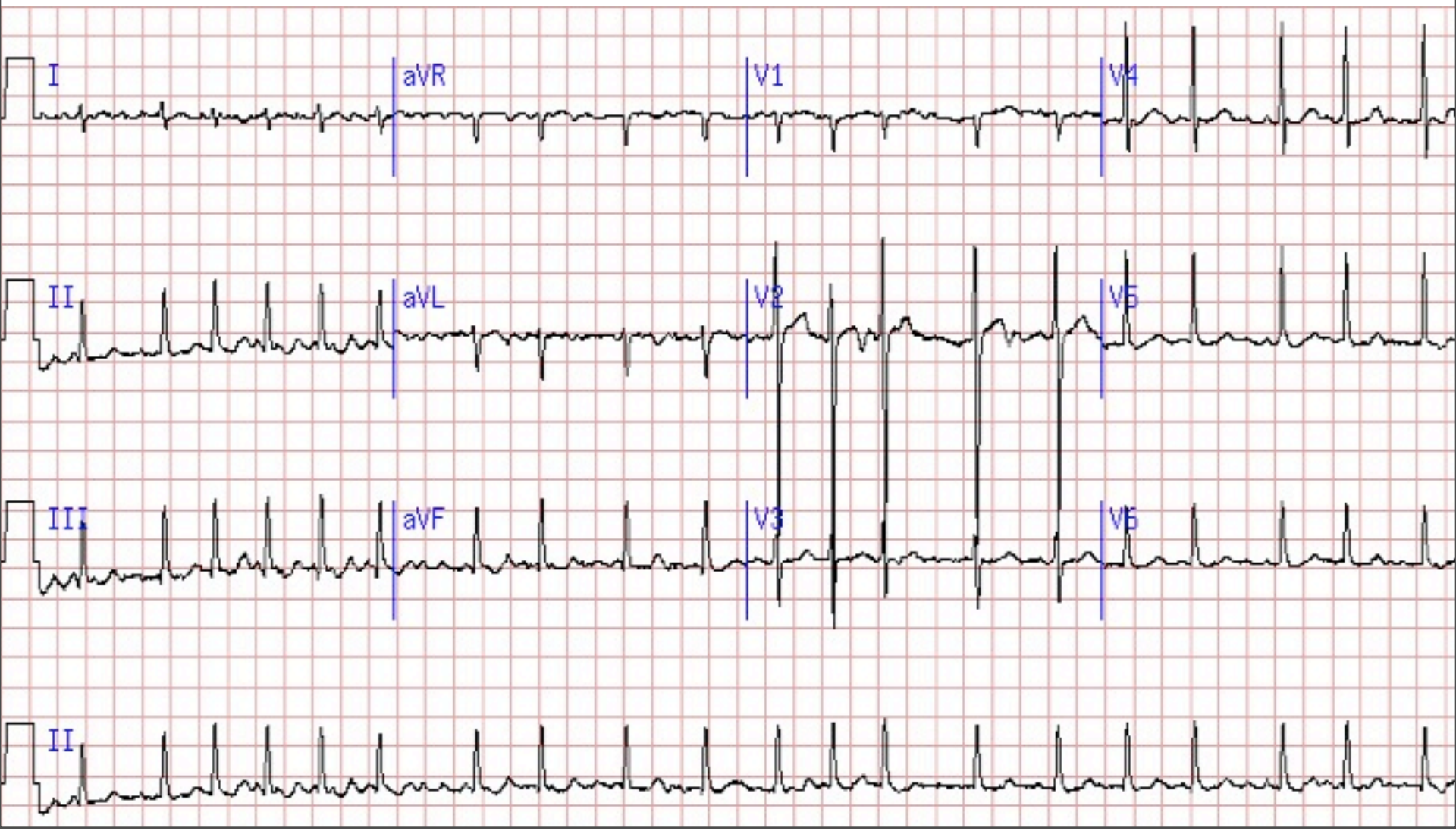
Atrial Fibrillation

Pharmacological therapy of AF

นพ. ธรณิศ จันทรารัตน์
รพ. พระมงกุฎเกล้า


I
aVR
V1
V4
II
aVL
V2
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III
aVF
V3
V6
II

AF Prevalence by Age and Sex

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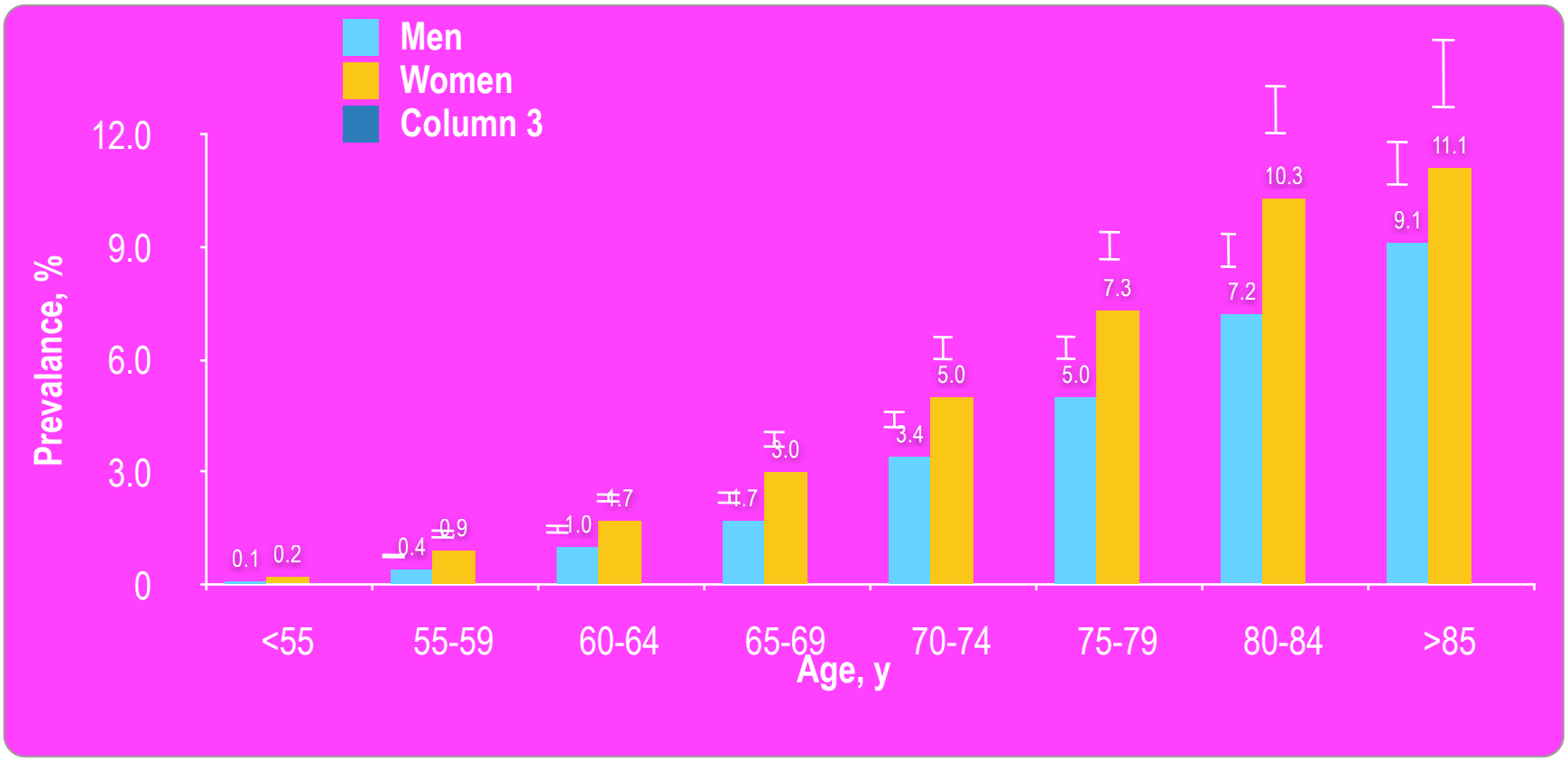


Go AS, et al. *JAMA.* 2001;285:2370-2375.

Principle of Treatment

- Anticoagulant for Stroke Prevention
- Rate or Rhythm control

Definition of AF

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 d.
Longstanding persistent AF	• Continuous AF of >12 mo duration.
Permanent AF	• Permanent AF is used when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF. • Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preferences evolve.

Anticoagulants

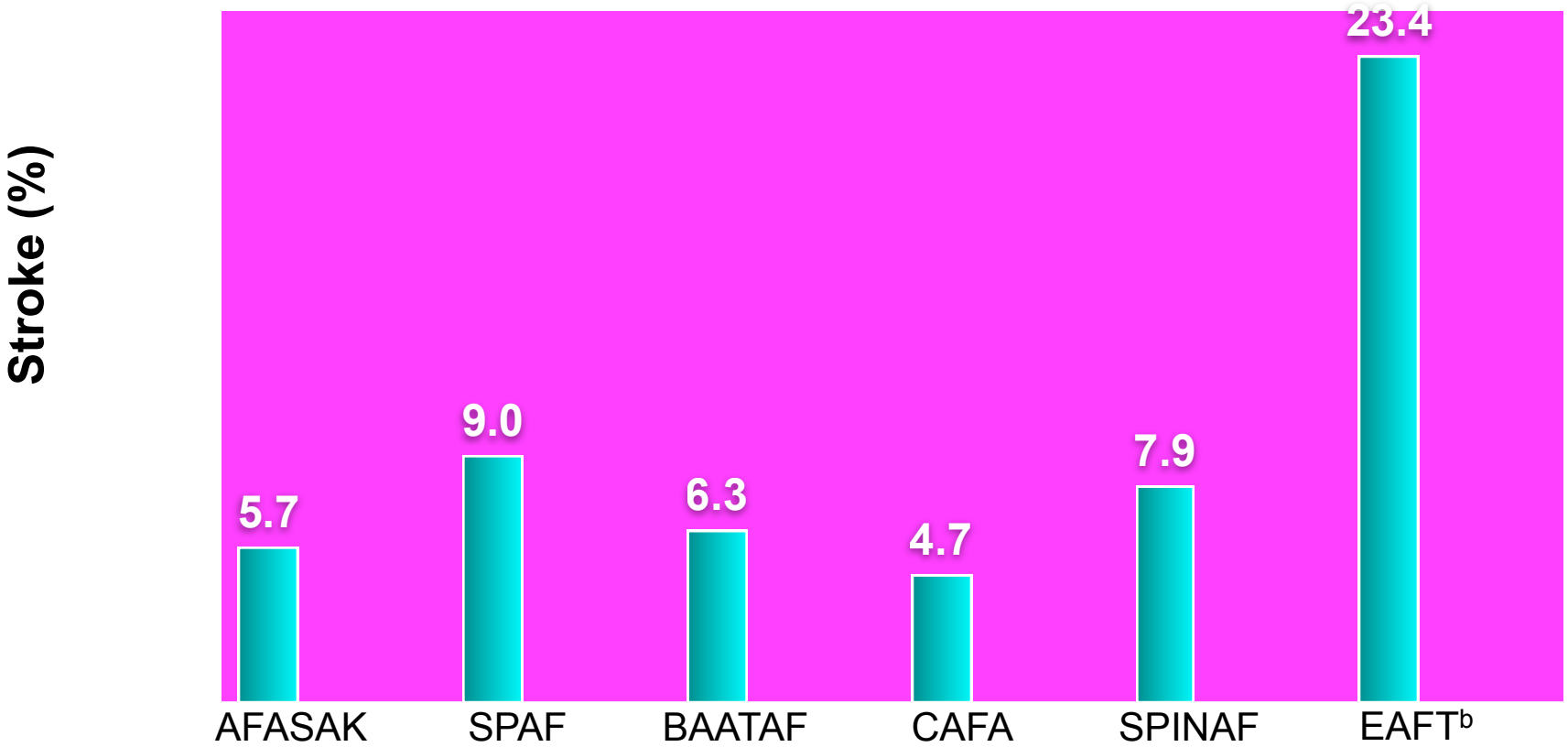
- **Warfarin**
- **NOACs**
- **Aspirin**
- **Clopidogrel**

