How to manage atrial fibrillation (AF) in 2019

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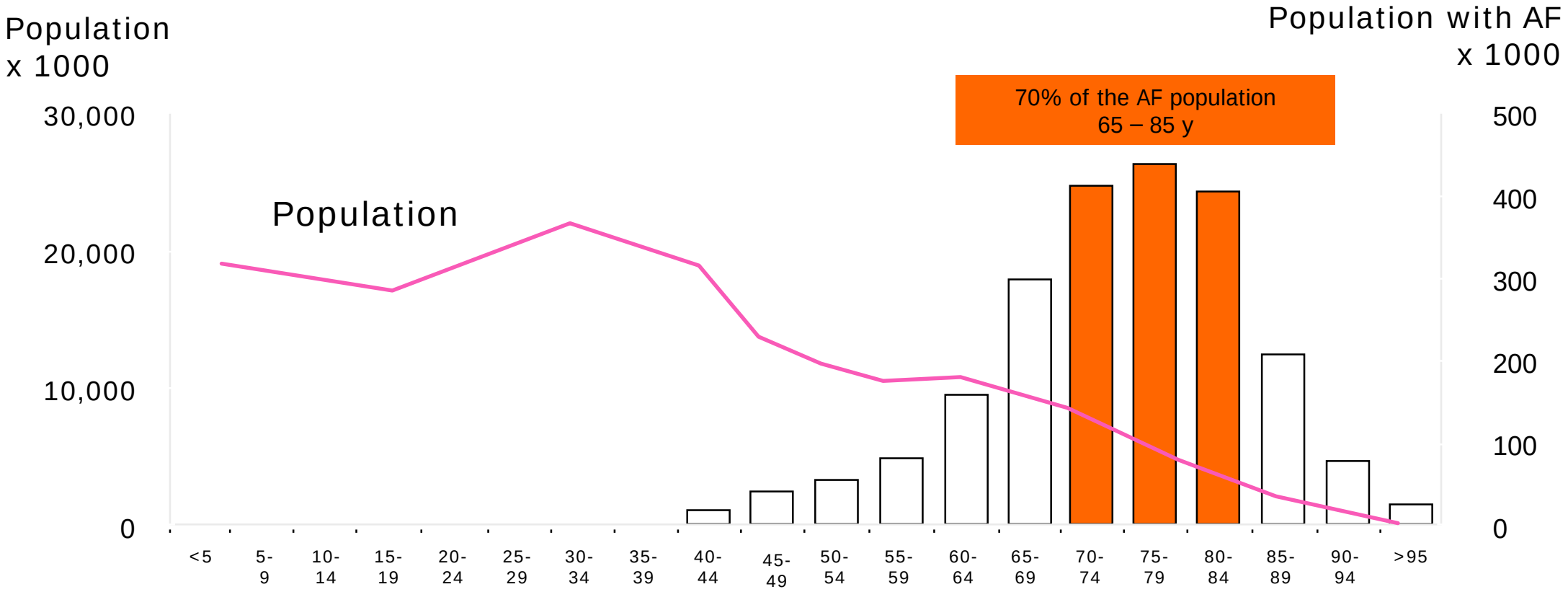
Epidemiology

Epidemiology

- 2010: 20.9 million of men and 12.6 millions of women[1]
- Higher incidence and prevalence in developed countries[1]
- 25% of middle aged adults in Europe and US will develop AF[2]
- Prevalence of AF 3% in adults >20 years with greater prevalence in older persons[3]
- Higher prevalence in patients with conditions such as **hypertension**, **heart failure**, **coronary artery disease**, **valvular heart disease**, **obesity**, **diabetes mellitus**, **chronic kidney disease**[4]

1. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, Gillum RF, Kim YH, McAnulty JH Jr, Zheng ZJ, Forouzanfar MH, Naghavi M, Mensah GA, Ezzati M, Murray CJ. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014;129:837–847.
2. Heeringa J, van der Kuip DA, Hofman A, Kors JA, van Herpen G, Stricker BH, Stijnen T, Lip GY, Witteman JC. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006;27:949–953.
3. Bjorck S, Palaszewski B, Friberg L, Bergfeldt L. Atrial fibrillation, stroke risk, and warfarin therapy revisited: a population-based study. Stroke 2013;44:3103–3108.
4. Ball J, Carrington MJ, McMurray JJ, Stewart S. Atrial fibrillation: profile and burden of an evolving epidemic in the 21st century. Int J Cardiol 2013;167:1807–1824.

