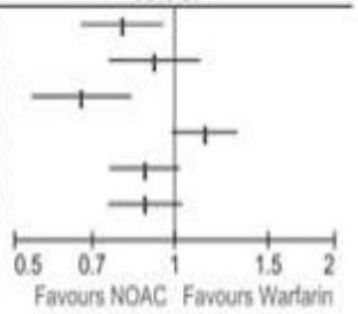
Bid = twice-daily dose; CrCl = creatinine clearance as per Cockcroft Gault formulas; kg = kilogram; mg = milligram.

Chan et al. New oral anticoagulatns for stroke prevention in atrial fibrillation. Thromb Haemost 2014; 111: 798-807

DOAC Events Summary

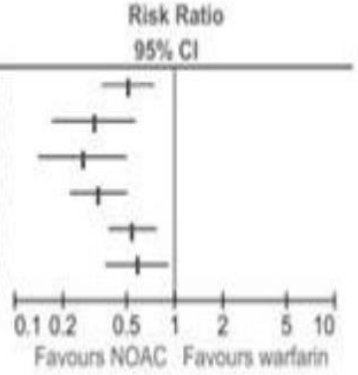
A. Primary Efficacy Outcome

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

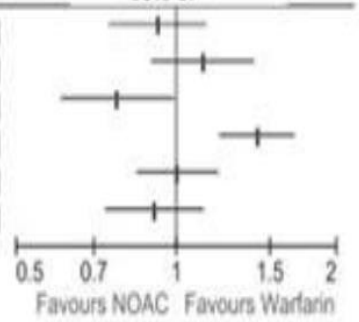
Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	40	9120	78	9081	0.51 [0.35, 0.75]
Dabigatran 110mg bid	14	6015	45	6022	0.31 [0.17, 0.57]
Dabigatran 150mg bid	12	6076	45	6022	0.26 [0.14, 0.50]
Edoxaban 30mg daily	30	7034	90	7036	0.33 [0.22, 0.50]
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]



DOAC Events Summary

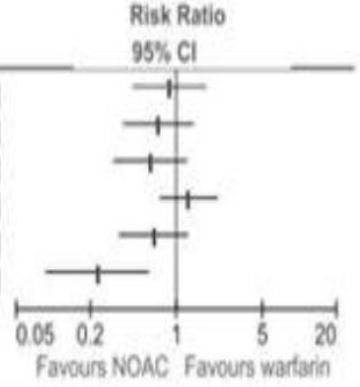
C. Non-haemorrhagic stroke

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

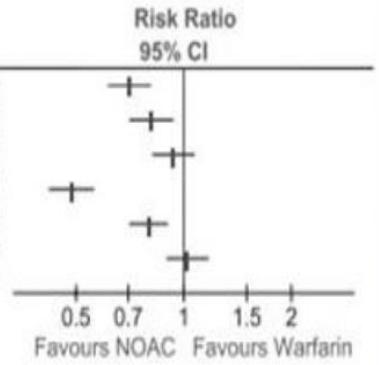
Study or Subgroup	NOAC Events	NOAC Total	Warfarin Events	Warfarin Total	Risk Ratio 95% CI
Apixaban 5mg bid	15	9120	17	9081	0.88 [0.44, 1.76]
Dabigatran 110mg bid	15	6015	21	6022	0.72 [0.37, 1.39]
Dabigatran 150mg bid	13	6076	21	6022	0.61 [0.31, 1.22]
Edoxaban 30mg daily	29	7034	23	7036	1.26 [0.73, 2.18]
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]



DOAC Bleeding Summary

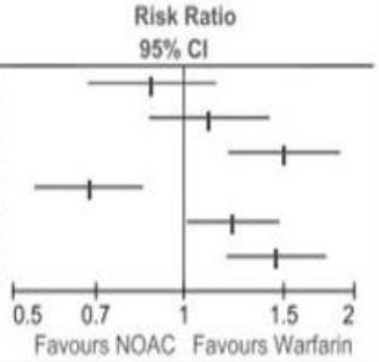
A. Major bleeding

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]