AF and Risk for Stroke

- The annual rate of ischemic stroke is **approximately 5%** among people with nonvalvular AF, 2 to 7 times that of people without AF
- The rate of brain ischemia (TIAs and "silent" strokes) exceeds 7%
- Long-term follow-up studies:
  - In the Framingham study, people with rheumatic heart disease and AF had a 17-fold increase in stroke risk compared with age-matched controls and a 5-fold increase compared with those who had nonrheumatic AF

Fuster V, et al. *Circulation.* 2006;114:257-354.

Stroke Rates in Placebo-Treated Patients With AF



[a]Patients not anticoagulated; [b]Secondary prevention.

Hart et al. *Ann Intern Med. Ann Intern Med*. 2007;146:857-867.

CHA_2DS_2-VASc	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Aged 65–74 years	1
Sex category (i.e. female gender)	1
Maximum score	9

Anticoagulation in AF: Stroke Risk Reductions

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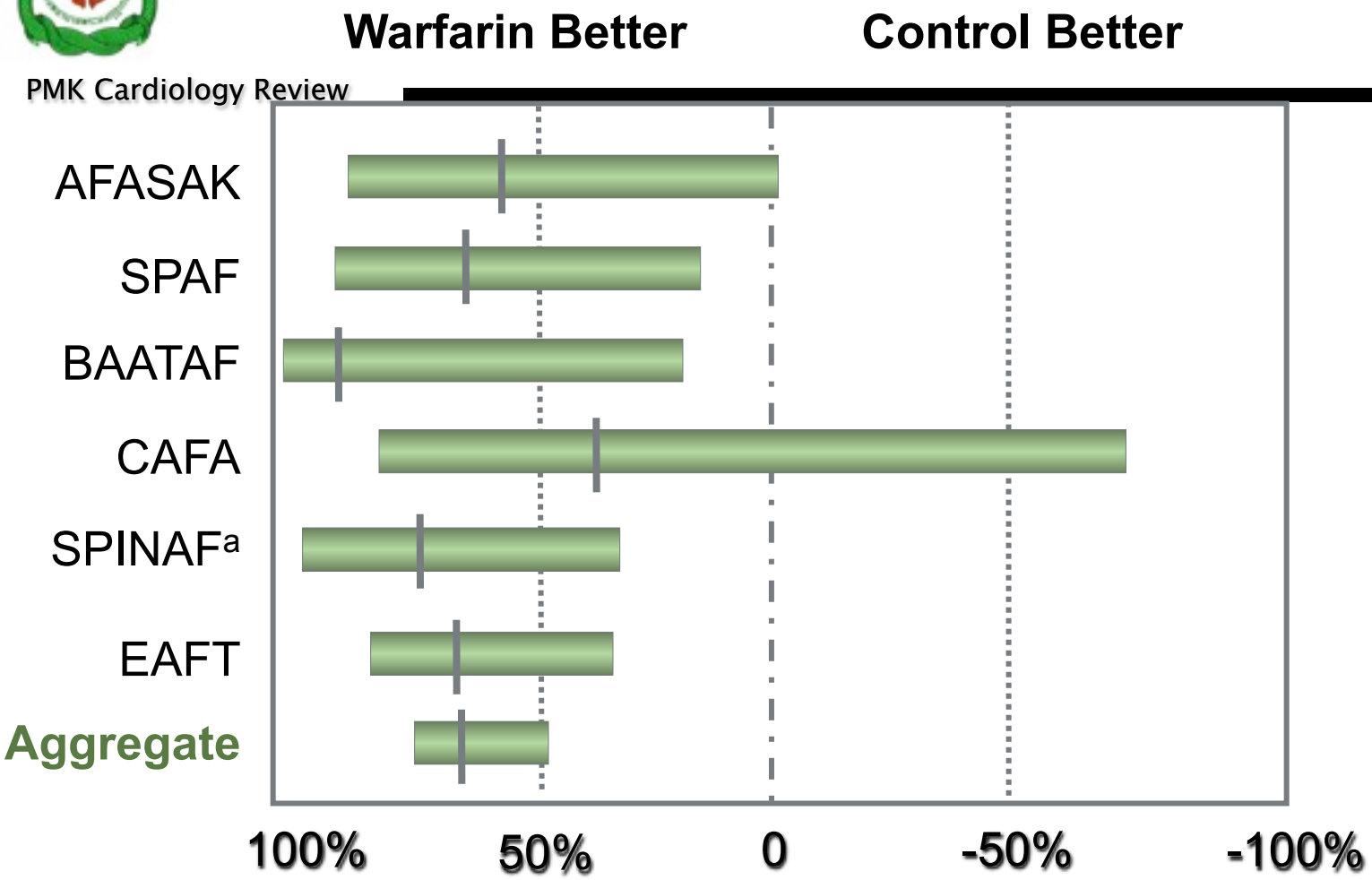

[a]Only SPINAF used placebo-controlled, double-blind design; no women included.

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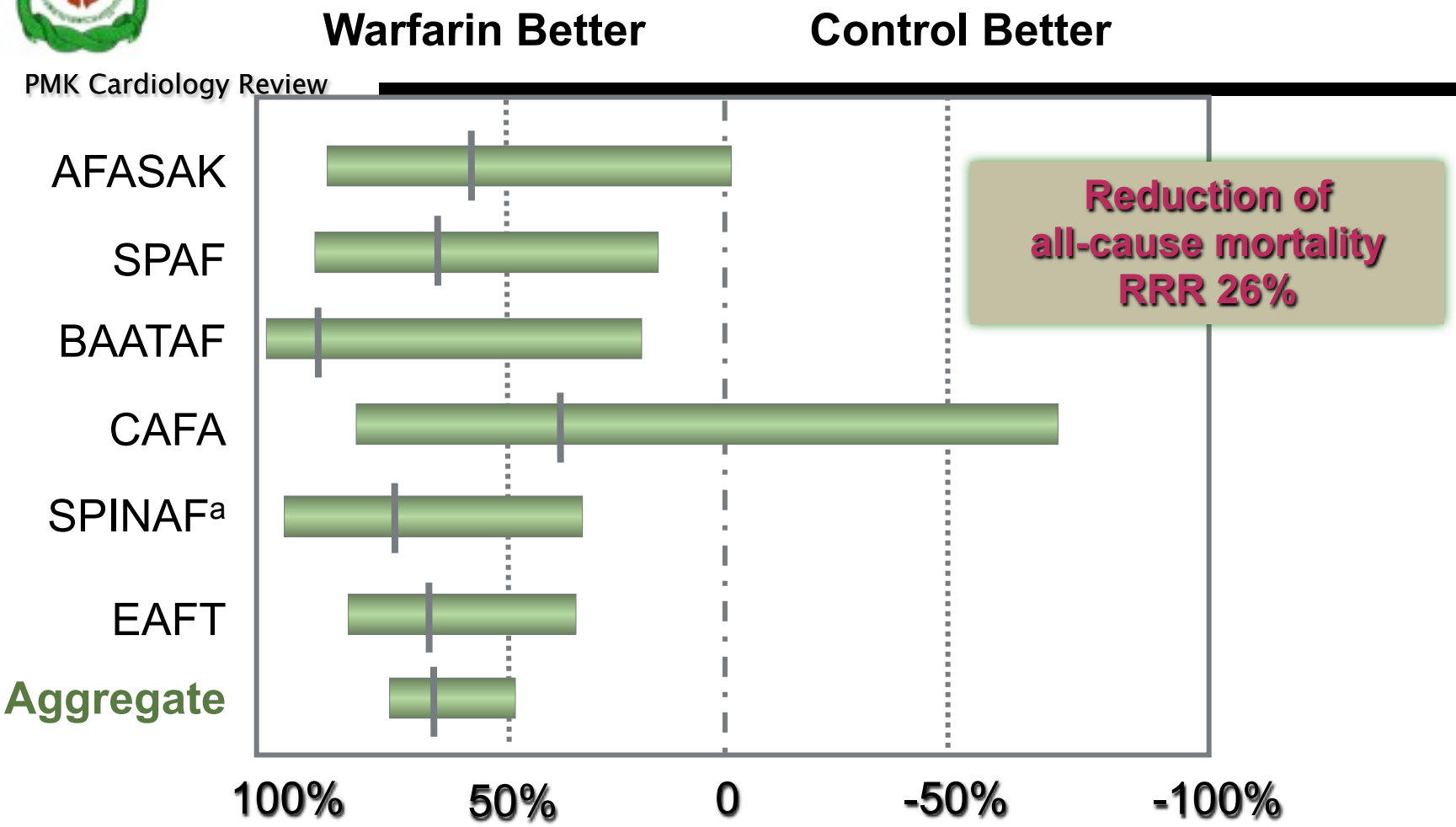

