

STROKE PREVENTION IN AF



4.5 minutes



Right internal carotid artery

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INCIDENCE OF PREVIOUSLY UNDIAGNOSED ATRIAL FIBRILLATION USING INSERTABLE CARDIAC MONITORS IN A HIGH-RISK POPULATION

Patients with no AF history but deemed to be at risk for AFIB

Afib risk factors

CAD
Renal impairment
Sleep apnea
COPD

CHADS2 score >3

Primary end point - **AF lasting >6 minutes** and was assessed at 18 months

Characteristic	Patients With Device Insertion, No. (%) (n = 394)
Demographic characteristics	
Male	206 (52.3)
Age, y	
Mean (SD)	71.6 (9.8)
<65	88 (22.3)
65-75	131 (33.3)
>75	175 (44.4)
Left ventricular ejection fraction	58.9 (8.1)
CHADS₂ score	
Mean (SD)	2.9 (0.8)
1	1 (0.3)
2	158 (40.0)
3	130 (33.2)
≥4	105 (26.6)
CHA₂DS₂-VASc score	
Mean (SD)	4.4 (1.3)
2	25 (6.3)
3	79 (20.1)
4	112 (28.4)
5	100 (25.4)
6	53 (13.5)
≥7	25 (6.3)

JAMA Cardiology | Original Investigation Incidence of Previously Undiagnosed Atrial Fibrillation Using Insertable Cardiac Monitors in a High-Risk Population The REVEAL AF Study

James A. Reiffel, MD, Raul Verma, MD, Peter B. Kowey, MD, Jonathan L. Halperin, MD, Bernard J. Gersh, MD, PhD, Rolf Wichter, MD, Erika Probst, MD, Paul D. Ziegler, MD, for the REVEAL AF Investigators

IMPORTANCE In approximately 20% of atrial fibrillation (AF)-related ischemic strokes, stroke is the first clinical manifestation of AF. Strategies are needed to identify and therapeutically address previously undetected AF.

OBJECTIVE To quantify the incidence of AF in patients at high risk for but without previously known AF using an insertable cardiac monitor.

DESIGN, SETTING, AND PARTICIPANTS This prospective, single-arm, multicenter study was conducted from November 2012 to January 2017. Visits took place at 57 centers in the United States and Europe. Patients with a CHADS₂ score of 3 or greater (or 2 with at least 1 additional risk factor) were enrolled. Approximately 90% had nonspecific symptoms potentially compatible with AF, such as fatigue, dyspnea, and/or palpitations.

Invited Commentary
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Supplemental content

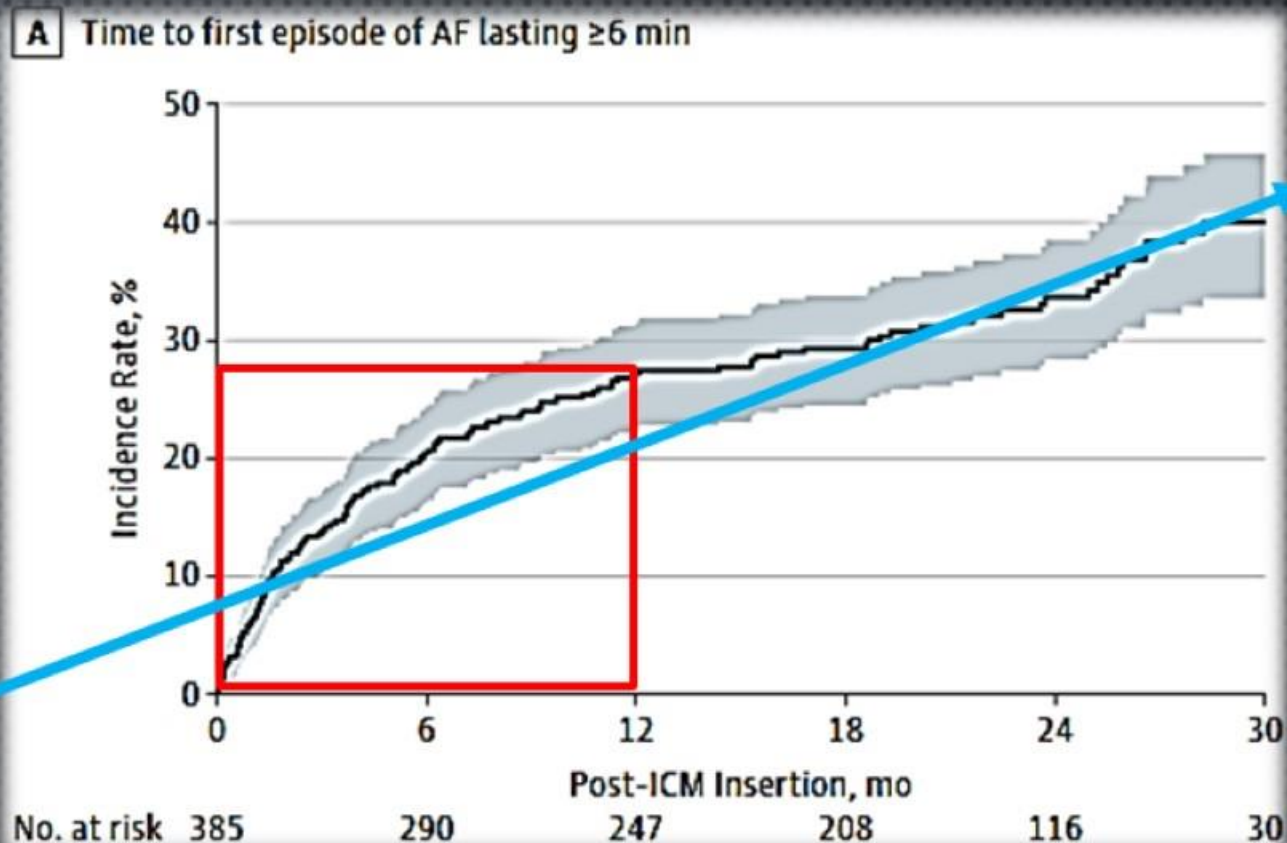
Medical history	
Renal dysfunction	64 (16.2)
Congestive heart failure	81 (20.6)
Coronary artery disease	233 (59.1)
Prior coronary artery bypass grafting or percutaneous coronary intervention	165 (41.9)
Hypertension	369 (93.7)
Chronic obstructive pulmonary disease	76 (19.3)
Sleep apnea	104 (26.4)
Diabetes	248 (62.9)
Valve disease (any, clinical or laboratory)	222 (56.3)
Prior valve surgery	12 (3.0)