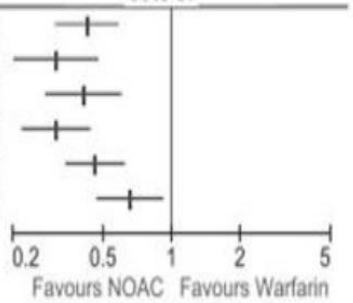


Chan et al. New oral anticoagulatns for stroke prevention in atrial fibrillation. Thromb Haemost 2014; 111: 798-807

DOAC Bleeding 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]



tygacil bkgrnd

Chan et al. New oral anticoagulatns for stroke prevention in atrial fibrillation. Thromb Haemost 2014; 111: 798-807

Selecting an Oral Anticoagulant 1

Setting	Anticoagulant consideration
Good-excellent warfarin control (TTR ≥65%)	Warfarin
Below average warfarin control (TTR <65%)	?? Not specifically studied
Severe renal dysfunction	Warfarin
Mechanical heart valve	Warfarin
Age >75	Warfarin, ? new OAC (riva)
Poor compliance	Warfarin

Selecting an Oral Anticoagulant 2

Setting	Anticoagulant consideration
High risk of IC bleeding	?? (lower dose new OAC, LMWH)
High risk of extracranial bleeding	Warfarin or LMWH
Compliant, healthy patients <70	Warf, dabi, riva
Cost a concern	Warfarin

Guidelines for Management of AF

Effectiveness and Safety of Dabigatran, Rivaroxaban, and Apixaban Versus Warfarin in Nonvalvular Atrial Fibrillation

Xiaoxi Yao, PhD; Neena S. Abraham, MD, MSCE; Lindsey R. Sangaralingham, MPH; M. Fernanda Bellolio, MD, MS; Robert D. McBane, MD; Nilay D. Shah, PhD; Peter A. Noseworthy, MD

Background—The introduction of non–vitamin K antagonist oral anticoagulants has been a major advance for stroke prevention in atrial fibrillation; however, outcomes achieved in clinical trials may not translate to routine practice. We aimed to evaluate the effectiveness and safety of dabigatran, rivaroxaban, and apixaban by comparing each agent with warfarin.

Methods and Results—Using a large US insurance database, we identified privately insured a[tygacil bkgrnd]e Advantage patients with nonvalvular atrial fibrillation who were users of apixaban, dabigatran, rivaroxaban, or warfarin between October 1, 2010, and June 30, 2015. We created 3 matched cohorts using 1:1 propensity score matching: apixaban versus warfarin (n=15 390), dabigatran versus warfarin (n=28 614), and rivaroxaban versus warfarin (n=32 350). Using Cox proportional hazards regression, we found that for stroke or systemic embolism, apixaban was associated with lower risk (hazard ratio [HR] 0.67, 95% CI 0.46–0.98, *P*=0.04), but dabigatran and rivaroxaban were associated with a similar risk (dabigatran: HR 0.98, 95% CI 0.76–1.26, *P*=0.98; rivaroxaban: HR 0.93, 95% CI 0.72–1.19, *P*=0.56). For major bleeding, apixaban and dabigatran were associated with lower risk (apixaban: HR 0.45, 95% CI 0.34–0.59, *P*<0.001; dabigatran: HR 0.79, 95% CI 0.67–0.94, *P*<0.01), and rivaroxaban was associated with a similar risk (HR 1.04, 95% CI 0.90–1.20], *P*=0.60). All non–vitamin K antagonist oral anticoagulants were associated with a lower risk of intracranial bleeding.