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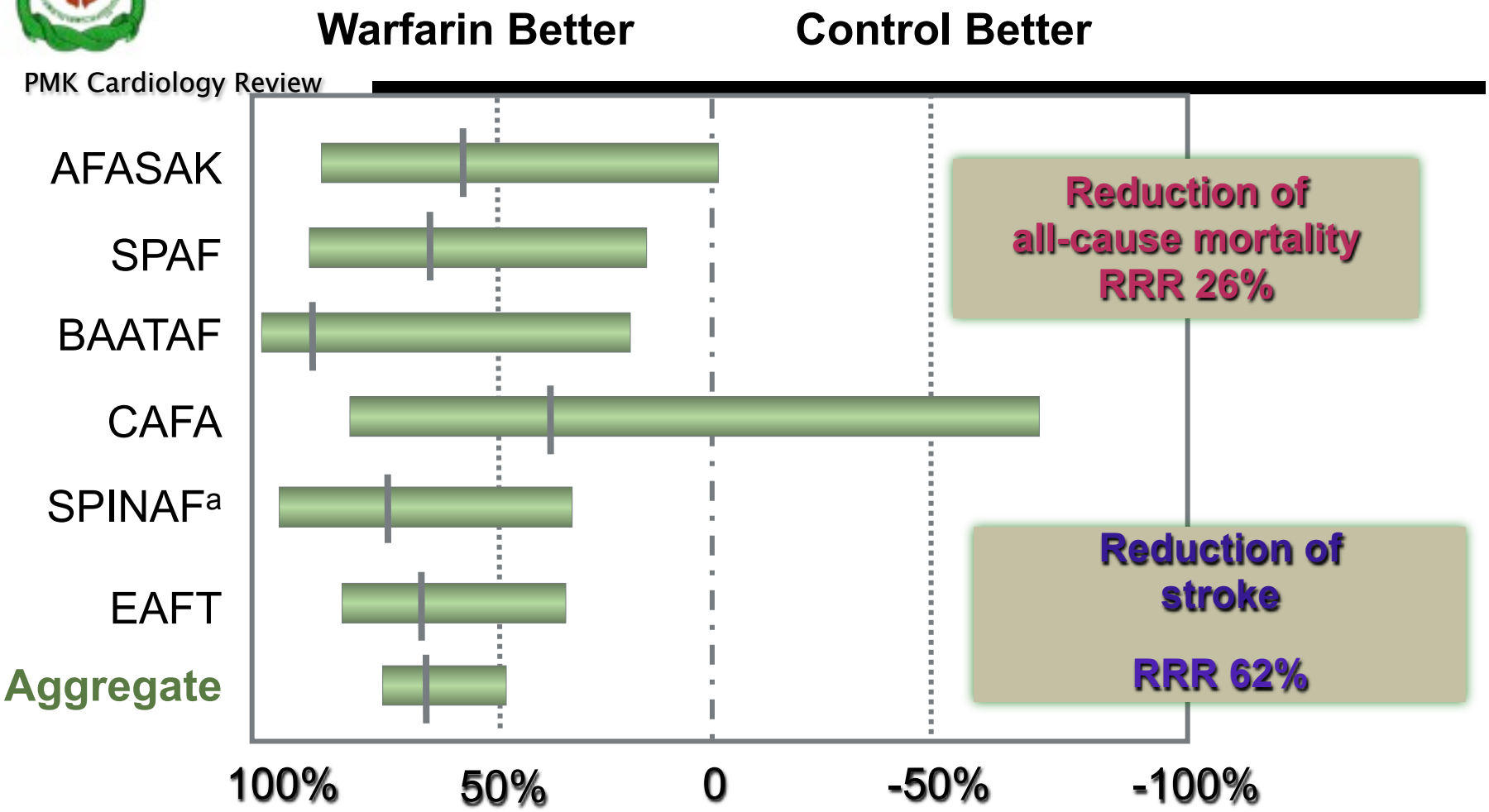

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BACKGROUND

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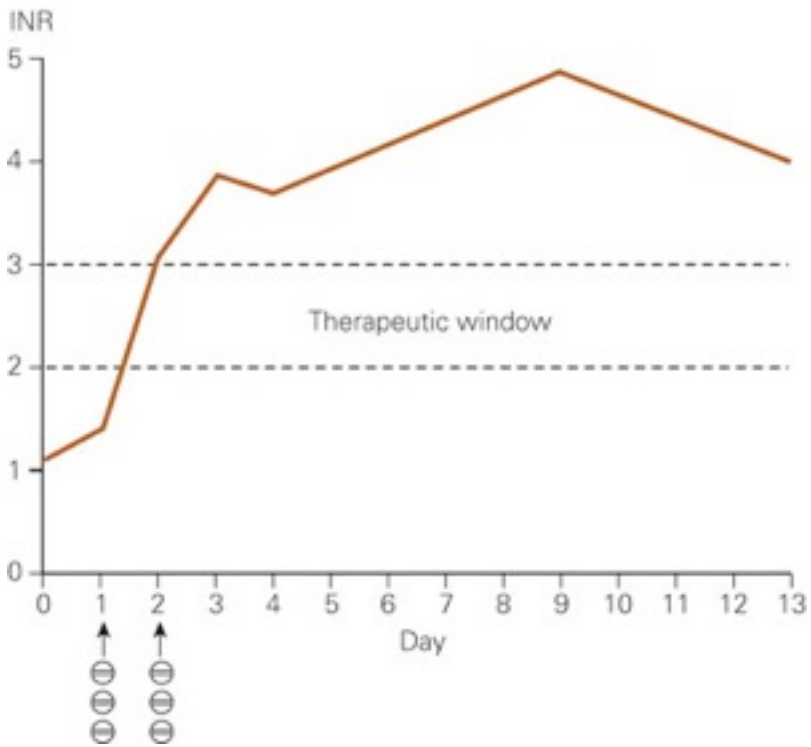
Warfarin



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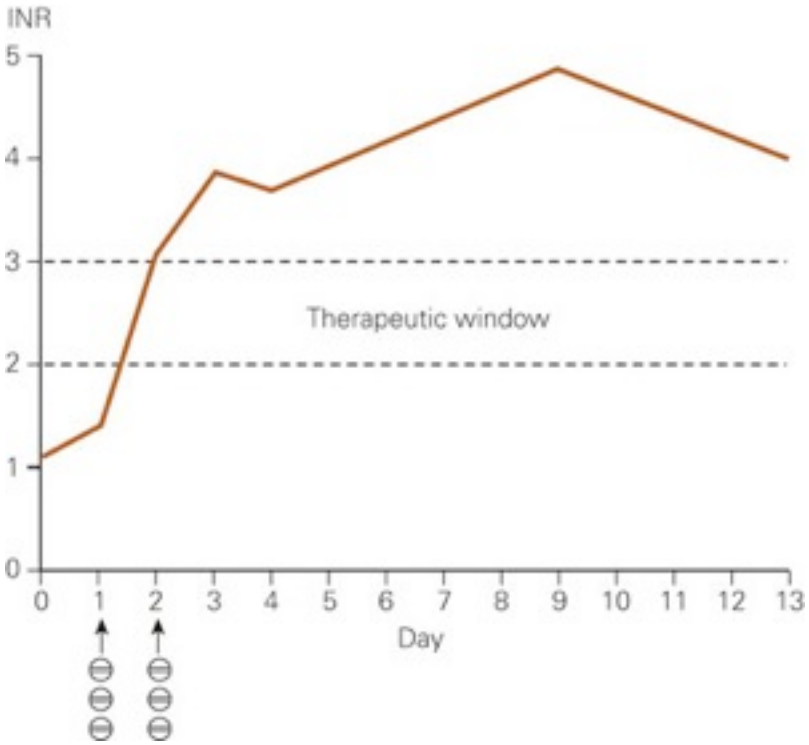
Warfarin



BACKGROUND

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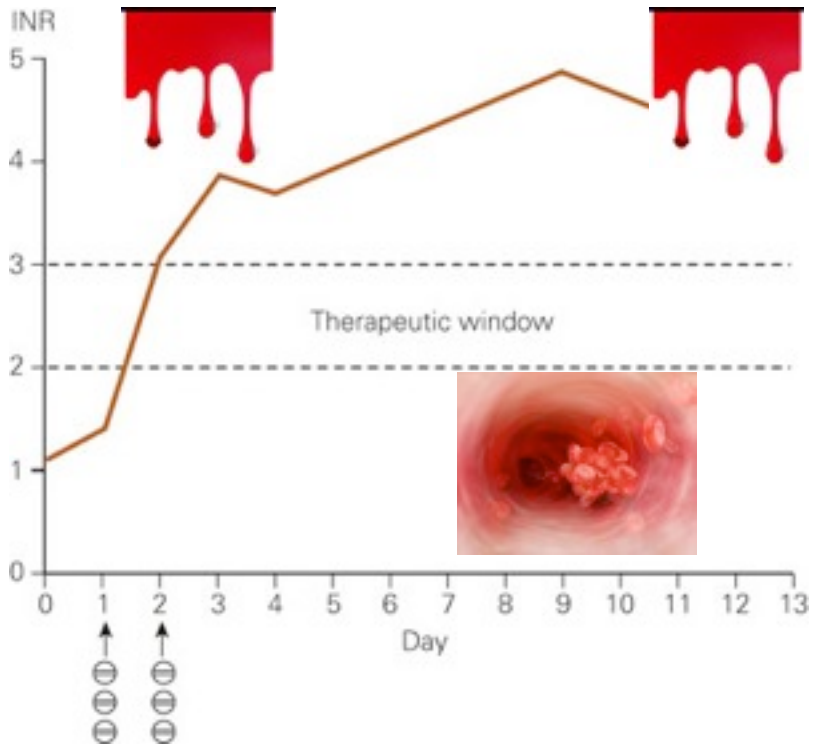

Substantial risk of major bleedings

(approximately **1.2%** per year)

Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. Chest 2001; 119:194S–206S.

BACKGROUND

Warfarin

Bleeding

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Table 5. Incidence Rates of Ischemic Stroke and Intracranial Hemorrhage among Patients with Nonvalvular Atrial Fibrillation Who Were Taking Warfarin, According to the International Normalized Ratio (INR) at the Time of the Stroke.*

INR	Person-yr†	Stroke (95% CI) (N=152)	Person-yr†	Intracranial Hemorrhage (95% CI) (N=58)
		rate/100 person-yr		*rate/100 person-yr*
<1.5	556	7.7 (5.7–10.4)	561	0.5 (0.2–1.7)
1.5–1.9	2847	1.9 (1.4–2.4)	2867	0.3 (0.1–0.6)
2.0–2.5	5357	0.4 (0.3–0.7)	5400	0.3 (0.2–0.4)
2.6–3.0	2388	0.9 (0.6–1.4)	2409	0.5 (0.3–0.9)
3.1–3.5	834	0.7 (0.3–1.6)	843	0.6 (0.3–1.4)
3.6–3.9	243	0.4 (0.1–2.9)	247	0.4 (0.1–2.9)
4.0–4.5	144	1.4 (0.4–5.5)	147	2.7 (1.0–7.3)
>4.5	115	2.6 (0.8–8.1)	118	9.4 (5.2–16.9)

Hylek, EM *et al*. *N Engl J Med*. 2003;349:1019-2614

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NOVEL ANTICOAGULANTS FOR STROKE PREVENTION IN AF

	Dabigatran (RE-LY)[70, 71]	Rivaroxaban (ROCKET-AF)[3]	Apixaban (ARISTOTLE)[4]
Drug characteristics			
Mechanism	Oral direct thrombin inhibitor	Oral direct factor Xa inhibitor	Oral direct factor Xa inhibitor
Bioavailability, %	6	60–80	50
Time to peak levels, h	3	3	3
Half-life, h	12–17	5–13	9–14
Excretion	80% renal	2/3 liver, 1/3 renal	25% renal, 75% faecal
Dose	150 mg b.i.d.	20 mg o.d.	5 mg b.i.d.
Dose in renal impairment	110 mg b.i.d.	15 mg o.d. (if CrCl 30-49 mL/min)	2.5 mg b.i.d.
Special considerations	Intestinal absorption is pH-dependent and is reduced in patients taking proton pump inhibitors	Higher levels expected in patients with renal or hepatic failure	
	Increased risk of bleeding in patients taking verapamil/amiodarone/quinidine/ketoconazole	Activity lower in fasted patients so should be taken after food	

*** Adjusted based on renal function** **1.** Connolly SJ, et al. *N Engl J Med* 2009;361:1139-1151; **2.** www.clinicaltrials.gov, clinical trial identifier: NCT00781391; **3.** Eikelboom JW, et al. *Am Heart J* 2010;159:348-353; **4.** ROCKET-AF Investigators. *Am Heart J* 2010;159:340-347; **5.** Lopes RD, et al. *Am Heart J* 2010;159:331-339; **6.** AMADEUS Investigators et al. *Lancet* 2008;371:315-321; 7. Sanofi-aventis press release: http://en.sanofi-aventis.com/binaries/20091221_rdupdate_en_tcm28-26977.pdf Accessed March 2010.