JAMA Cardiol. 2017;2(10):1120-1127



WHAT WAS THE PERCENT INCIDENCE OF ATRIAL FIBRILLATION @ 1 YEAR: (REVEAL STUDY)

1. <2%
2. 5%
3. 10%
4. 15%
5. >25%

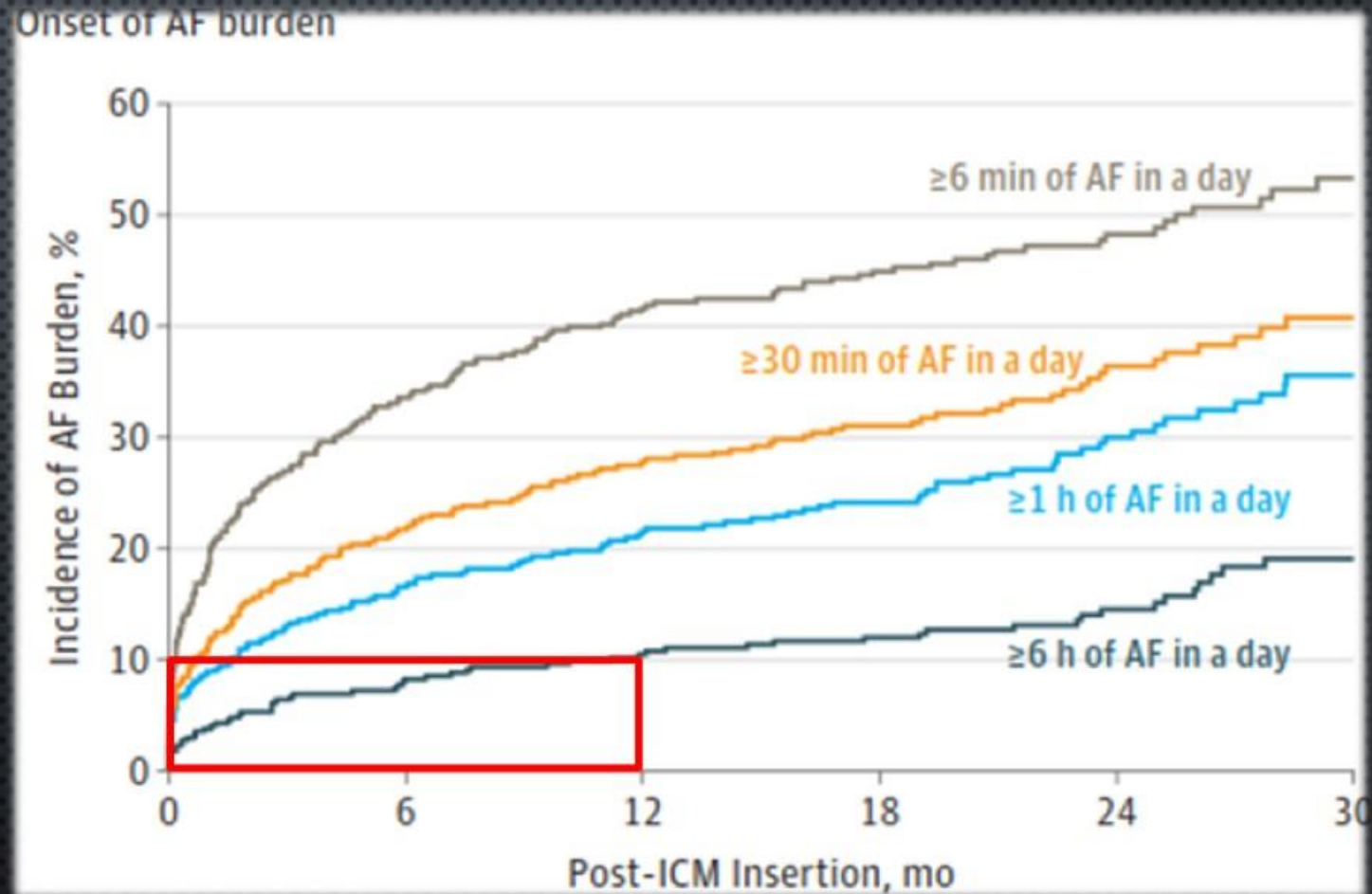


JAMA Cardiol. 2017;2(10):1120-1127



WHAT WAS THE PERCENT INCIDENCE OF ATRIAL FIBRILLATION LASTING **MORE THAN 6 HOURS @ 1 YEAR** YEAR: (REVEAL STUDY)

1. <2%
2. 5%
3. 10%
4. 15%
5. >25%



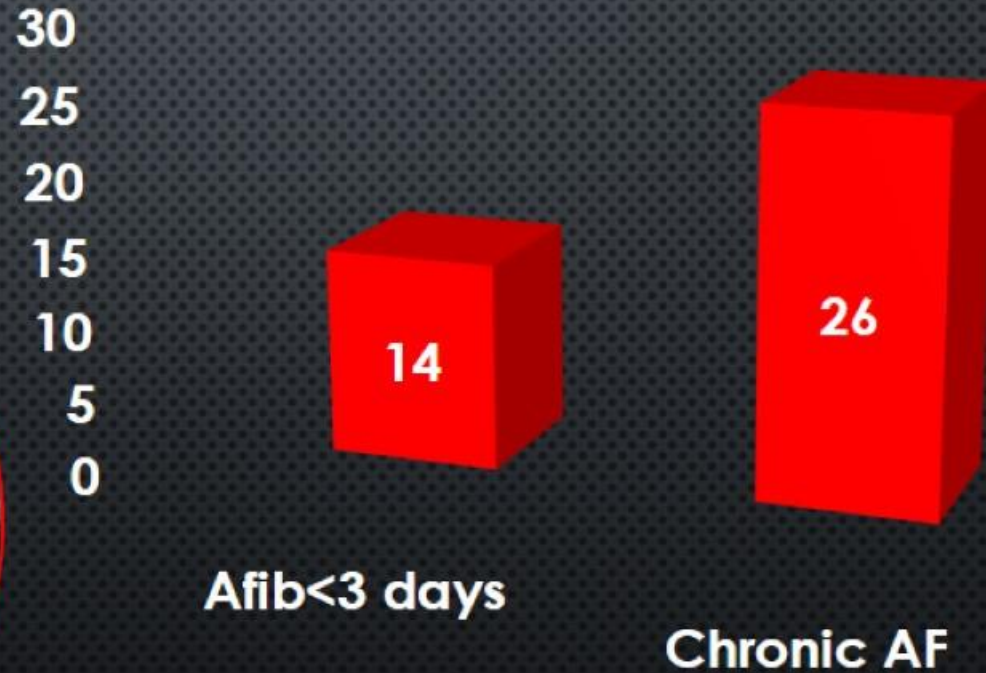
JAMA Cardiol. 2017;2(10):1120-1127



WHAT IS THE INCIDENCE OF LEFT ATRIAL APPENDAGE THROMBUS IN PATIENTS WITH ATRIAL FIBRILLATION?