Conclusions—In patients with nonvalvular atrial fibrillation, apixaban was associated with lower risks of both stroke and major bleeding, dabigatran was associated with similar risk of stroke but lower risk of major bleeding, and rivaroxaban was associated with similar risks of both stroke and major bleeding in comparison to warfarin. **(*J Am Heart Assoc.* 2016;5:e003725 doi: 10.1161/JAHA.116.003725)**

Format: Abstract

Full text links

Full Text
www.ajhp.org

Am J Health Syst Pharm. 2017 Aug 15;74(16):1237-1244. doi: 10.2146/ajhp160756. Epub 2017 Jun 26.

Trends in utilization of warfarin and direct oral anticoagulants in older adult patients with atrial fibrillation.

Alalwan AA[1], Voils SA[2], Hartzema AG[1].

Author information

Abstract

PURPOSE: Results of a study to determine trends in oral anticoagulant (OAC) use and OAC switching in patients with atrial fibrillation (AF) or atrial flutter are presented.

METHODS: Warfarin has been the most prescribed anticoagulant in patients with AF for decades. Since 2010, several direct OACs (DOACs) have gained U.S. marketing approval for stroke prevention in AF or atrial flutter. A cross-sectional longitudinal analysis was conducted using healthcare and prescription claims databases to characterize OAC use and rates of OAC and DOAC switching during the period 2008-14 in cohorts of Medicare beneficiaries 65 years of age or older with AF or atrial flutter.

RESULTS: Overall, 66% of patients with AF or atrial flutter were receiving OACs during the study period. The prevalence of warfarin use decreased from 69.8% in 2008 to 42.2% in 2014. This decrease in warfarin use was paralleled by an increase in dabigatran use, which rose from 1.3% in 2010 to 12.1% in 2011 and then declined to 7.6% in 2014. The prevalence of rivaroxaban use increased from 0.13% in 2011 to 13.87% in 2014. Among anticoagulated patients, an average of 6% annually were switched from one OAC to another.

CONCLUSION: Overall OAC utilization in patients with AF or atrial flutter remained steady over the study period. Beginning in 2010, a gradual decrease in use of warfarin was paralleled by an increase in use of DOACs.

KEYWORDS: anticoagulants/therapeutic use; atrial fibrillation; drug utilization; geriatrics; prevalence; vitamin K/antagonists & inhibitors

PMID: 28652320 DOI: 10.2146/ajhp160756

Patient Preference and Adherence

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ORIGINAL RESEARCH

A survey of reasons for continuing warfarin therapy in the era of direct oral anticoagulants in Japanese patients with atrial fibrillation: the SELECT study

This article was published in the following Dove Press journal:
Patient Preference and Adherence