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Study characteristics			
Study design	Randomized, open-label	Randomized, double-blind	Randomized, double-blind
Number of patients	18 111	14 264	18 201
Follow-up period, years	2	1.9	1.8
Randomized groups	Dose-adjusted warfarin vs. blinded doses of dabigatran (150 mg b.i.d., 110 mg b.i.d.)	Dose-adjusted warfarin vs. rivaroxaban 20 mg o.d.	Dose-adjusted warfarin vs. apixaban 5 mg b.i.d.
Baseline patient characteristics			
Age, years	71.5 ± 8.7 (mean ± SD)	73 (65–78) [median (interquartile range)]	70 (63–76) [median (interquartile rang
Male sex, %	63.6	61.3	64.5
$CHADS_2$ (mean)	2.1	3.5	2.1

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Outcomes (% per year)							
	Warfarin	Dabigatran 150	Dabigatran 110	Warfarin	Rivaroxaban	Warfarin	Apixaban
	(*n* = 6022)	(*n* = 6076)	(*n* = 6015)	(*n* = 7133)	(*n* = 7131)	(*n* = 9081)	(*n* = 9120)
		(RR, 95% CI; *P* value)	(RR, 95% CI; *P* value)		(HR, 95% CI; *P* value)		(HR, 95% CI; *P* value)
Stroke/systemic embolism	1.69	1.11 (0.66, 0.53–0.82; *P* for superiority <0.001)	1.53 (0.91, 0.74–1.11; *P* for non-inferiority <0.001)	2.4	2.1 (0.88, 0.75–1.03; *P* for non-inferiority <0.001, *P* for superiority = 0.12) (ITT)	1.6	1.27 (0.79, 0.66–0.95; *P* <0.001 for non-inferiority, *P* = 0.01 for superiority)
Ischaemic stroke	1.2	0.92 (0.76, 0.60–0.98; *P* = 0.03)	1.34 (1.11, 0.89–1.40; *P* = 0.35)	1.42	1.34 (0.94; 0.75–1.17; *P* = 0.581)	1.05	0.97 (0.92, 0.74–1.13; *P* = 0.42)
Haemorrhagic stroke	0.38	0.10 (0.26, 0.14–0.49; *P* <0.001)	0.12 (0.31, 0.17–0.56; *P* <0.001)	0.44	0.26 (0.59; 0.37–0.93; *P* =0.024)	0.47	0.24 (0.51, 0.35–0.75; *P* <0.001)
Major bleeding	3.36	3.11 (0.93, 0.81–1.07; *P* = 0.31)	2.71 (0.80, 0.69–0.93; *P* = 0.003)	3.4	3.6 (*P* = 0.58)	3.09	2.13 (0.69, 0.60–0.80; *P* <0.001)
Intracranial bleeding	0.74	0.30 (0.40, 0.27–0.60; *P* <0.001)	0.23 (0.31, 0.20–0.47; *P* <0.001)	0.7	0.5 (0.67; 0.47–0.93; *P* = 0.02)	0.80	0.33 (0.42, 0.30–0.58; *P* <0.001)
Extracranial bleeding	2.67	2.84 (1.07, 0.92–1.25;	2.51 (0.94, 0.80–1.10;	–	–	–	–

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Outcomes (% per year)							
Gastrointestinal bleeding	1.02	1.51 (1.50, 1.19–1.89; *P* <0.001)	1.12 (1.10, 0.86–1.41; *P* = 0.43)	2.2	3.2 (*P* <0.001)	0.86	0.76 (0.89, 0.70–1.15; *P* = 0.37)
Myocardial infarction	0.64	0.81 (1.27, 0.94-1.71; *P* = 0.12)	0.82 (1.29, 096-1.75; *P* = 0.09)	1.1	0.9 (0.81; 0.63–1.06; *P* = 0.12)	0.61	0.53 (0.88, 0.66–1.17; *P* = 0.37)
Death from any cause	4.13	3.64 (0.88, 0.77–1.00; *P* = 0.051)	3.75 (0.91, 0.80–1.03; *P* = 0.13)	2.2	1.9 (0.85; 0.70–1.02; *P* = 0.07)	3.94	3.52 (0.89, 0.80–0.99; *P* = 0.047)
% Discontinuation at the end of follow-up	10.2	15.5	14.5	22.2	23.7	27.5	25.3
% Discontinuation/year	5.1	7.8	7.3	11.7	12.5	15.3	14.1

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Efficacy and Safety of the Novel Oral Anticoagulants in Atrial Fibrillation : A Systematic Review and Meta-Analysis of the Literature

Francesco Dentali, Nicoletta Riva, Mark Crowther, Alexander G.G. Turpie, Gregory Y.H. Lip and Walter Ageno

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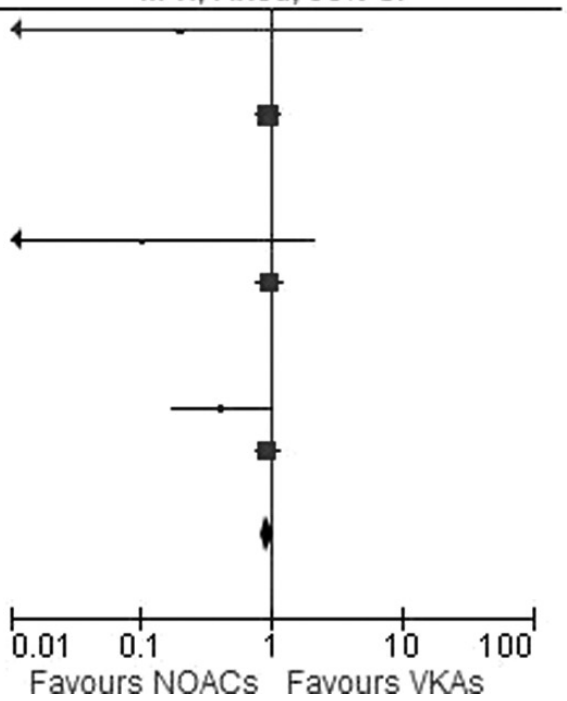
B Ischemic stroke

Study or Subgroup	NOACs Events	NOACs Total	VKAs Events	VKAs Total	Weight	Risk Ratio M-H, Fixed, 95% CI
NCT01136408 (D)	0	104	1	62	0.4%	0.20 [0.01, 4.84]
PETRO	0	166	0	70		Not estimable
RE-LY	255	12091	134	6022	34.6%	0.95 [0.77, 1.17]
CHUNG	0	159	0	75		Not estimable
YAMASHITA	0	260	0	125		Not estimable
ARISTOTLE-J	0	148	2	74	0.6%	0.10 [0.00, 2.07]
ARISTOTLE	149	9120	155	9081	30.0%	0.96 [0.77, 1.20]
NCT00973245 (R1)	0	75	0	27		Not estimable
NCT00973323 (R2)	0	50	0	26		Not estimable
J-ROCKET-AF	7	637	17	637	3.3%	0.41 [0.17, 0.99]
ROCKET-AF	149	7061	161	7082	31.1%	0.93 [0.74, 1.16]
Total (95% CI)		**29871**		**23281**	**100.0%**	**0.92 [0.81, 1.04]**
Total events	560		470			

Heterogeneity: Chi² = 6.40, df = 5 (P = 0.27); I² = 22%

Test for overall effect: Z = 1.35 (P = 0.18)

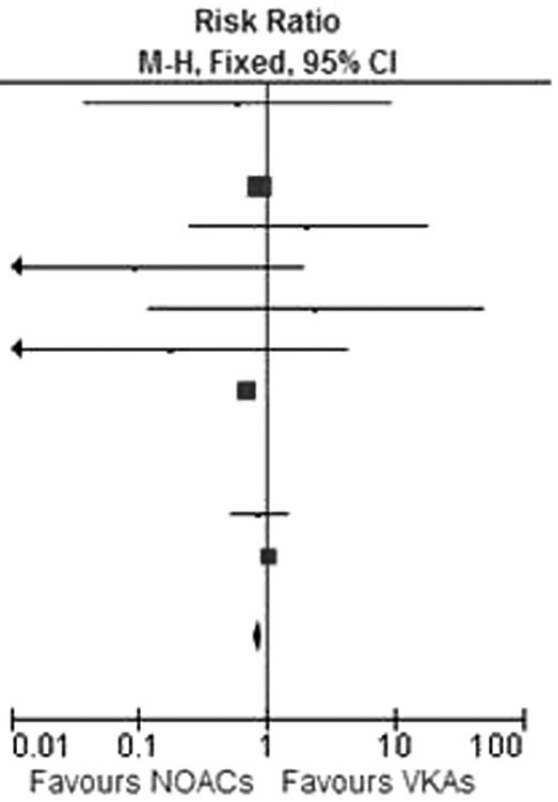


A Major bleeding

Study or Subgroup	NOACs Events	NOACs Total	VKAs Events	VKAs Total	Weight	Risk Ratio M-H, Fixed, 95% CI
NCT01136408 (D)	1	104	1	62	0.1%	0.60 [0.04, 9.36]
PETRO	0	166	0	70		Not estimable
RE-LY	741	12091	421	6022	38.8%	0.88 [0.78, 0.98]
WEITZ	6	713	1	250	0.1%	2.10 [0.25, 17.39]
CHUNG	0	159	2	75	0.2%	0.10 [0.00, 1.95]
YAMASHITA	2	260	0	125	0.0%	2.41 [0.12, 49.90]
ARISTOTLE-J	0	143	1	75	0.1%	0.18 [0.01, 4.27]
ARISTOTLE	327	9088	462	9052	31.9%	0.70 [0.61, 0.81]
NCT00973245 (R1)	0	75	0	27		Not estimable
NCT00973323 (R2)	0	50	0	26		Not estimable
J-ROCKET-AF	26	639	30	639	2.1%	0.87 [0.52, 1.45]
ROCKET-AF	395	7111	386	7125	26.6%	1.03 [0.89, 1.18]
Total (95% CI)		30599		23548	100.0%	0.86 [0.80, 0.93]
Total events	1498		1304			