Percentage with LAA thrombus

1. <2%
2. 5%
3. 10%
4. 15-25%
5. >25%



JACC 1995;25:452-9

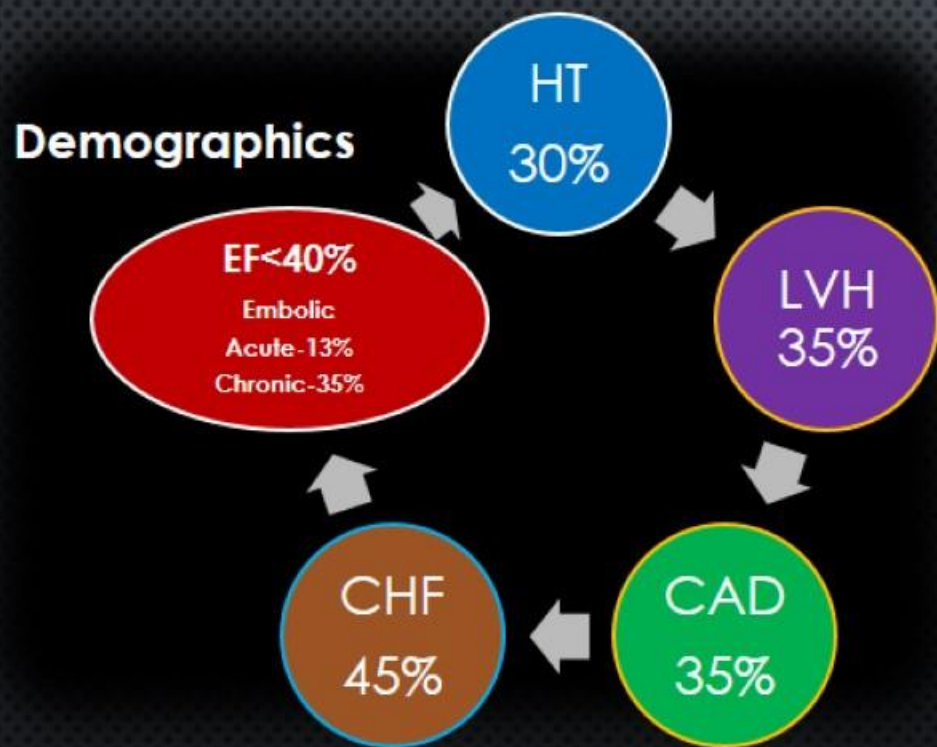


INCIDENCE OF LAA THROMBUS IS COMMON: AFIB PATIENTS

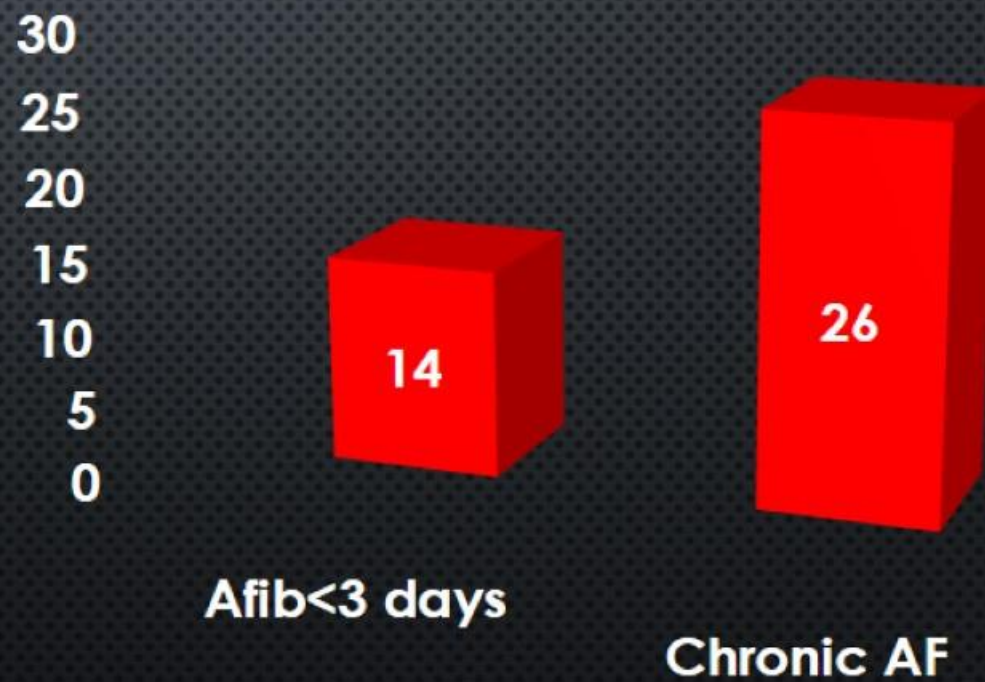
Left Atrial Appendage Thrombus Is Not Uncommon in Patients With Acute Atrial Fibrillation and a Recent Embolic Event: A Transesophageal Echocardiographic Study

MARCUS F. STODDARD, MD, FACC, PHILLIP R. DAWKINS, MD,
CHARLES R. PRINCE, MD, FACC, NASER M. AMMASH, MD
Louisville, Kentucky

- 317 PATIENTS WITH EKG AFIB REFERRED FOR ECHO



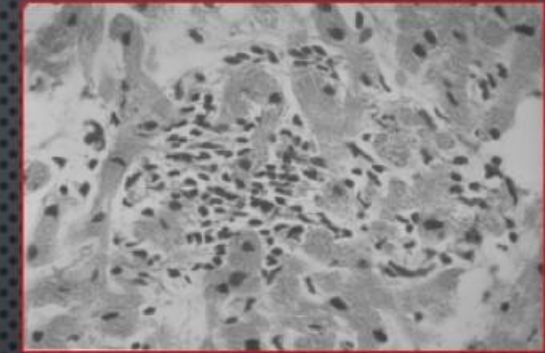
Percentage with LAA thrombus



PROTHROMBOTIC STATE IN ATRIAL FIBRILLATION

Abnormal blood constituents

Platelet activation
Hematocrit
Thrombosis
Inflammation/IL6
D-Dimer
Prothrombin



Atrial myocarditis. Clusters of lymphomononuclear infiltrates are observed with focal necrosis of the adjacent myocytes (hematoxylin and eosin stain, $\times 250$).