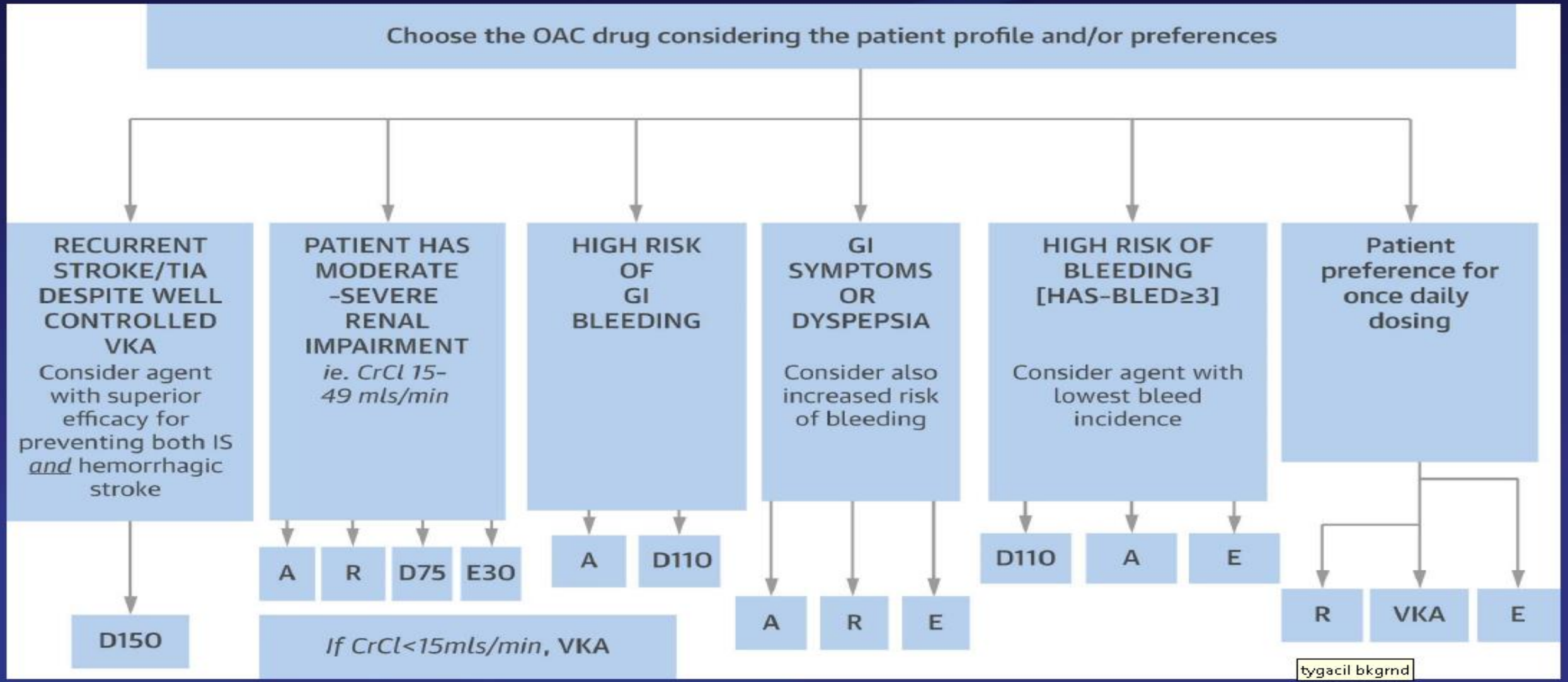
Takanori Ikeda[1]
Masahiro Yasaka[2]
Makoto Kida[3]
Miki Imura[4]

Purpose: Although warfarin has historically been the standard of care for preventing ischemic stroke in patients with nonvalvular atrial fibrillation (NVAF), the use of direct oral anticoagulants (DOACs) is rapidly increasing. In this study, we examined the demographic and clinical characteristics of patients continuing warfarin therapy and investigated reasons for warfarin continuation.

Conclusion

Approximately half of the patients in this study received a recommendation from their physician to switch from warfarin to a DOAC, primarily on the basis of improved efficacy and safety, but elected not to change regimens because of the high price of DOACs. In the remaining half of the study population, physician preference or specific patient characteristics prevented a change of therapy. From the physician's perspective, stable INR control was the most important reason to continue warfarin, even if INR values were below the therapeutic range. For patients, lower cost and long-term positive experiences with warfarin constituted the rationale for warfarin preference. Ultimately, a healthy doctor–patient relationship that includes discussion of all treatment options and frequent communication about patient satisfaction with anticoagulation therapy is crucial for achieving medication adherence.

Anticoagulation Strategies



Who should remain on warfarin?

- Patient already receiving warfarin and stable whose INR is easy to control
- If dabigatran, rivaroxaban, apixaban or edoxaban not available
- Cost
- If patient not likely to comply with twice daily dosing (Dabigatran, Apixaban or edoxaban)
- Chronic kidney disease/ESRD (GFR < 15 ml/min)

Guidelines for Management of AF

Barriers to Treatment-

- Patients are often reluctant
- Physicians' overestimation of the risks of anticoagulation is the most consistently cited explanation for warfarin under-use
- Physicians' risk perceptions may be influenced by their experiences with warfarin use
  - For example, in one small survey, physicians who reported having patients experience adverse events from anticoagulation were less likely to prescribe warfarin
- Different types of adverse events may have more influence on practice than others
  1. Bleeding in a patient to whom a physician prescribed warfarin
  2. Thromboembolic stroke in patient to whom a physician did not prescribe warfarin