Heterogeneity: $Chi^2 = 18.58$, $df = 8$ ($P = 0.02$); $I^2 = 57\%$

Test for overall effect: $Z = 4.03$ ($P < 0.0001$)

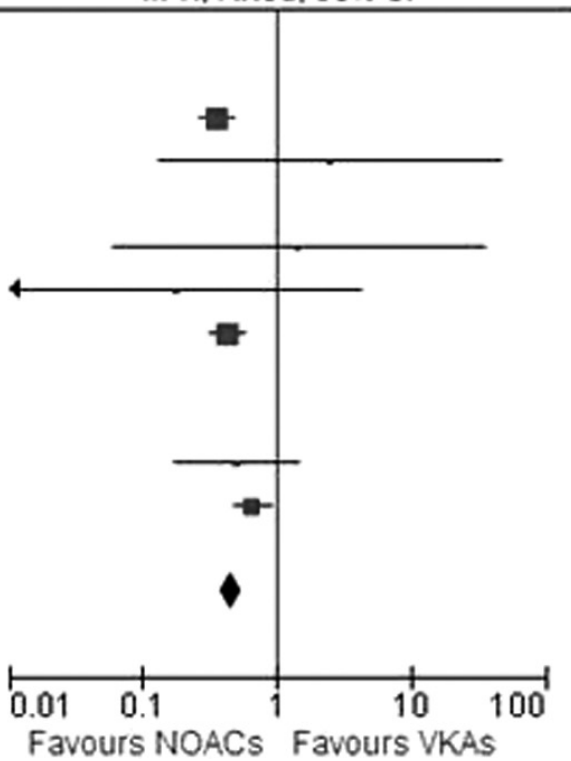


Intracranial bleeding

Study or Subgroup	NOACs Events	NOACs Total	VKAs Events	VKAs Total	Weight	Risk Ratio M-H, Fixed, 95% CI
NCT01136408 (D)	0	104	0	62		Not estimable
PETRO	0	166	0	70		Not estimable
RE-LY	64	12091	90	6022	35.4%	0.35 [0.26, 0.49]
WEITZ	3	713	0	250	0.2%	2.46 [0.13, 47.47]
CHUNG	0	159	0	75		Not estimable
YAMASHITA	1	260	0	125	0.2%	1.45 [0.06, 35.30]
ARISTOTLE-J	0	143	1	75	0.6%	0.18 [0.01, 4.27]
ARISTOTLE	52	9088	122	9052	36.0%	0.42 [0.31, 0.59]
NCT00973245 (R1)	0	75	0	27		Not estimable
NCT00973323 (R2)	0	50	0	26		Not estimable
J-ROCKET-AF	5	639	10	639	2.9%	0.50 [0.17, 1.45]
ROCKET-AF	55	7111	84	7125	24.7%	0.66 [0.47, 0.92]
Total (95% CI)		30599		23548	100.0%	0.46 [0.39, 0.56]
Total events	180		307			

Heterogeneity: $Chi^2 = 9.15$, $df = 6$ ($P = 0.17$); $I^2 = 34\%$

Test for overall effect: $Z = 8.22$ ($P < 0.00001$)



European Heart Journal
doi:10.1093/eurheartj/ehs253

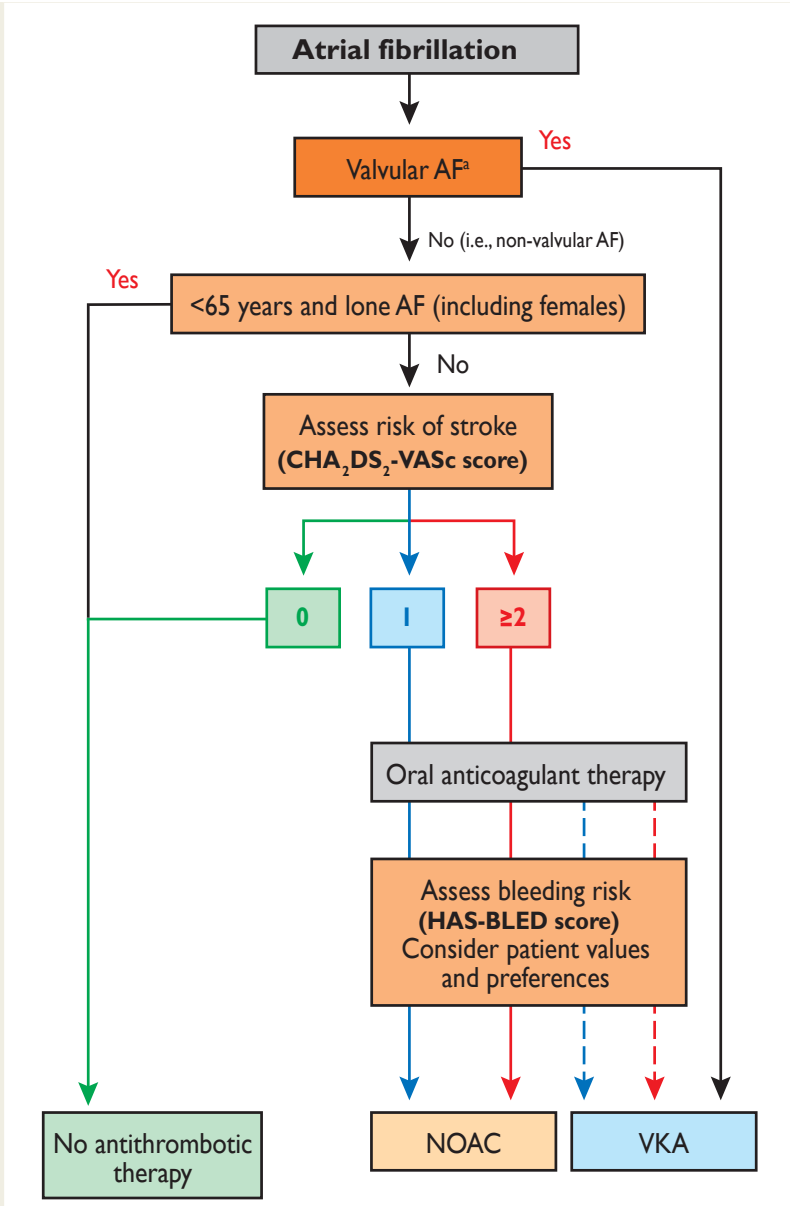
2012 focused update of the ESC Guidelines for the management of atrial fibrillation

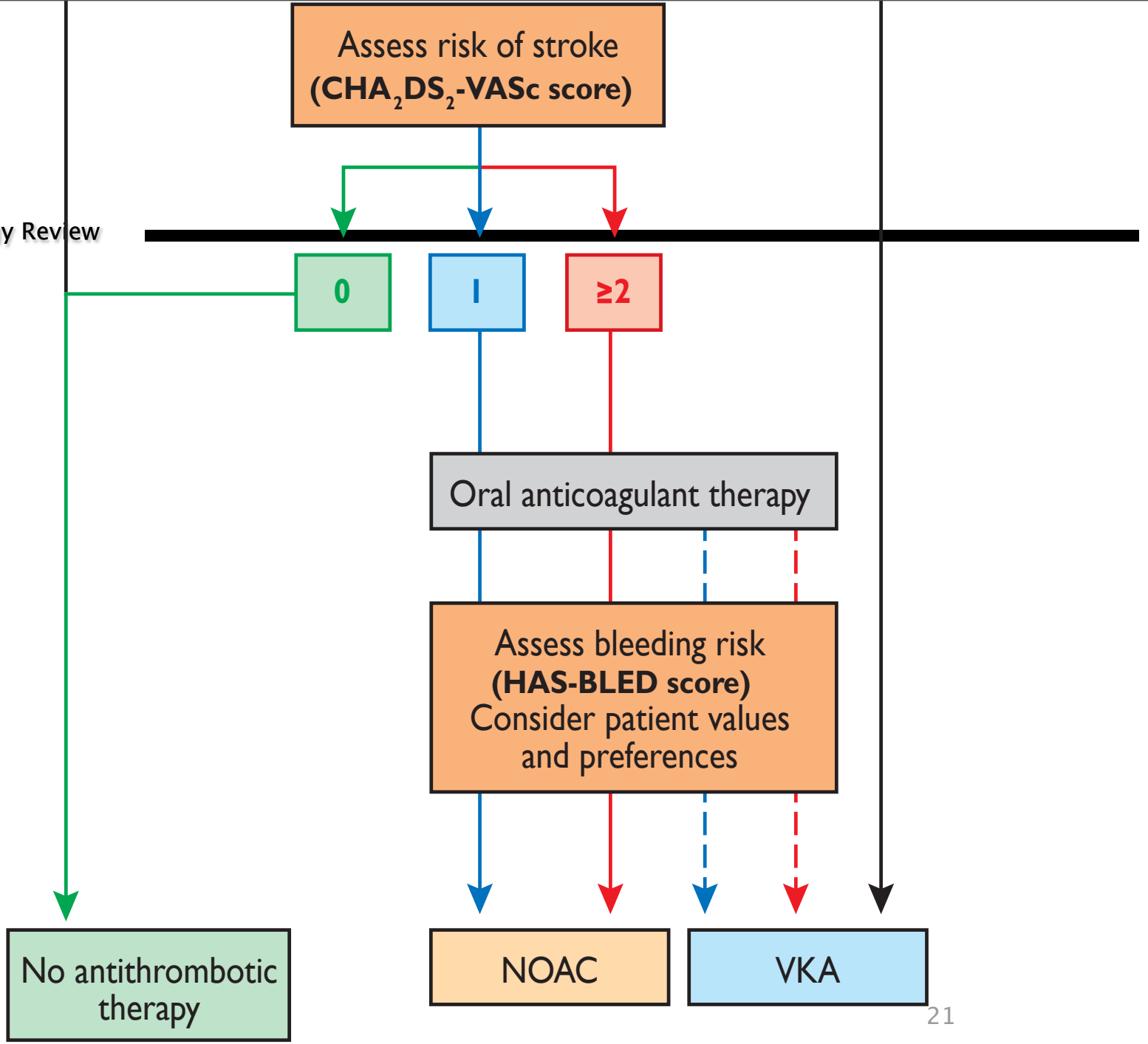
An update of the 2010 ESC Guidelines for the management of atrial fibrillation
Developed with the special contribution of the European Heart Rhythm Association

Authors/Task Force Members: A. John Camm (Chairperson) (UK)*, Gregory Y.H. Lip (UK), Raffaele De Caterina (Italy), Irene Savelieva (UK), Dan Atar (Norway), Stefan H. Hohnloser (Germany), Gerhard Hindricks (Germany), Paulus Kirchhof (UK)

ESC 2012 Focus Update

PMK Cardiology




Assess risk of stroke
(CHA2DS2-VASc score)
0
1
≥2
Oral anticoagulant therapy
Assess bleeding risk
(HAS-BLED score)
Consider patient values
and preferences
No antithrombotic
therapy
NOAC
VKA