Virchow's triad for thrombogenesis

Abnormal vessel wall

Fibrotic changes of the LAA appendage

Areas of erosion of the endothelium and clusters of clot

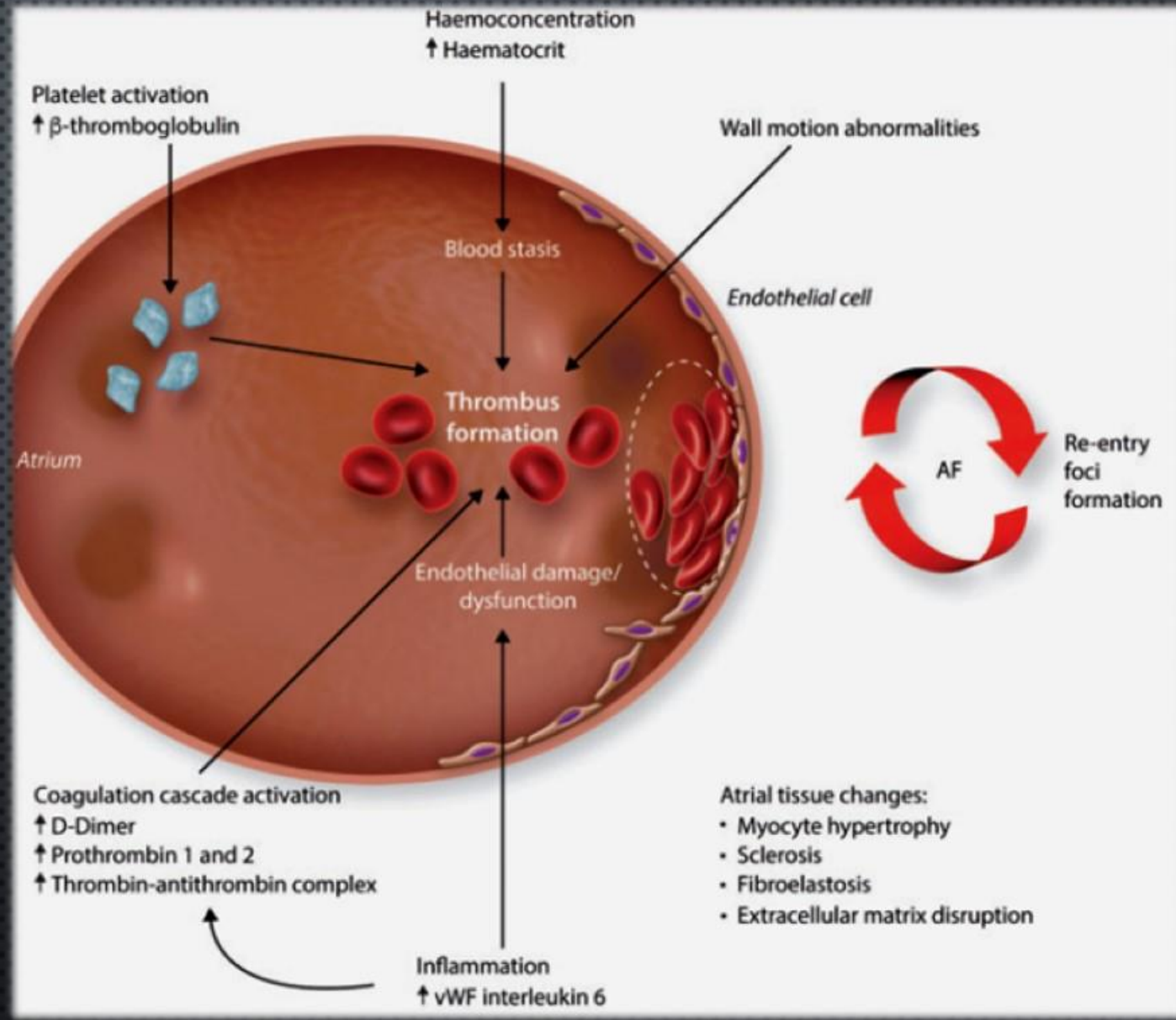
Abnormal blood flow

Cardiovascular Research (2019) 115, 31–45
Circulation 1997;96:1180-4



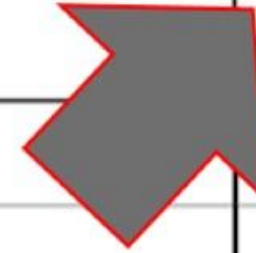
Table 4 Schematic representation of the strength of association of different biomarkers and outcomes in patients with AF

Biomarker	Stroke/systemic embolism	Mortality	Major bleeding
Cardiac biomarkers			
Troponin	+++	+++	+++
NT-proBNP	+++	+++	+
Renal dysfunction	+ / +++	++	++
Inflammation biomarkers			
CRP	+	+++	+
IL-6	++	+++	++
GDF-15	++	+++	+++
Galectin-3	+	+++	+
Endothelial function			
vWF	+	++	++
Coagulation			
D-dimer	++	++	++



CHA ₂ DS ₂ -VASc acronym	Score
Congestive HF	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65 to 74 years	1
Sex category (ie, female sex)	1
Maximum score	9

CHA ₂ DS ₂ -VASc acronym	Unadjusted ischemic stroke rate (% per year)*
0	0.2%
1	0.6%
2	2.2%
3	3.2%
4	4.8%
5	7.2%
6	9.7%
7	11.2%
8	10.8%
9	12.2%



18,201 patients with atrial fibrillation and at least one additional risk factor for stroke