Guidelines for Management of AF

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

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ABSTRACT

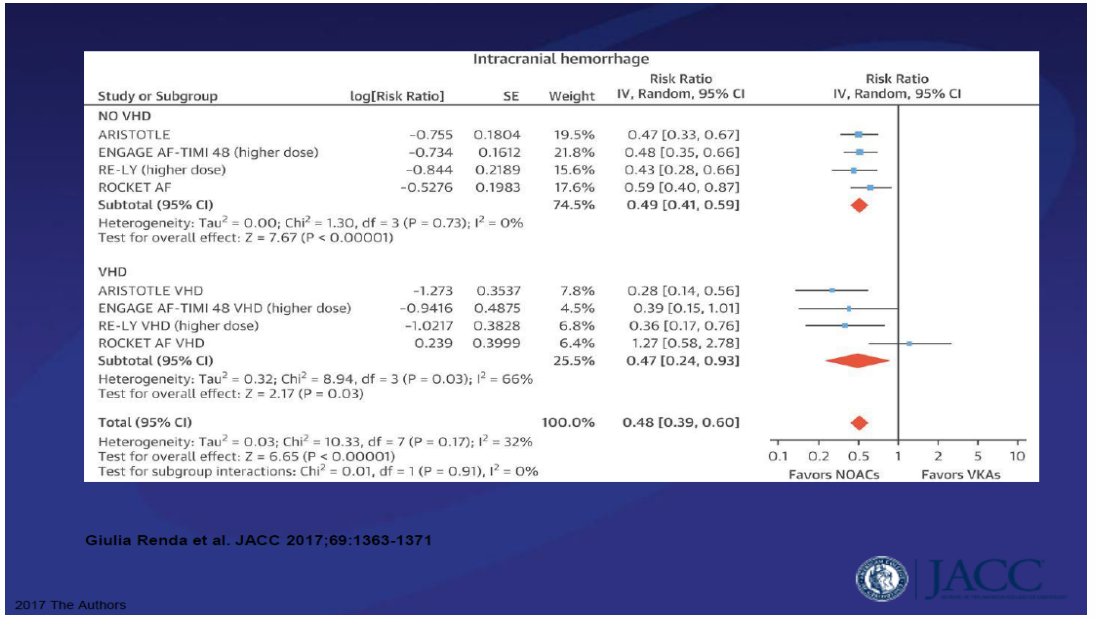
BACKGROUND Valvular heart disease (VHD) and atrial fibrillation (AF) often coexist. Phase III trials comparing non-vitamin K antagonist oral anticoagulants (NOACs) with warfarin excluded patients with moderate/severe mitral stenosis or mechanical heart valves, but variably included patients with other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

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

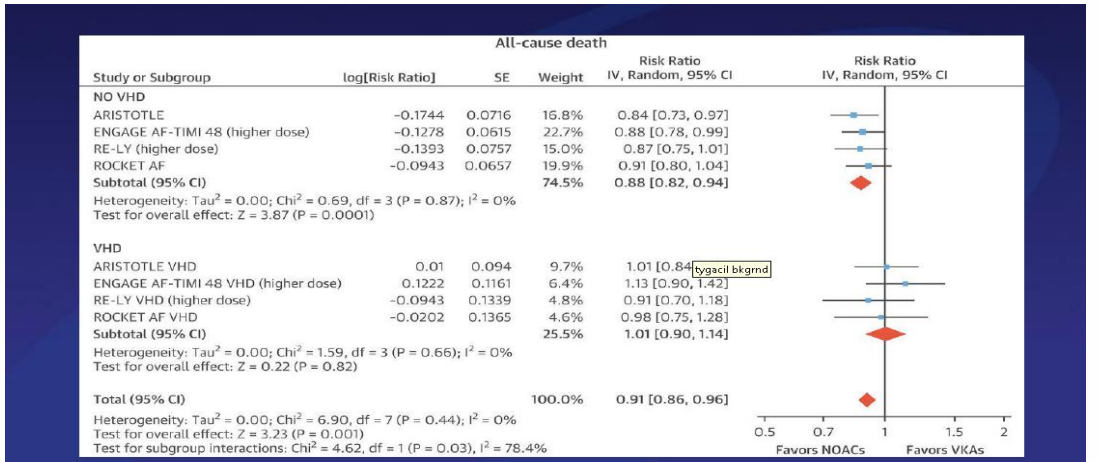
METHODS We performed a meta-analysis of the 4 phase III AF trials of the currently available NOACs versus warfarin in patients with coexisting VHD to assess pooled estimates of relative risk (RR) and 95% confidence intervals (CIs) for stroke/systemic embolic events (SSEE), major bleeding, intracranial 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.
(J Am Coll Cardiol 2017;69:1363-71)