Prevalence, Age distribution and Gender of patients with AF



- Based on data from 4 large population-based studies (PAF + sustained AF)
- Median age of pts with AF = 75 y old
- AF present in 2.3% of > 40 y, and 5.9% > 65 y old $\Rightarrow$ 2.3×10^6 in the US
- 50% of AF population is >75 y and 32% > 80 y old

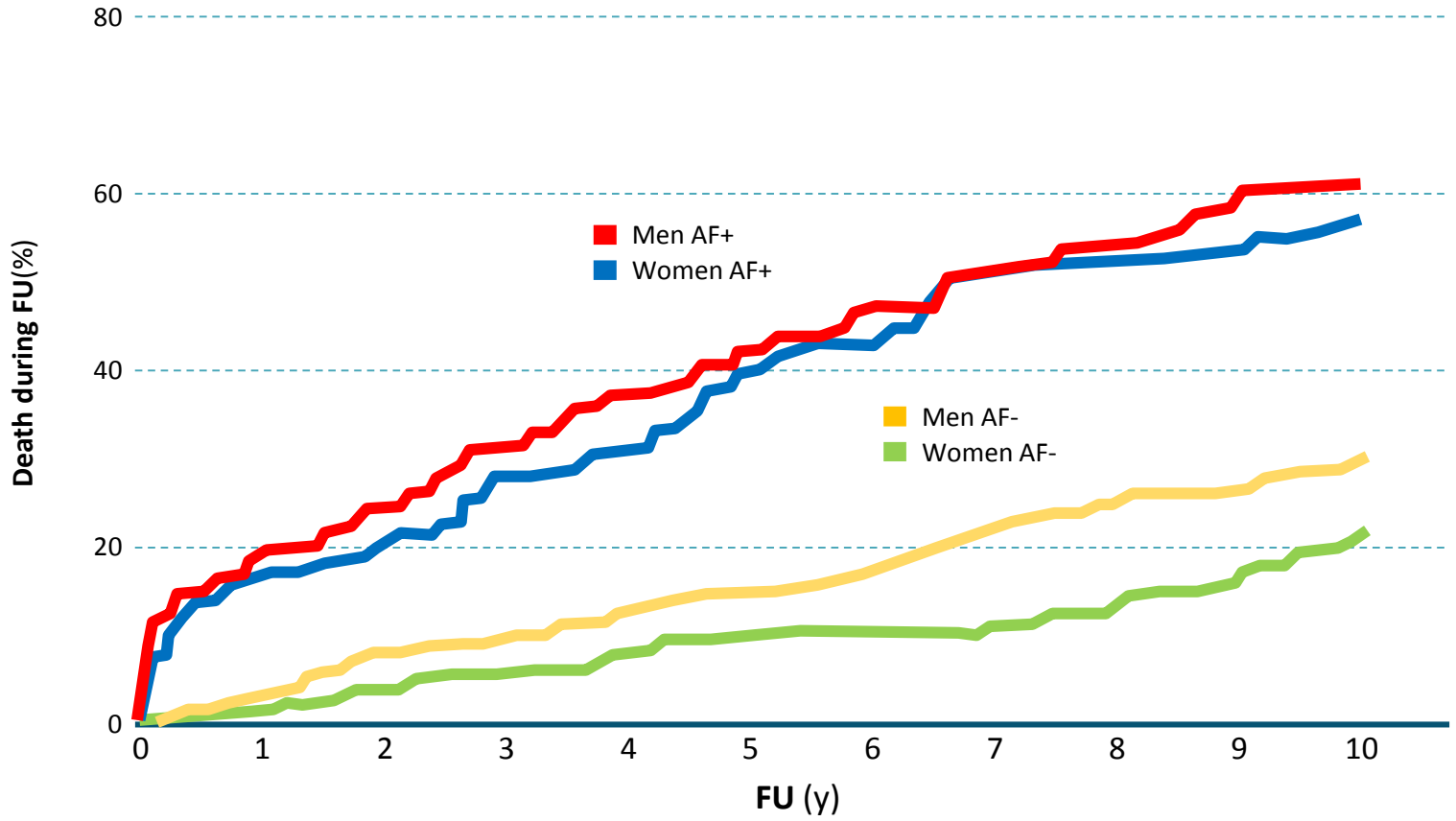
Feinberg WM et al. AIM 1995;155:469-73

Morbidity an Mortality

- AF associated with a **2 fold** increased risk of all-cause mortality (mostly SCD and HF) in women and **1.5 fold** increase in men[1]
- **Death** due to **stroke** can largely be mitigated by anticoagulation, while other CV deaths (**HF, sudden death**) remain common even in AF patients treated according to the current evidence base[2]
- AF also associated with increased morbidity such as **heart failure** and **stroke**[3]
- Left ventricular dysfunction is found in 20–30% of all AF patients
- **20-30% of patients with ischaemic stroke** have AF diagnosed before, during or after the initial event[4]
- White matter lesions in the brain, **cognitive impairment**, **decreased quality of life** and **depressed mood** are common in AF patients[5]
- **10-40%** of AF patients are hospitalized each year[6]