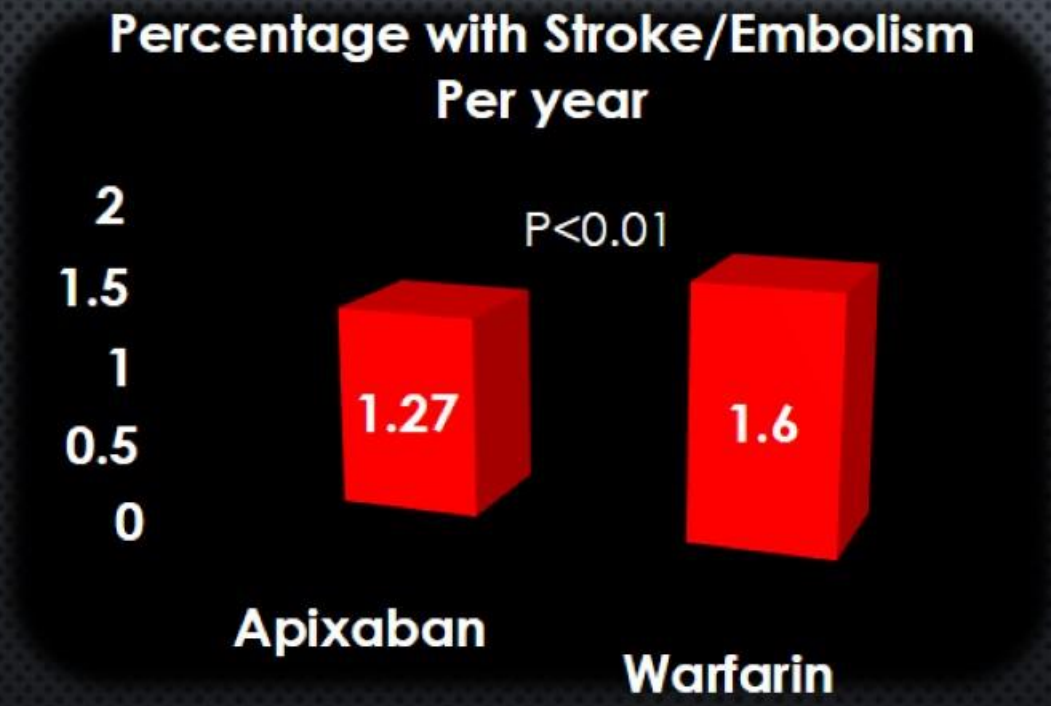
Primary outcome was ischemic or hemorrhagic stroke or systemic embolism

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Apixaban versus Warfarin in Patients with Atrial Fibrillation

Christopher B. Granger, M.D., John H. Alexander, M.D., M.H.S., John J.V. McMurray, M.D., Renato D. Lopes, M.D., Ph.D., Elaine M. Hylek, M.D., M.P.H., Michael Hanna, M.D., Hussein R. Al-Khalidi, Ph.D., Jack Ansell, M.D., Dan Atar, M.D., Alvaro Avezum, M.D., Ph.D., M. Cecilia Bahit, M.D., Rafael Diaz, M.D., J. Donald Easton, M.D., Justin A. Ezekowitz, M.B., B.Ch., Greg Flaker, M.D., David Garcia, M.D., Margarida Geraldes, Ph.D., Bernard J. Gersh, M.D., Sergey Golitsyn, M.D., Ph.D., Shinya Goto, M.D., Antonio G. Hermosillo, M.D., Stefan H. Hohnloser, M.D., John Horowitz, M.D., Puneet Mohan, M.D., Ph.D., Petr Jansky, M.D., Basil S. Lewis, M.D., Jose Luis Lopez-Sendon, M.D., Prem Pais, M.D., Alexander Parkhomenko, M.D., Freek W.A. Verheugt, M.D., Ph.D., Jun Zhu, M.D., and Lars Wallentin, M.D., Ph.D., for the ARISTOTLE Committees and Investigators*



N Engl J Med 2011;365:981-92

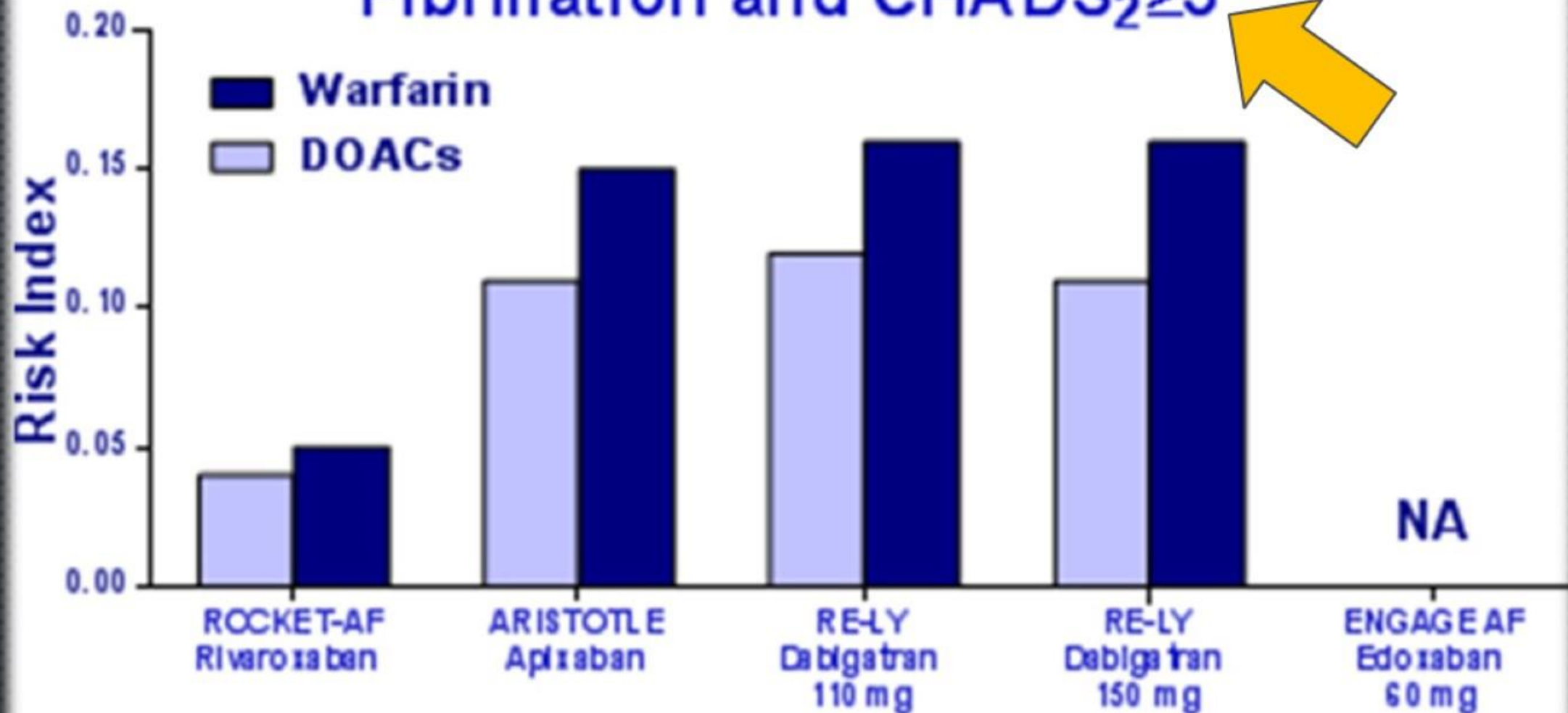
Major bleeding was 2.13% per year in the apixaban group, 3.09% per year in the warfarin group (hazard ratio, 0.69; 95% CI, 0.60 to 0.80; P < 0.001)