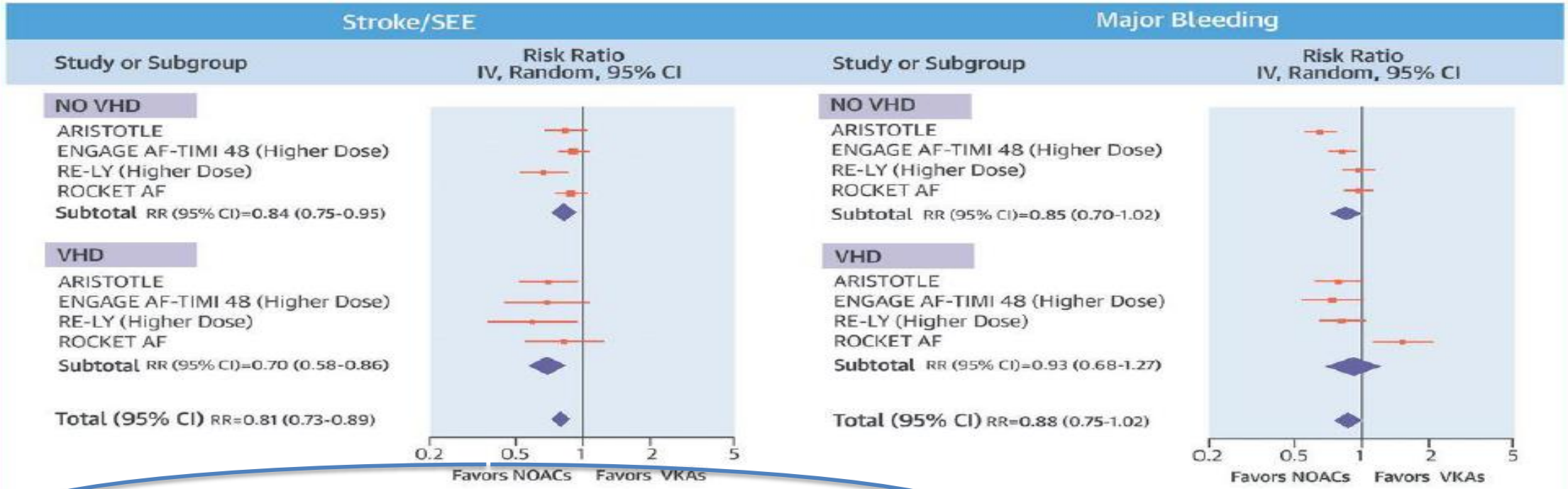


Giulia Renda et al. JACC 2017;69:1363-1371



Giulia Renda et al. JACC 2017;69:1363-1371

CENTRAL ILLUSTRATION: SSEE and Major Bleeding in Patients Without and With VHD, Treated With Higher-Dose NOACs or Warfarin



Renda, G. et al. J Am Coll Cardiol. 2017;69(11):1363–71.

Giulia Renda et al. JACC 2017;69:1363-1371

Guidelines for Management of AF

- 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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THANK YOU FOR YOUR ATTENTION

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