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

Recommendations	COR
Antithrombotic therapy based on shared decision-making, discussion of risks of stroke and bleeding, and patient's preferences	I
Antithrombotic therapy selection based on risk of thromboembolism	I
CHA_2DS_2-VASc score recommended to assess stroke risk	I
Warfarin recommended with mechanical heart valves. Target INR intensity should be based on the type and location of prosthesis	I

With prior stroke, TIA, or CHA_2DS_2-VASc score ≥2, oral anticoagulants recommended. Options include:	
• Warfarin	I
• Dabigatran, rivaroxaban, or apixaban	I
With warfarin, determine INR at least weekly during initiation and monthly when stable	I
Direct thrombin or factor Xa inhibitor recommended, if unable to maintain therapeutic INR	I
Re-evaluate the need for anticoagulation at periodic intervals	I

With nonvalvular AF and CHA_2DS_2-VASc score of 0, it is reasonable to omit antithrombotic therapy	IIa
With CHA_2DS_2-VASc score ≥2 and end-stage CKD (CrCl <15 mL/min) or on hemodialysis, it is reasonable to prescribe warfarin for oral anticoagulation	IIa

With nonvalvular AF and a CHA_2DS_2-VASc score of 1, no antithrombotic therapy or treatment with an oral anticoagulant or aspirin may be considered	IIb
With moderate-to-severe CKD and CHA_2DS_2-VASc scores of ≥2, reduced doses of direct thrombin or factor Xa inhibitors may be considered	IIb
For PCI,* BMS may be considered to minimize duration of DAPT	IIb
Following coronary revascularization in patients with CHA_2DS_2-VASc score of ≥2, it may be reasonable to use clopidogrel concurrently with oral anticoagulants, but without aspirin	IIb

Direct thrombin, dabigatran, and factor Xa inhibitor, rivaroxaban, are not recommended with AF and end-stage CKD or on hemodialysis because of the lack of evidence from clinical trials regarding the balance of risks and benefits	III: No Benefit
Direct thrombin inhibitor, dabigatran, should not be used with a mechanical heart valve	III: Harm

Doses of anticoagulant

Renal Function	**Warfarin** (92)	**Dabigatran**† (74)	**Rivaroxaban**† (75)	**Apixaban**† (76)
Normal/Mild Impairment	Dose adjusted for INR 2.0–3.0	150 mg BID (CrCl >30 mL/min)	20 mg QD with the evening meal (CrCl >50 mL/min)	5.0 or 2.5 mg BID‡
Moderate Impairment	Dose adjusted for INR 2.0–3.0	150 mg BID or 75 mg BID§ (CrCl >30 mL/min)	15 mg QD with the evening meal (CrCl 30–50 mL/min)	5.0 or 2.5 mg BID‡
Severe Impairment	Dose adjusted for INR 2.0–3.0‖	75 mg BID§ (CrCl 15–30 mL/min)	15 mg QD with the evening meal (CrCl 15–30 mL/min)	No recommendation, See section 4.2.2.2.¶
End-Stage CKD Not on Dialysis	Dose adjusted for INR 2.0–3.0‖	Not recommended¶ (CrCl <15 mL/min)	Not recommended¶ (CrCl <15 mL/min)	No recommendation, See section 4.2.2.2.¶
End-Stage CKD on Dialysis	Dose adjusted for INR 2.0–3.0‖	Not recommended¶ (CrCl <15 mL/min)	Not recommended¶ (CrCl <15 mL/min)	No recommendation, See section 4.2.2.2.¶#

Theoretical Benefit of Rhythm Control

Improved hemodynamics

Relief of symptoms

Improved exercise tolerance

Reduced risk of stroke

Avoidance of anticoagulants

Rhythm Control Strategies

- Electrical
- Pharmacological
- Radiofrequency ablation
- Upstream therapy

Electrical cardioversion

- Cardioversion is recommended when a rapid ventricular response to AF or atrial flutter does not respond promptly to pharmacological therapies and contributes to ongoing myocardial ischemia, hypotension, or HF.

- Cardioversion is recommended for patients with AF or atrial flutter and pre-excitation when tachycardia is associated with hemodynamic instability.

- **Elective case**

Rhythm Control

The New England Journal of Medicine

VOLUME 347 DECEMBER 5, 2002 NUMBER 23

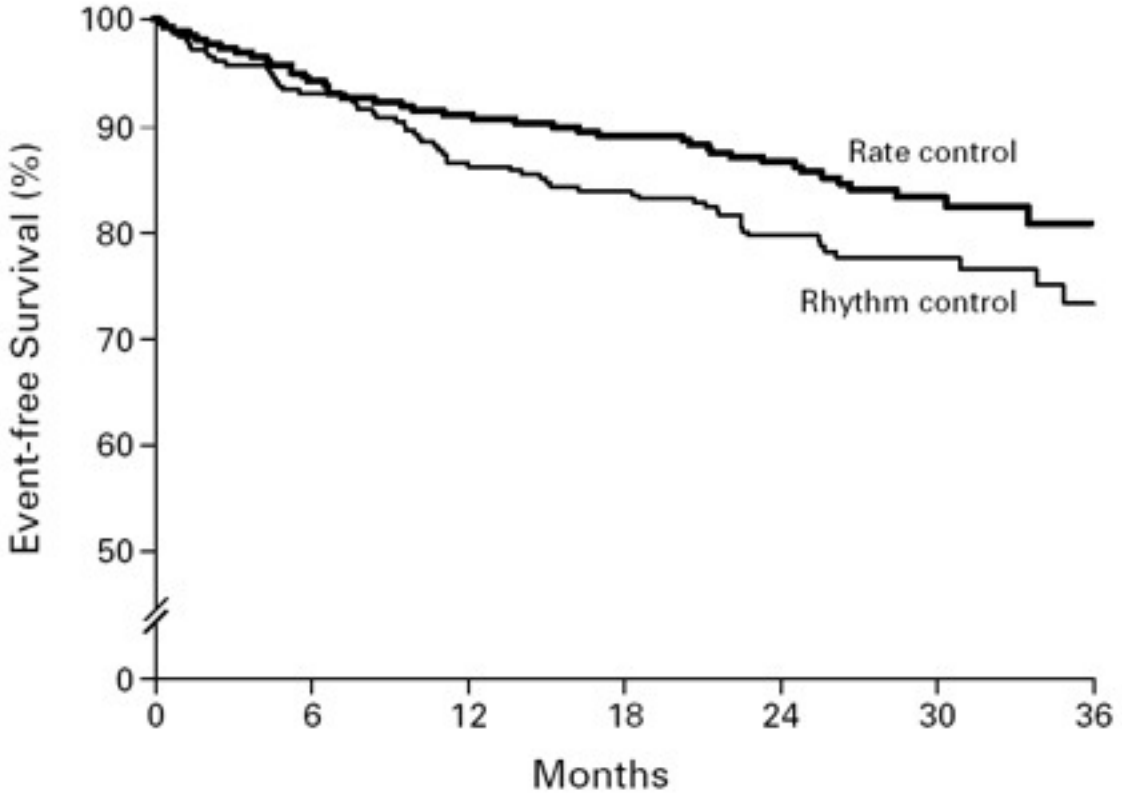
A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

ABSTRACT

Background There are two approaches to the treatment of atrial fibrillation: one is cardioversion and treatment with antiarrhythmic drugs to maintain sinus rhythm, and the other is the use of rate-controlling drugs, allowing atrial fibrillation to persist. In both approaches, the use of anticoagulant drugs is recommended

ATRIAL fibrillation is the most common sustained cardiac arrhythmia, yet the optimal strategy for its management remains uncertain.[1-4] During atrial fibrillation, most symptoms (but perhaps not all) are caused by a poorly controlled or irregular ventricular rate, and the associated risk of death is doubled in patients who have



No. at Risk							
Rate control	256	239	232	222	212	99	25
Rhythm control	266	243	224	218	207	85	24

Figure 2. Kaplan–Meier Curves for Event-free Survival in the Rate-Control and Rhythm-Control Groups.

AFFIRM Trial

-No survival advantage to rhythm control.

-Rhythm control patients were more likely to be hospitilized with adverse drug effects.

- Both groups had similar stroke risk (1% per yr)
  - Majority of strokes when warfarin stopped or INR subtherapeutic
  - Warfarin required long term even if sinus rhythm restored

-Torsades, bradycardic arrest more common with rhythm control.

Class III

- Antiarrhythmic drugs for rhythm control should not be continued when AF becomes permanent (Level of Evidence: C) including dronedarone

- Dronedarone should not be used for treatment of AF in patients with New York Heart Association (NYHA) class III and IV HF or patients who have had an episode of decompensated HF in the past 4 weeks

Upstream Therapy

- Class IIa
- An ACE inhibitor or angiotensin-receptor blocker (ARB) is reasonable for primary prevention of new-onset AF in patients with HF with reduced LVEF

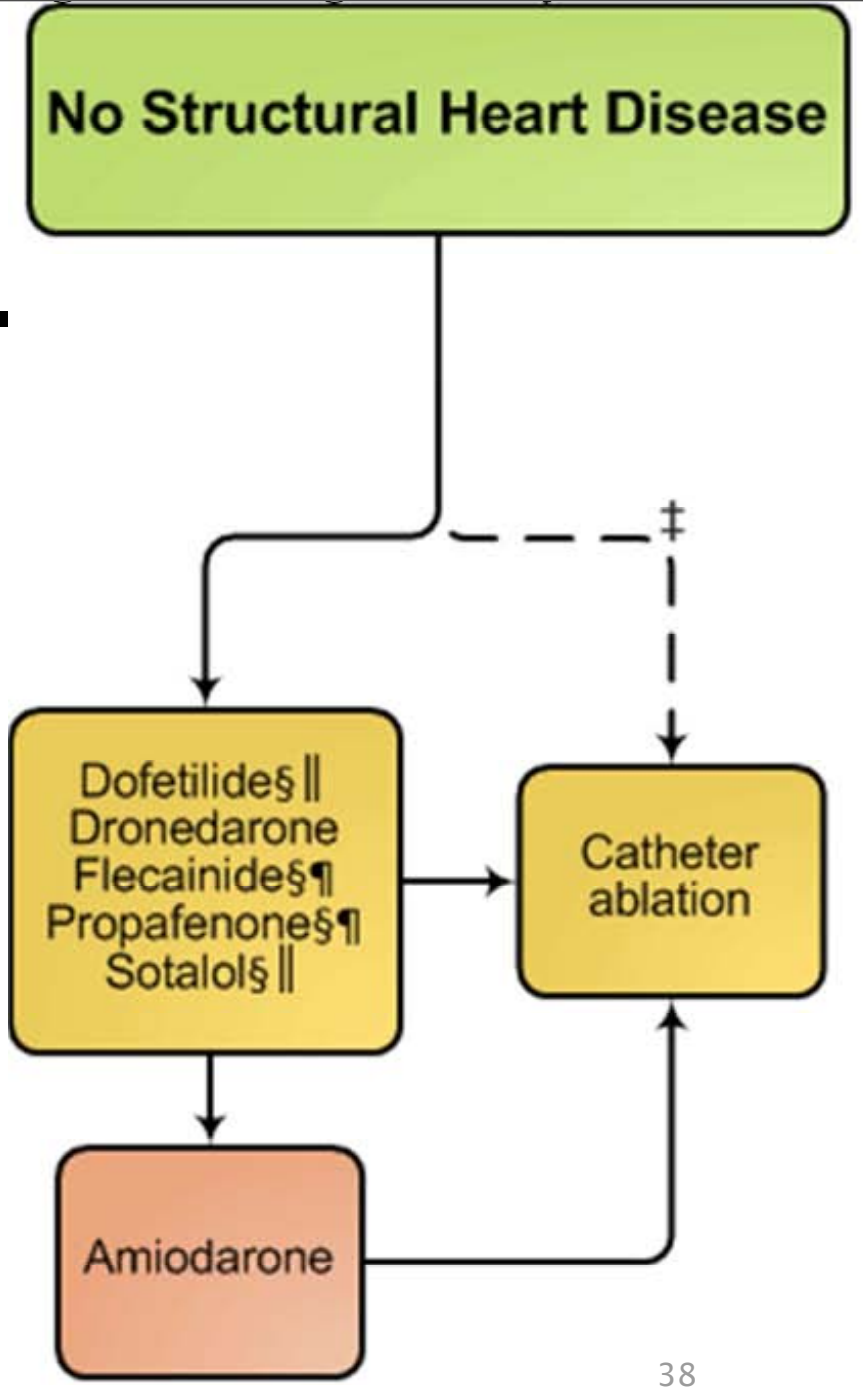
- Class IIb
- Therapy with an ACE inhibitor or ARB may be considered for primary prevention of new-onset AF in the setting of hypertension (150). (Level of Evidence: B) Statin therapy may be reasonable for primary prevention of new-onset AF after coronary artery surgery . (Level of Evidence: A)