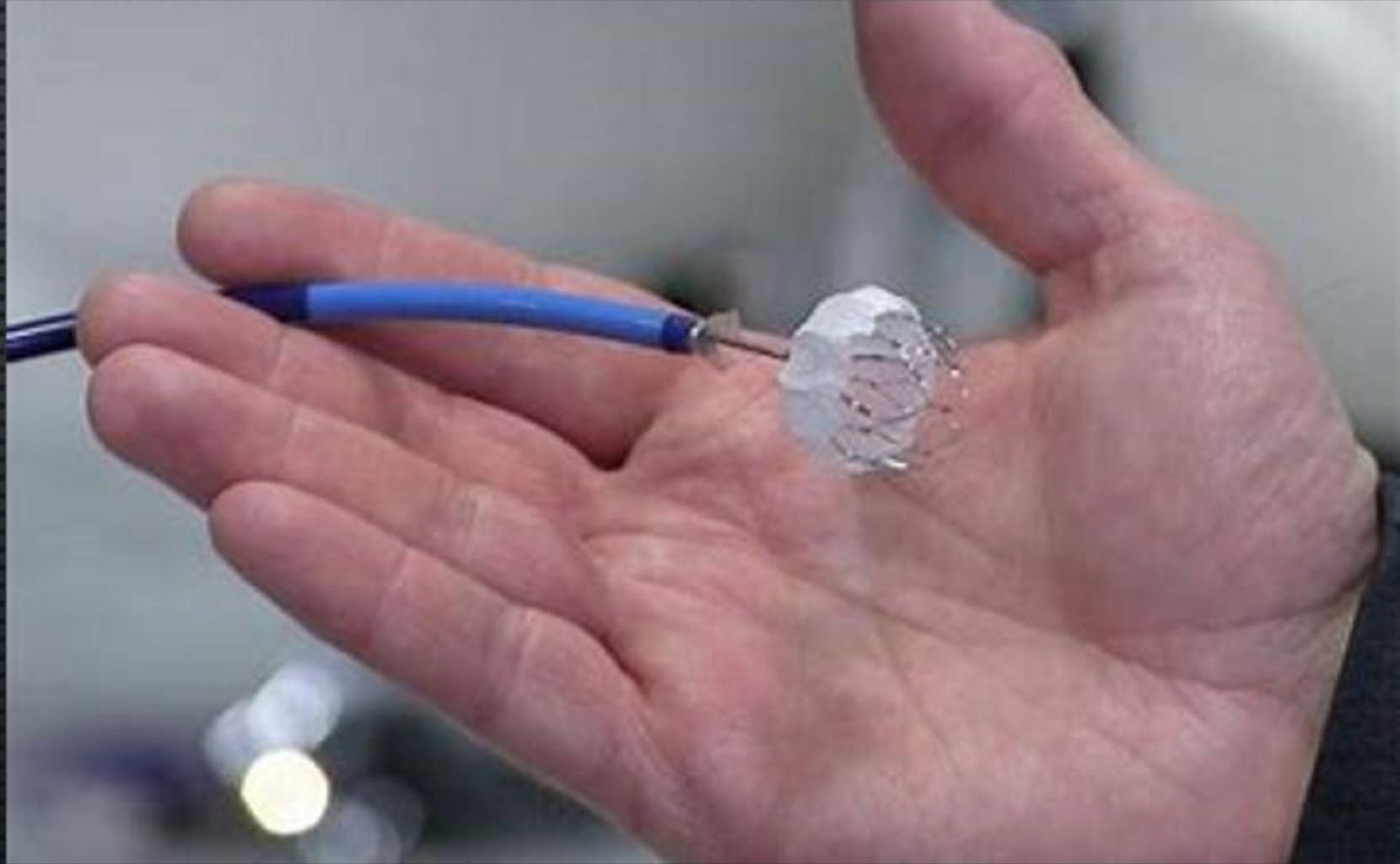
0.66 to 0.95; P < 0.001 for noninferiority; P = 0.01 for superiority