1. Benjamin EJ,Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 1998;98:946–952..
2. Kotecha D, Holmes J, Krum H, Altman DG, Manzano L, Cleland JG, Lip GY, Coats AJ, Andersson B, Kirchhof P, von Lueder TG, Wedel H, Rosano G, Shibata MC, Rigby A, Flather MD, Beta-Blockers in Heart Failure Collaborative Group. Efficacy of beta blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. Lancet 2014;384:2235–2243.
3. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the longterm risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. Am J Med 2002;113:359–364.
4. Grond M, Jauss M, Hamann G, Stark E, Veltkamp R, Nabavi D, Horn M,Weimar C, Kohrmann M,Wachter R, Rosin L, Kirchhof P. Improved detection of silent atrial fibrillation using 72-hour Holter ECG in patients with ischemic stroke: a prospective multicenter cohort study. Stroke 2013;44:3357–3364.
5. Ball J, Carrington MJ, Stewart S, SAFETY investigators. Mild cognitive impairment in high-risk patients with chronic atrial fibrillation: a forgotten component of clinical management? Heart 2013;99:542–547.
6. Kirchhof P, Schmalowsky J, Pittrow D, Rosin L, Kirch W, Wegscheider K, Meinertz T. Management of patients wtih atrial fibrillation by primary care physicians in Germany: 1-year results of the ATRIUM registry. Clin Cardiol 2014;37: 277–284.

AF and Mortality



Framingham. Benjamin et al. Circulation 1998;98:946-952

Pathophysiology and mechanism of AF

Pathophysiology

External stressors induce a slow but progressive process of **structural remodelling** in the **atria**