Upstream Therapy

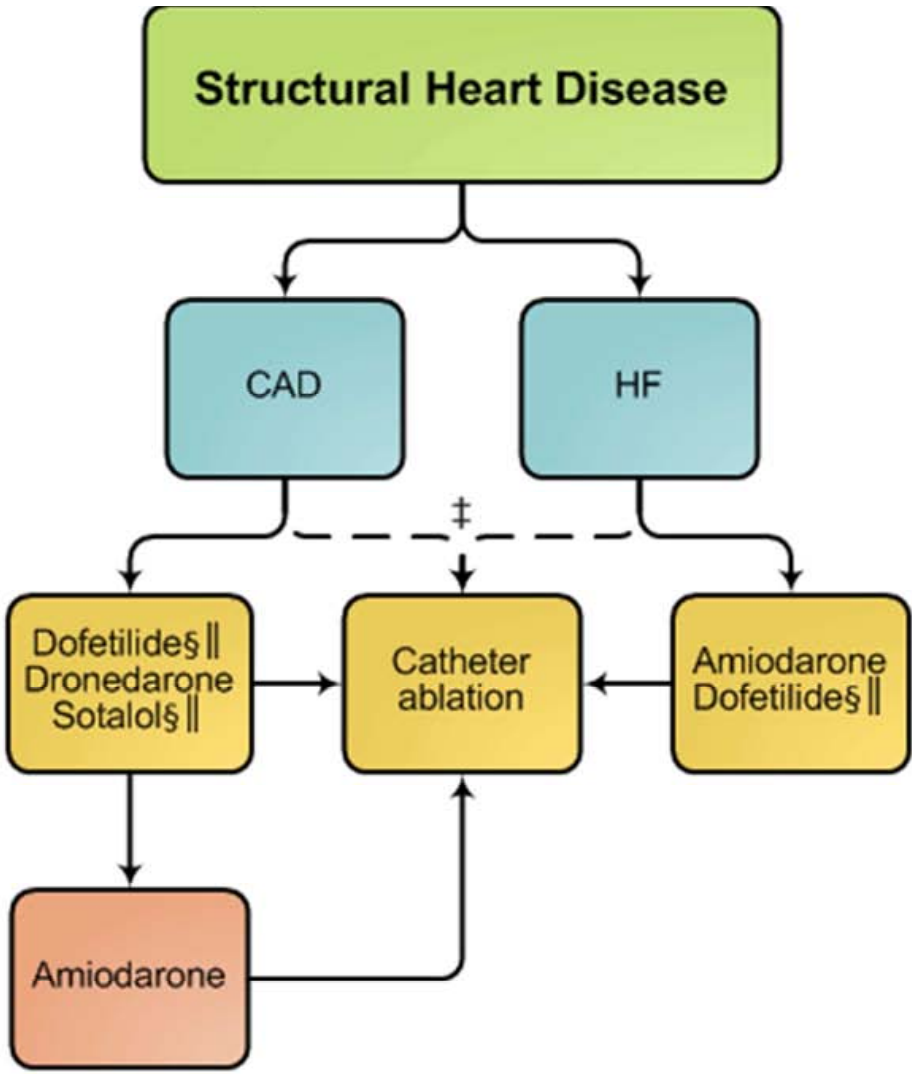
- Class III

- Therapy with an ACE inhibitor, ARB, or statin is not beneficial for primary prevention of AF in patients without cardiovascular disease

ACC 2014


No Structural Heart Disease
‡
Dofetilide§‖
Dronedarone
Flecainide§¶
Propafenone§¶
Sotalol§‖
Catheter ablation
Amiodarone

ACC 2014


Structural Heart Disease
CAD
HF
‡
Dofetilide§‖
Dronedarone
Sotalol§‖
Catheter ablation
Amiodarone
Dofetilide§‖
Amiodarone

PMK Cardiol

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

Isabelle C. Van Gelder, M.D., Hessel F. Groenveld, M.D., Harry J.G.M. Crijns, M.D., Ype S. Tuininga, M.D., Jan G.P. Tijssen, Ph.D., A. Marco Alings, M.D., Hans L. Hillege, M.D., Johanna A. Bergsma-Kadijk, M.Sc., Jan H. Cornel, M.D., Otto Kamp, M.D., Raymond Tukkie, M.D., Hans A. Bosker, M.D., Dirk J. Van Veldhuisen, M.D., and Maarten P. Van den Berg, M.D., for the RACE II Investigators*

ABSTRACT

BACKGROUND

Rate control is often the therapy of choice for atrial fibrillation. Guidelines recommend strict rate control, but this is not based on clinical evidence. We hypothesized that lenient rate control is not inferior to strict rate control for preventing cardiovascular morbidity and mortality in patients with permanent atrial fibrillation.

METHODS

We randomly assigned 614 patients with permanent atrial fibrillation to undergo a lenient rate-control strategy (resting heart rate <110 beats per minute) or a strict rate-control strategy (resting heart rate <80 beats per minute and heart rate during moderate exercise <110 beats per minute). The primary outcome was a composite of death from cardiovascular causes, hospitalization for heart failure, and stroke, systemic embolism, bleeding, and life-threatening arrhythmic events. The duration of follow-up was at least 2 years, with a maximum of 3 years.

From the Department of Cardiology (I.C.V.G., H.F.G., H.L.H., D.J.V.V., M.P.V.B.) and the Trial Coordination Center, Department of Epidemiology (H.L.H., J.A.B.-K.), University Medical Center Groningen, University of Groningen, Groningen; the Interuniversity Cardiology Institute of the Netherlands, Utrecht (I.C.V.G.); Maastricht University Medical Center, Maastricht (H.J.G.M.C.); Deventer Hospital, Deventer (Y.S.T.); Academic Medical Center, University of Amsterdam (J.G.P.T.), and VU University Medical Center (O.K.) — both in Amsterdam; Amphia Hospital, Breda (A.M.A.); Medical Center, Alkmaar (J.H.C.); Kennemer Hospital, Haarlem (R.T.); and Rijnstate Hospital, Arnhem (H.A.B.) — all in the Netherlands. Ad-

Lenient
Hr < 110 bpm

Strict
Rest hr < 80
Mod exerc hr < 110

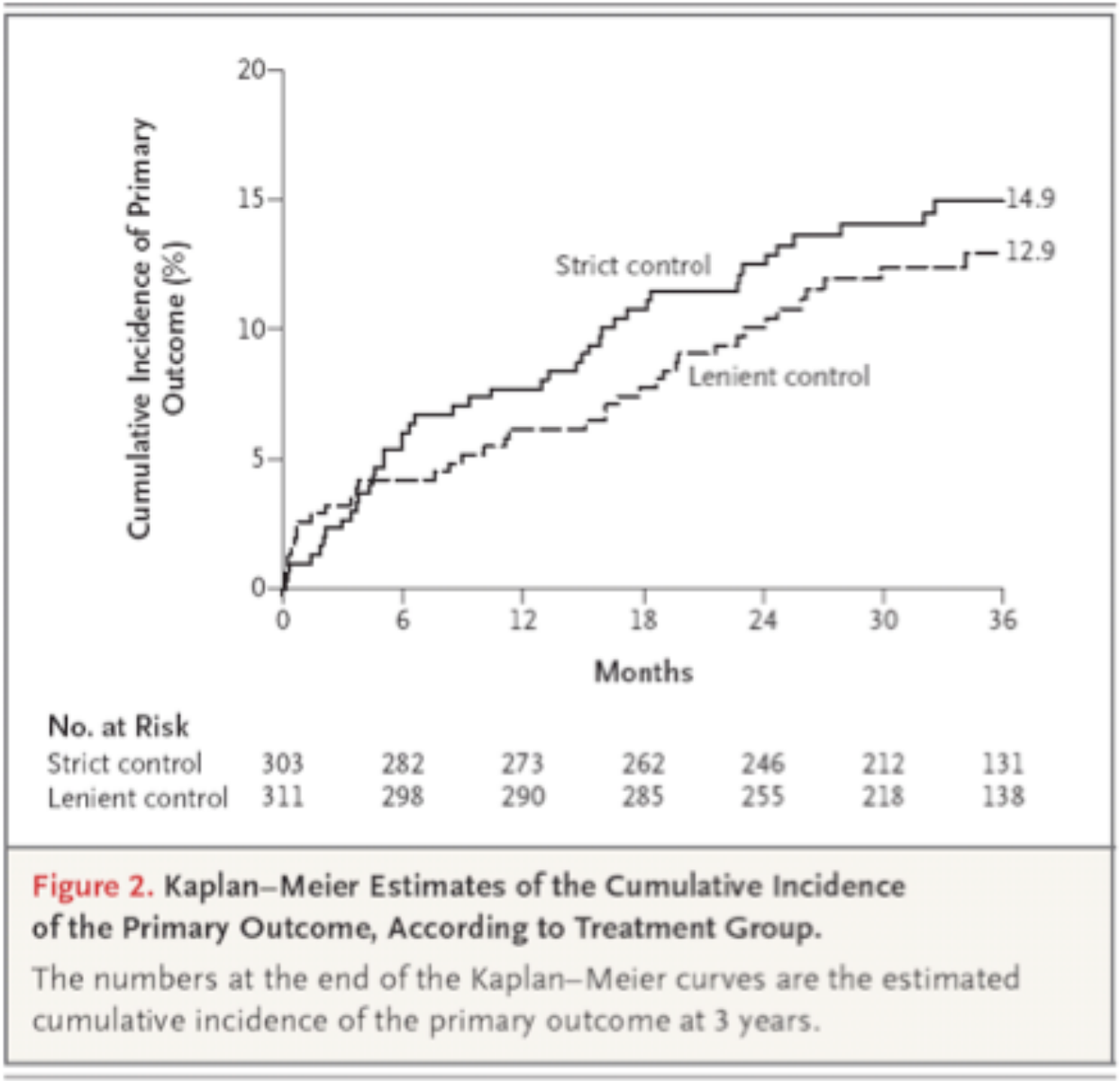


Figure 2. Kaplan–Meier Estimates of the Cumulative Incidence of the Primary Outcome, According to Treatment Group.