CHADs-~30% each group



Stroke/SEE in Patients With Atrial Fibrillation and CHADS₂ ≥ 3





WATCHMAN

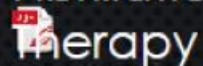


5-Year Outcomes After Left Atrial Appendage Closure

TABLE 1 Patient Demographics

	PROTECT AF			PREVAIL			Combined Cohort		
	Device (n = 463)	Control (n = 244)	p Value	Device (n = 269)	Control (n = 138)	p Value	Device (n = 732)	Control (n = 382)	p Value
Age, yrs	71.7 ± 8.8	72.7 ± 9.2	0.18	74.0 ± 7.4	74.9 ± 7.2	0.26	72.6 ± 8.4	73.5 ± 8.6	0.09
Male	70.4	70.1	0.93	67.7	74.6	0.15	69.4	71.7	0.42
CHADS ₂ score	2.2 ± 1.2	2.3 ± 1.2	0.07	2.6 ± 1.0	2.6 ± 1.0	0.48	2.3 ± 1.1	2.4 ± 1.2	0.06
Risk factors									
CHF	26.8	27.0	0.94	23.4	23.2	0.96	25.5	25.7	0.97
Hypertension	89.6	90.2	0.82	88.5	97.1	0.003	89.2	92.7	0.06
Age ≥75 yrs	36.9	41.4	0.25	46.5	46.4	0.99	40.4	43.2	0.38
Diabetes	24.4	29.5	0.14	33.8	29.7	0.40	27.9	29.6	0.55
Prior stroke/TIA	17.7	20.1	0.44	29.7	29.7	1.00	22.1	23.6	0.59
CHA ₂ DS ₂ -VASc score	3.4 ± 1.5	3.7 ± 1.6	0.02	4.0 ± 1.2	4.1 ± 1.2	0.4	3.6 ± 1.4	3.9 ± 1.5	0.02
AF pattern									
Paroxysmal	43.2	40.6	0.50	48.7	51.4	0.60	45.2	44.5	0.82
Persistent	21.0	20.5	0.89	31.6	28.3	0.49	24.9	23.3	0.56
Permanent	34.6	38.1	0.35	15.6	15.9	0.93	27.6	30.1	0.38
Unknown	1.3	0.8	0.72	1.5	0.7	0.50	1.4	0.8	0.56
Paced	0	0	—	2.6	3.6	0.55	1.0	1.3	0.56