Stroke

Diabetes

Heart failure

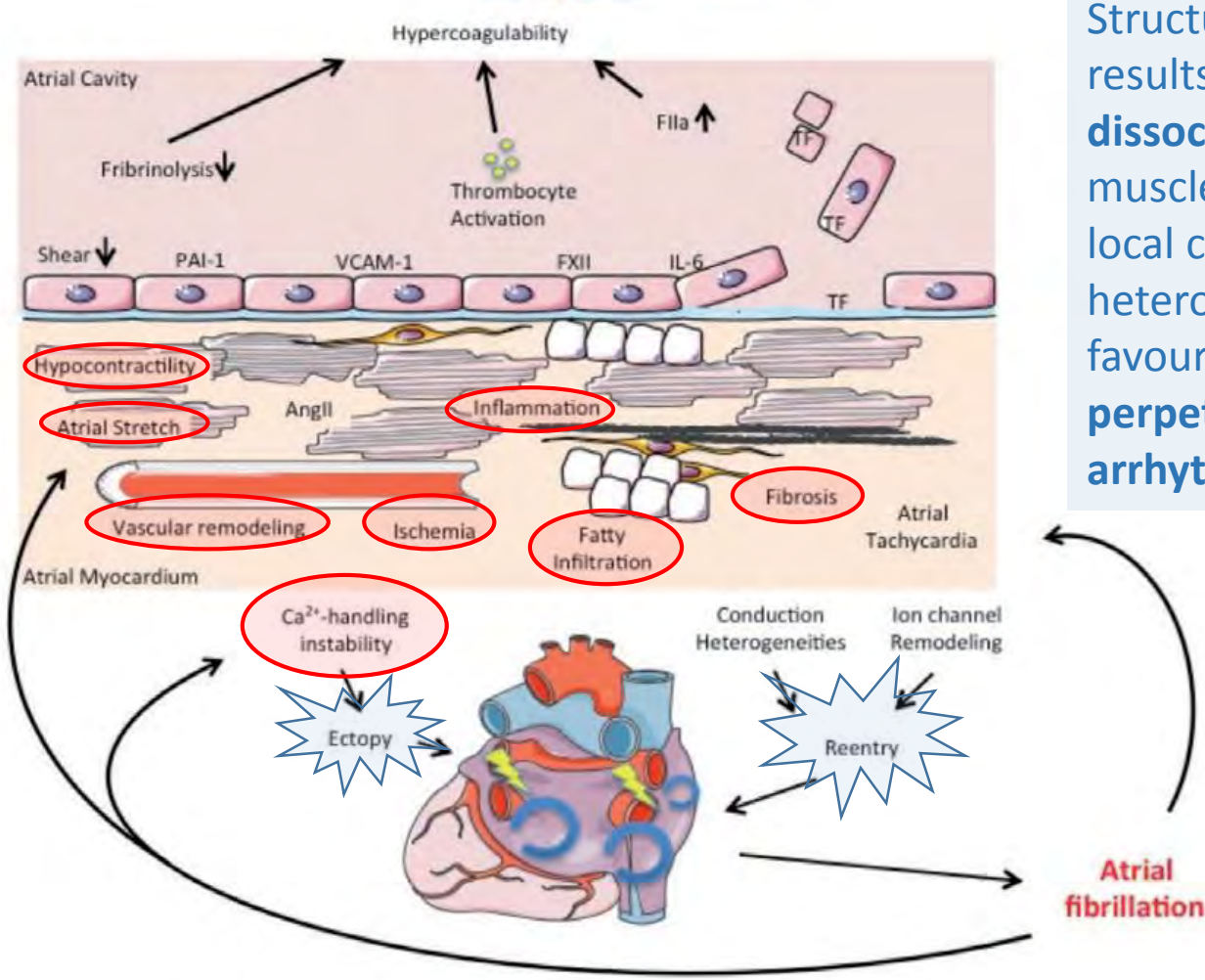
Obesity

Coronary artery disease

Hypertension

Ageing

Genetic predisposition

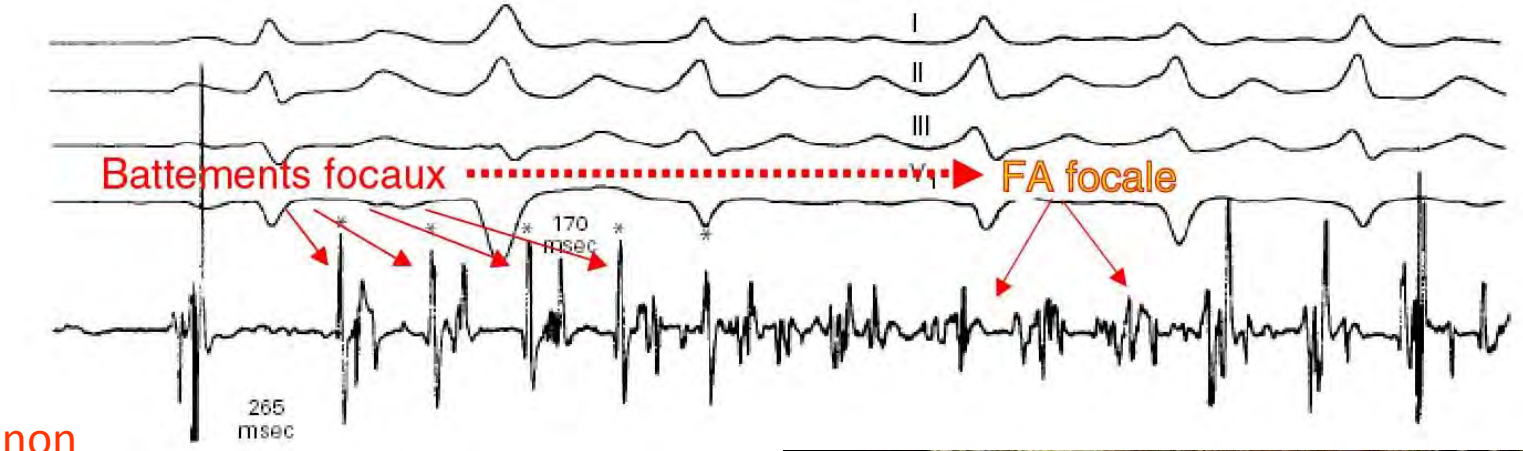


Structural remodelling results in **electrical dissociation** between muscle bundles and local conduction heterogeneities, favouring **re-entry and perpetuation of the arrhythmia**