The numbers at the end of the Kaplan–Meier curves are the estimated cumulative incidence of the primary outcome at 3 years.

Primary Outcomes

Cardiac death
CHF
Stroke
Systemic embolism
Major bleed
Syncope
Sust VT
Cardiac arrest
Life threat compl of antiarrhythmic
Pacemaker

Secondary Outcomes

Symptoms

Rate Control: Recommendations ACC/AHA 2014

- Class I

- Control of the ventricular rate using a **beta blocker or nondihydropyridine calcium channel antagonist** is recommended for patients with paroxysmal, persistent, or permanent AF (Level of Evidence: B)

- Intravenous administration of a beta blocker or nondihydropyridine calcium channel blocker is recommended to slow the ventricular heart rate in the acute setting in patients without pre- excitation. In hemodynamically unstable patients, electrical cardioversion is indicated. (Level of Evidence: B)

- In patients who experience AF-related symptoms during activity, the adequacy of heart rate control should be assessed during exertion, adjusting pharmacological treatment as necessary to keep the ventricular rate within the physiological range.

Class IIa

- A heart rate control (resting heart rate <80 bpm) strategy is reasonable for symptomatic management of AF
- Intravenous amiodarone can be useful for rate control in critically ill patients without pre- excitation
- AV nodal ablation with permanent ventricular pacing is reasonable to control the heart rate when pharmacological therapy is inadequate and rhythm control is not achievable
-

Class IIb

- A lenient rate-control strategy (resting heart rate <110 bpm) may be reasonable as long as patients remain asymptomatic and LV systolic function is preserved

- Oral amiodarone may be useful for ventricular rate control when other measures are unsuccessful or contraindicated.

Class III

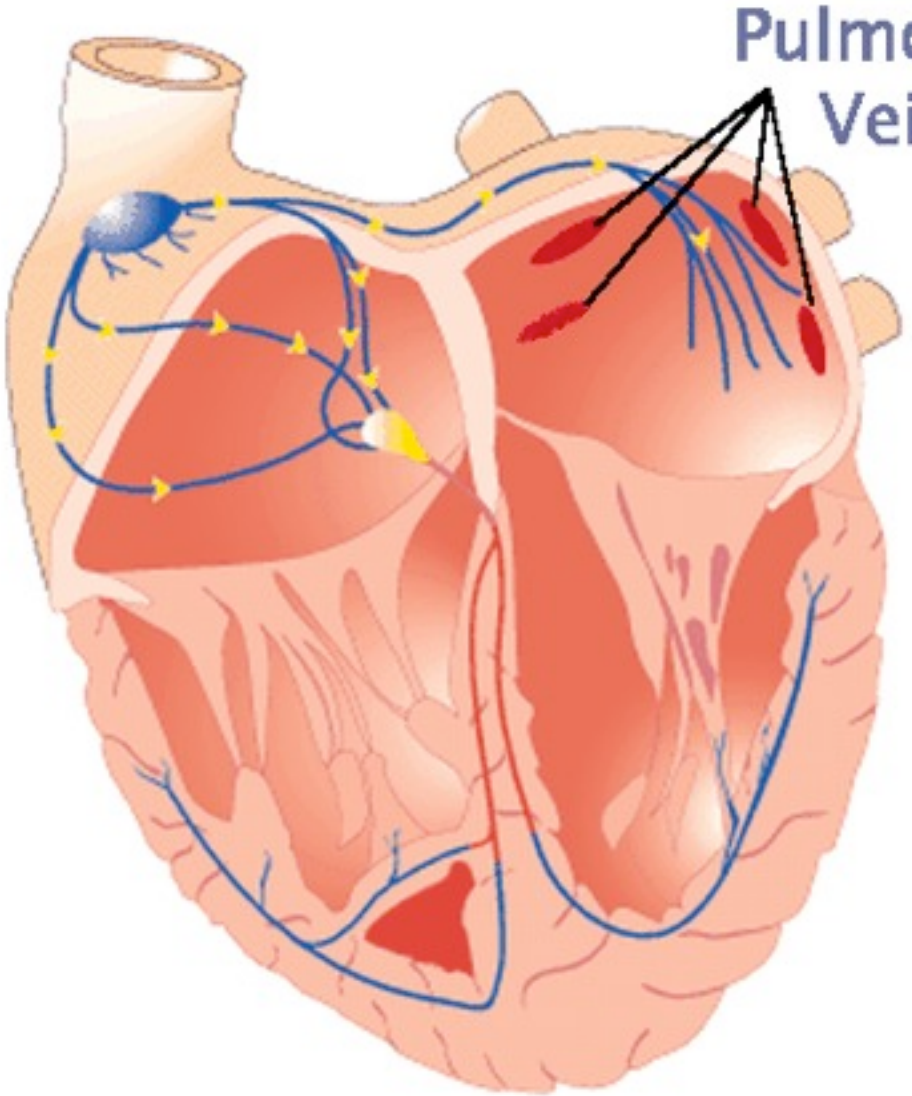
- 1. AV nodal ablation with permanent ventricular pacing should not be performed to improve rate control without prior attempts to achieve rate control with medications. (Level of Evidence: C)

- 2.Nondihydropyridine calcium channel antagonists should not be used in patients with decompensated HF as these may lead to further hemodynamic compromise. (Level of Evidence: C)

- 3.In patients with pre-excitation and AF, digoxin, nondihydropyridine calcium channel antagonists, or intravenous amiodarone should not be administered as they may increase the ventricular response and may result in ventricular fibrillation

- 4.Dronedarone should not be used to control the ventricular rate in patients with permanent AF as it increases the risk of the combined endpoint of stroke, MI, systemic embolism, or cardiovascular death

What is atrial fibrillation ablation?



Atrial fibrillation

a. Triggers

p. veins

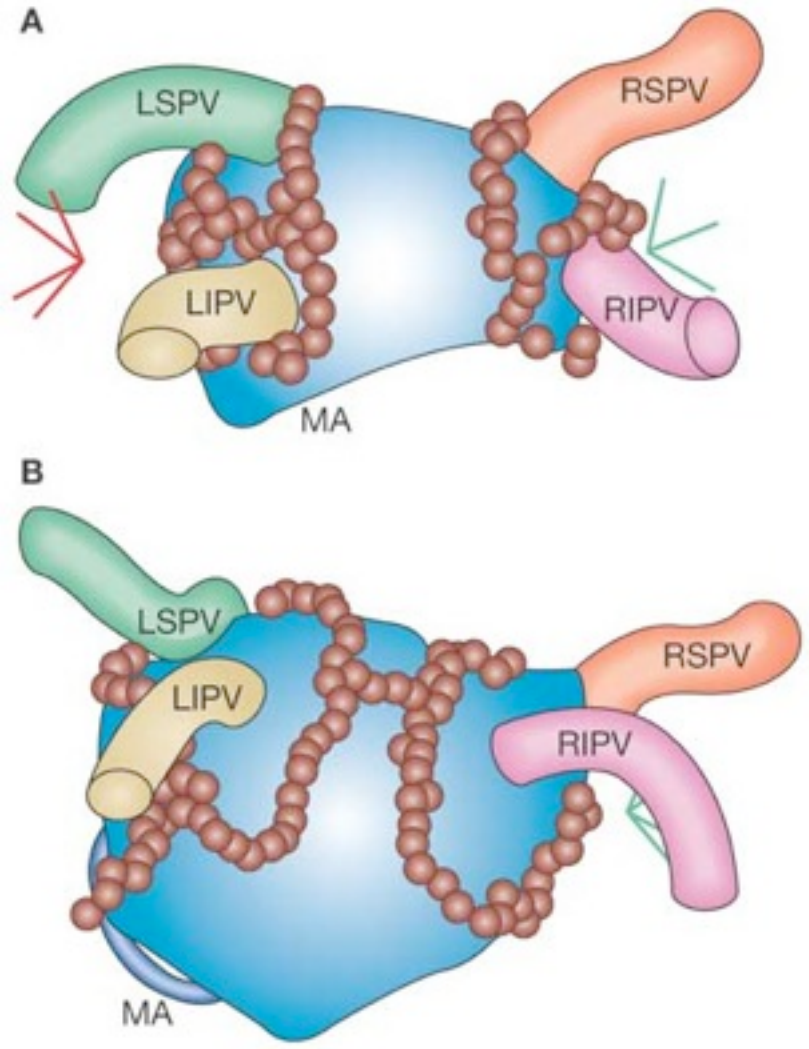
b. Sustainer

left atrium

enlarged

fibrosed

Anatomic Carto Map of Let atrium – ablation points



From: Dong et al.: Nature Clinical Practice Cardiovacular Medicine 2005, 2, 159-166

When to consider ablation? ACC/AHA 2014

- Class I
- 1. AF catheter ablation is useful for symptomatic paroxysmal AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm control strategy is desired

- 2. Prior to consideration of AF catheter ablation, assessment of the procedural risks and outcomes relevant to the individual patient is recommended.

- Class IIa
- AF catheter ablation is reasonable for selected patients with symptomatic persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication

- In patients with recurrent symptomatic paroxysmal AF, catheter ablation is a reasonable initial rhythm control strategy prior to therapeutic trials of antiarrhythmic drug therapy, after weighing risks and outcomes of drug and ablation therapy

- Class IIb
- AF catheter ablation may be considered for symptomatic long-standing (>12 months) persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication, when a rhythm control strategy is desired

- AF catheter ablation may be considered prior to initiation of antiarrhythmic drug therapy with a class I or III antiarrhythmic medication for symptomatic persistent AF, when a rhythm control strategy is desired.

- Class III

- AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and following the procedure.

- AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation.

Who does best ?

- ✓ Paroxysmal AF
- ✓ Younger (<70 years)
- ✓ Minimal structural heart disease
- ✓ Able to tolerate procedure and follow-up

Atrial fibrillation ablation issues

- Complication rate 1-5%
  - Tamponade – atrial perforation
  - TIA, stroke
  - Major bleed
  - Creation of atrial flutter (up to 8%)
  - Vascular access complications
  - Pulmonary vein stenosis (lower incidence than initial)
  - Aorto-esophageal fistula
  - Fatal 1/1000
- Lengthy procedure
  - 4-5 hours