PREVAIL -Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin



therapy

PROTECT AF -WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation

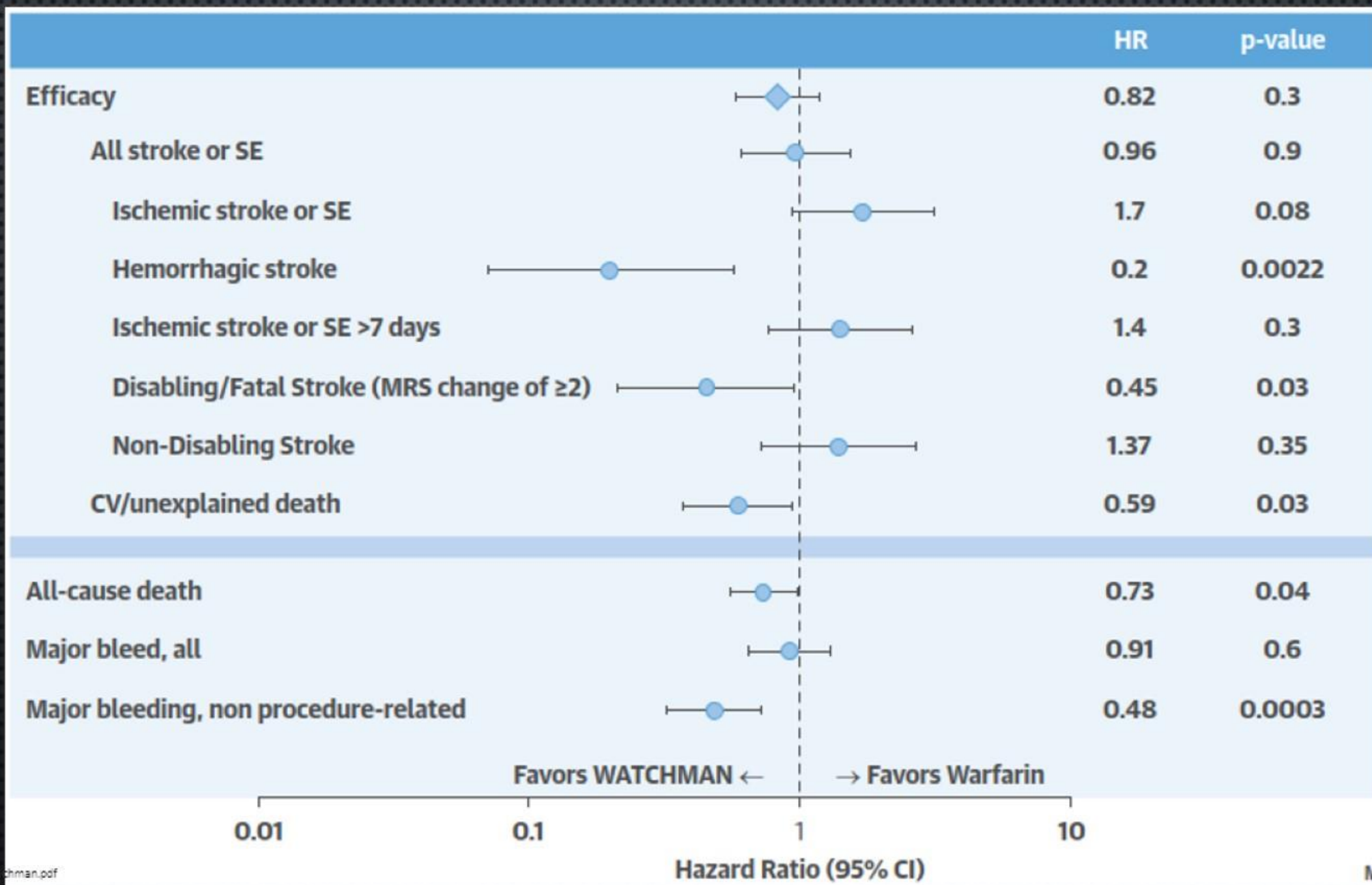


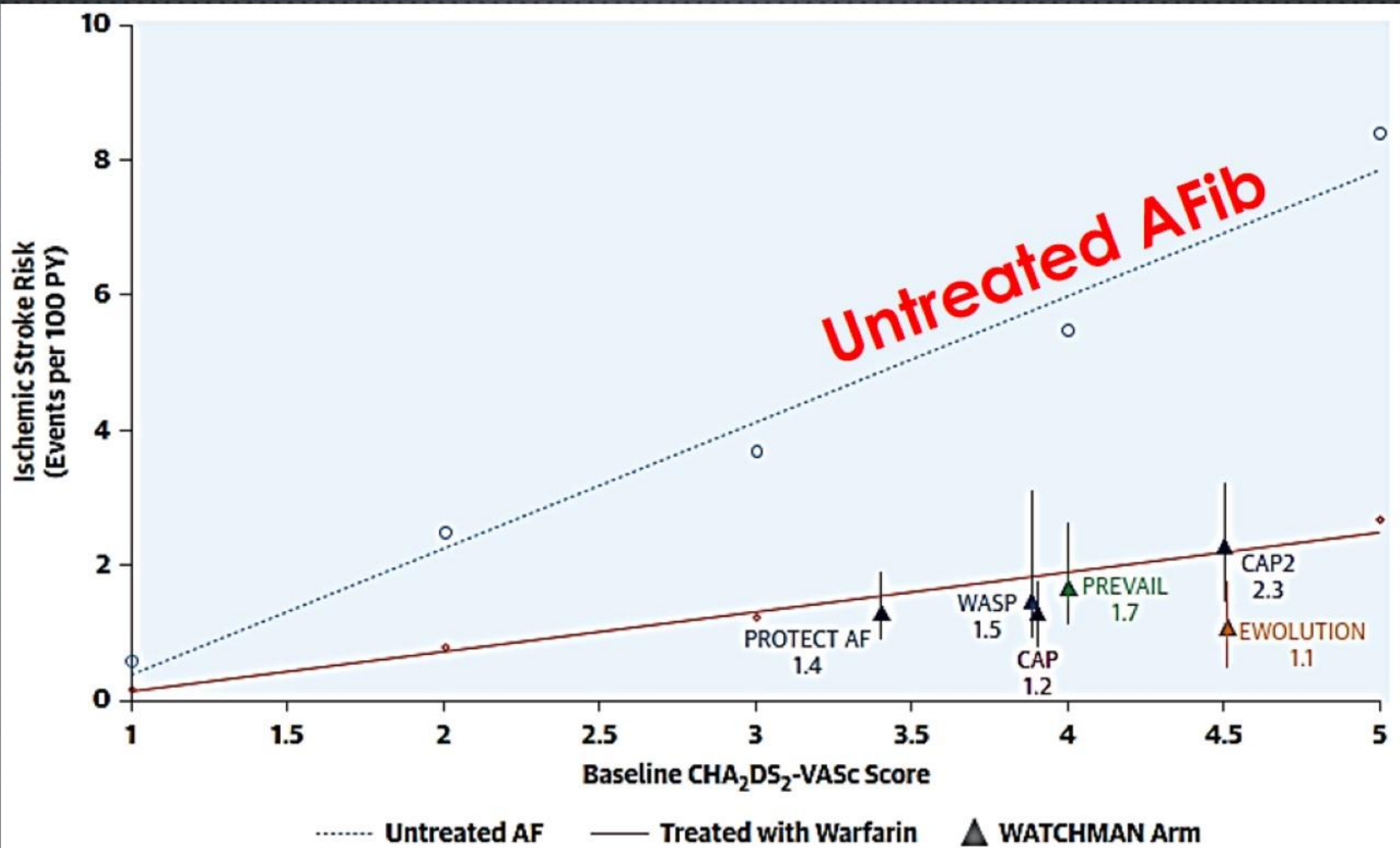
WATCHMAN

TABLE 4 5-Year Patient-Level Meta-Analysis of PROTECT AF and PREVAIL (2:1 Randomization)

	Device Group (n = 732)		Control Group (n = 382)		Hazard Ratio (95% Confidence Interval)	p Value
	No. of Events	Rate (per 100 PY)	No. of Events	Rate (per 100 PY)		
Efficacy: stroke/SE/CV death	79/2,856.0	2.8%	50/1,472.8	3.4%	0.82 (0.58-1.17)	0.27
All stroke or SE	49/2,849.4	1.7%	27/1,472.9	1.8%	0.96 (0.60-1.54)	0.87
Ischemic stroke or SE	45/2,850.2	1.6%	14/1,479.1	0.95%	1.71 (0.94-3.11)	0.08
Hemorrhagic stroke	5/2,954.8	0.17%	13/1,499.0	0.87%	0.20 (0.07-0.56)	0.0022
Ischemic stroke or SE >7 days	37/2,862.1	1.3%	14/1,479.1	0.95%	1.40 (0.76-2.59)	0.28
Disabling stroke	13/2,943.0	0.44%	15/1,493.8	1.0%	0.45 (0.21-0.94)	0.03
Nondisabling stroke	31/2,879.1	1.1%	12/1,484.3	0.81%	1.38 (0.71-2.68)	0.35
CV/unexplained death	39/2,960.5	1.3%	33/1,505.2	2.2%	0.59 (0.37-0.94)	0.027
All-cause death	106/2,961.6	3.6%	73/1,505.2	4.9%	0.73 (0.54-0.98)	0.035
Major bleeding, all	85/2,748.4	3.1%	50/1,414.7	3.5%	0.91 (0.64-1.29)	0.60
Major bleeding, non-procedure-related	48/2,853.6	1.7%	51/1,411.3	3.6%	0.48 (0.32-0.71)	0.0003

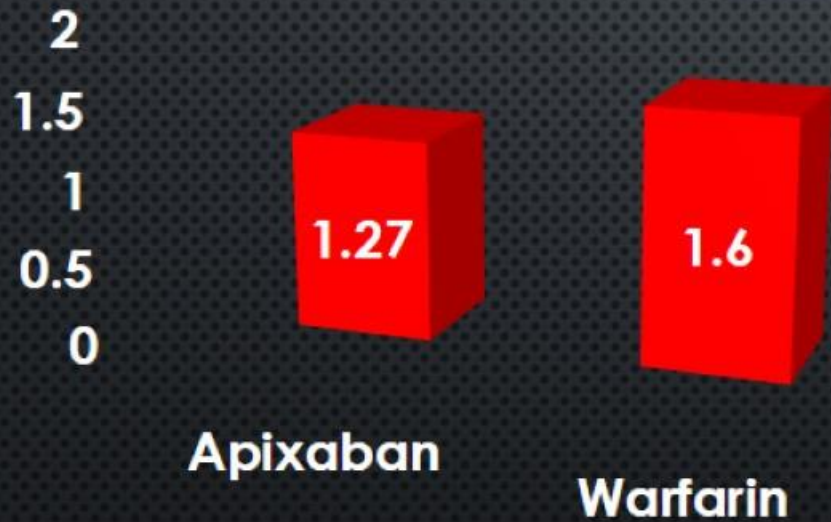






Cannot compare these trials different patients

Percentage with Stroke/Embolism
Per year



Percentage with Stroke/Embolism
5 years