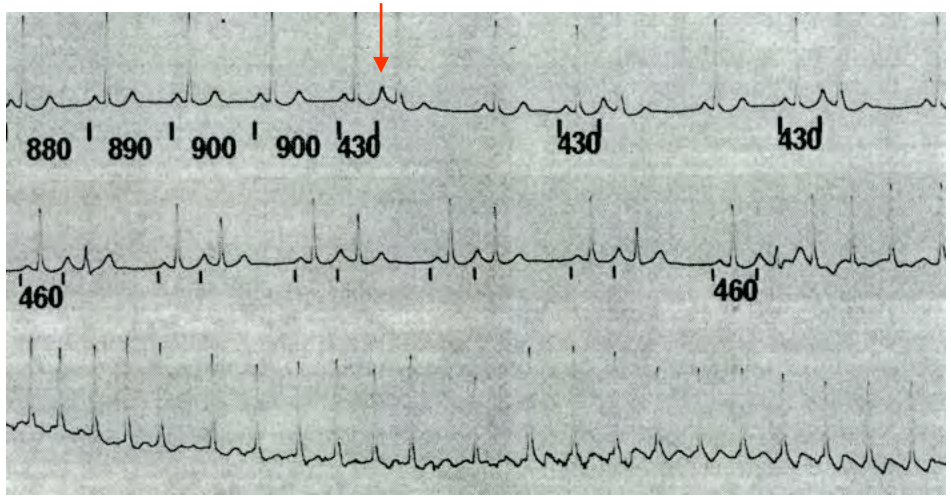
Initiation of atrial fibrillation

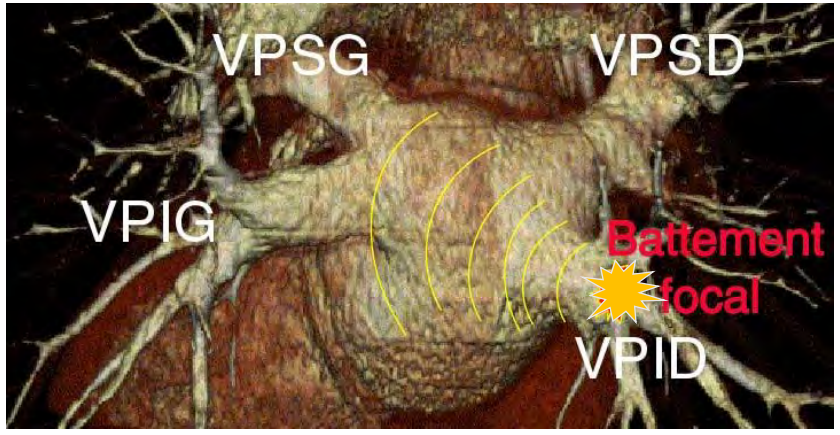
SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS

Haïssaguerre M et al. NEJM 1998



P on T Phenomenon

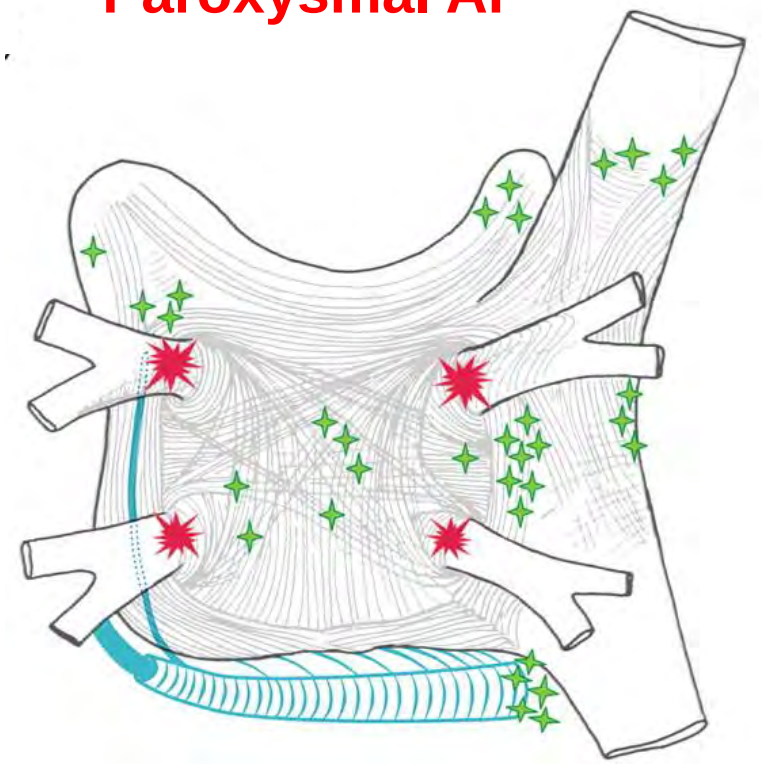




Mechanism of focal activity might involve both **triggered** activity and **localized reentry**

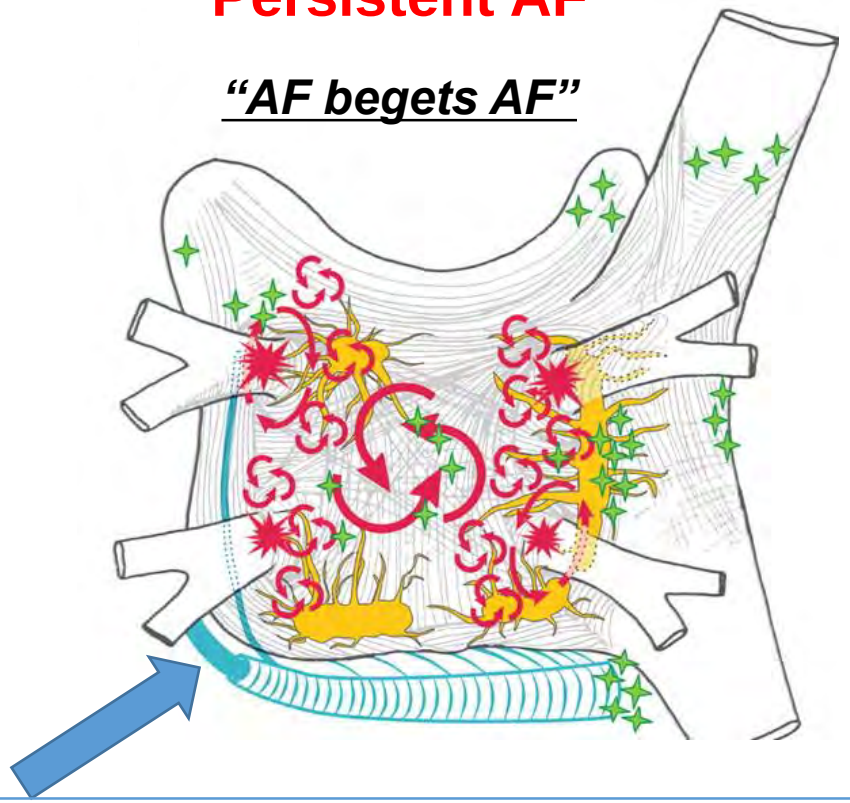
Different Mechanism of Paroxysmal AF vs Persistent AF

Paroxysmal AF



Persistent AF

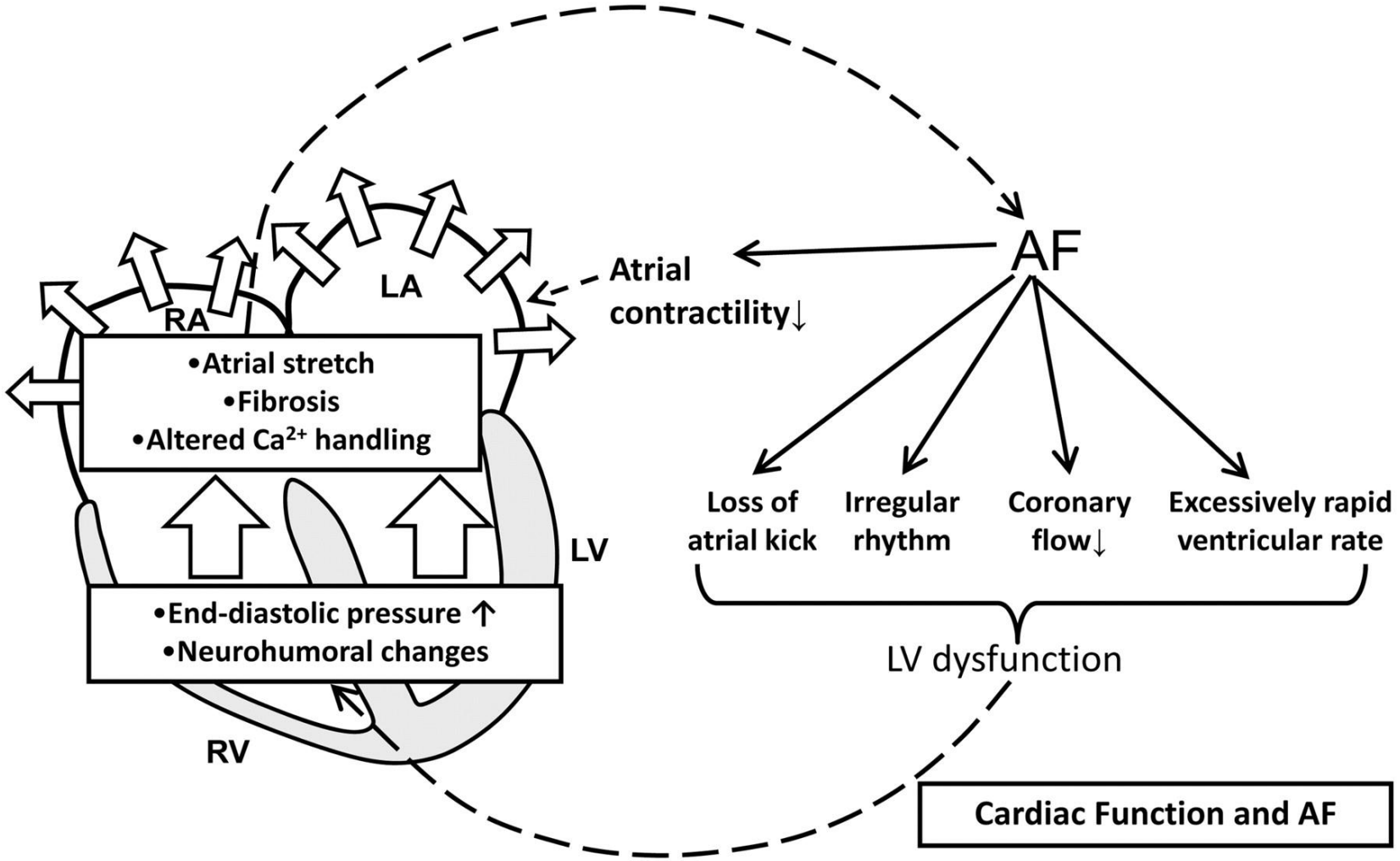
"AF begets AF"



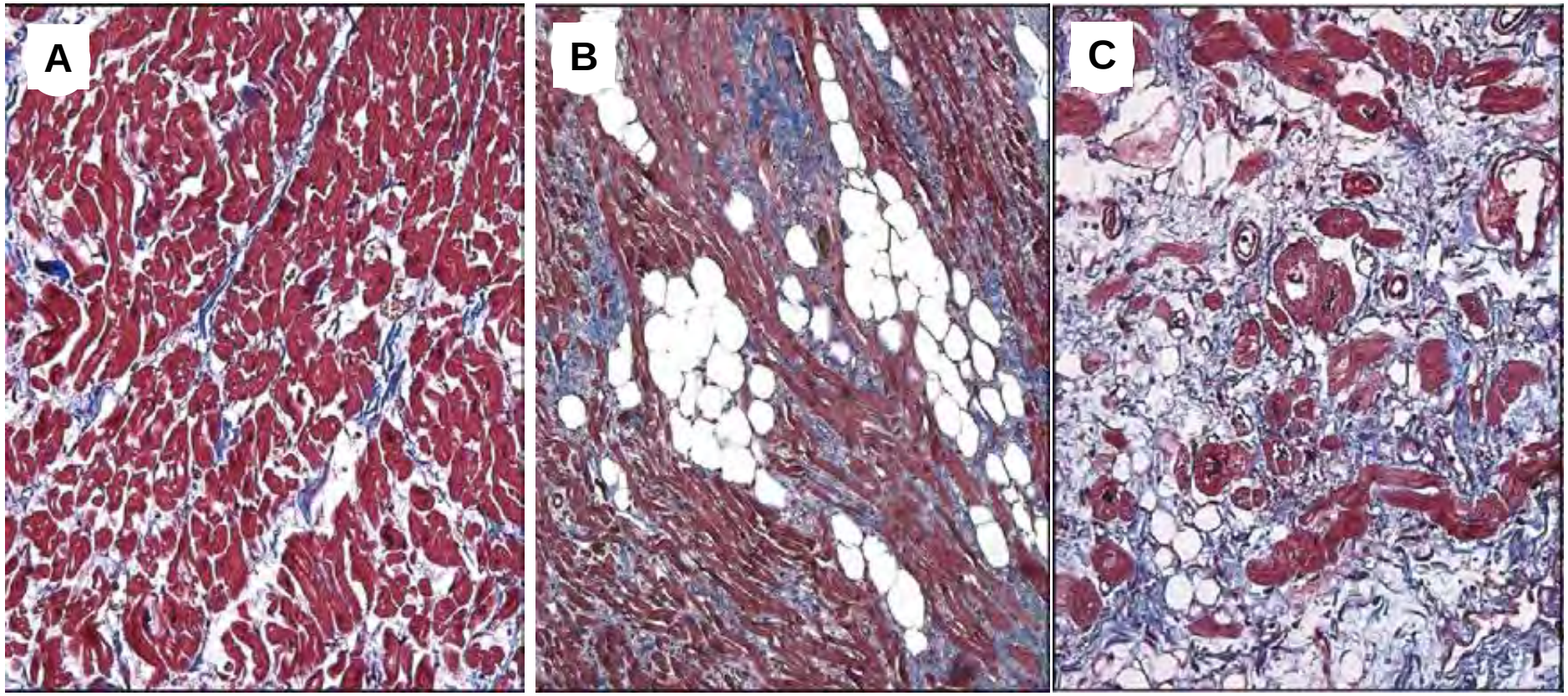
- Limited success of PV isolation (40-50%?)
- AF persists du to tissue and electrical remodelling:
  - AF itself(« AF begets AF »)
  - Secondary factors (HTN, valvular heart disesase…)

HRS-EHRA-Expert Consensus AF Ablation 2012

“AF begets AF”


AF
Atrial contractility↓
LA
RA
•Atrial stretch
•Fibrosis
•Altered Ca^{2+} handling
LV
•End-diastolic pressure ↑
•Neurohumoral changes
RV
Loss of atrial kick
Irregular rhythm
Coronary flow↓
Excessively rapid ventricular rate
LV dysfunction
Cardiac Function and AF

Fibrosis: Substrate of Persistent AF



w/o AF *5%*

Paroxysmal AF *14%*

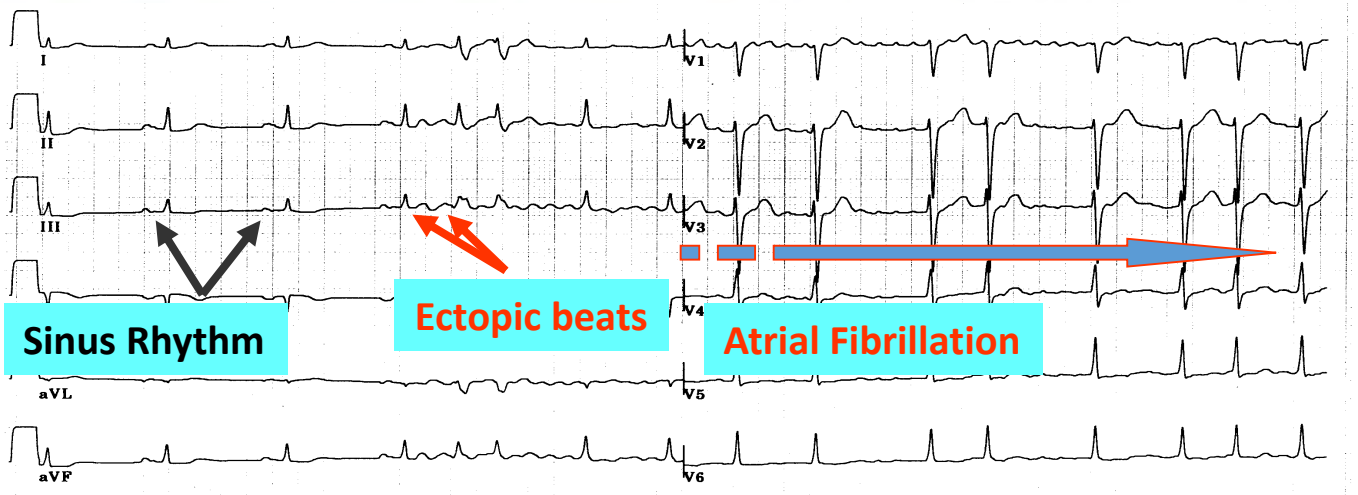
Permanent AF *51%*

Structural abnormalities *of the LA (****fibrosis, fatty tissue****) are associated with the* ***persistent*** *character of the AF and the* ***size of the LA*** *without association with age.* *Platonov P. et al., JACC 2011*

Definition

Definition

The diagnosis of AF requires rhythm documentation using an electrocardiogram (ECG) showing the typical pattern of AF: Absolutely irregular RR intervals and no discernible, distinct P waves. ECG-documented AF was the entry criterion in trials forming the evidence for these guidelines. By accepted convention, an episode lasting at least 30 s is diagnostic. Individuals with AF may be



2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

European Heart Journal (2016) **37**, 2893–2962
doi:10.1093/eurheartj/ehw210

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Patterns of atrial fibrillation

- **First diagnosed AF**:
  - AF that has **not been diagnosed before**, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms.
- **Paroxysmal AF**:
  - **Self-terminating**, in most cases **within 48 hours**. Some AF paroxysms may continue for up to 7 days. AF episodes that are **cardioverted within 7 days** should be considered paroxysmal.
- **Persistent AF:**
  - AF that lasts **longer than 7 days**, including episodes that are **terminated by cardioversion**, either with drugs or by direct current cardioversion, **after 7 days** or more.
- **Long-standing persistent AF:**
  - Continuous AF lasting for **≥1 year** when it is decided to adopt a **rhythm control** strategy.
- **Permanent AF:**
  - AF that is **accepted** by the patient (and physician). Hence**, rhythm control** interventions are, by definition, **not pursued** in patients with permanent AF. Should a rhythm control strategy be adopted, the arrhythmia would be re-classified as 'long-standing persistent AF'.

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AF Type	Clinical presentation	Pathophysiology
AF secondary to structural heart disease	AF in patients with **LV systolic or diastolic dysfunction**, long-standing **hypertension** with LVH, and/or other **structural heart disease**. The onset of AF in these patients is a common cause of hospitalization and a predictor of poor outcome.	**Increased atrial pressure and atrial structural remodelling**, together with activation of the sympathetic and reninangiotensin system.
Focal AF	Patients with **repetitive atrial runs** and frequent, s**hort episodes of paroxysmal** atrial fibrillation. Often **highly symptomatic**, **younger patients** with distinguishable atrial waves (coarse AF), atrial ectopy, and/ or atrial tachycardia deteriorating in AF.	**Localized triggers**, in most cases originating from the **pulmonary veins**, initiate AF. AF due to one or a few re-entrant drivers is also considered to be part of this type of AF.
Polygenic AF	AF in **carriers of common gene variants** that have been associated with **early onset AF**.	Currently under study. The presence of selected gene variants may also influence treatment outcomes.
Post-operative AF	New onset of AF (**usually self-terminating) after major (typically cardiac) surgery** in patients who were in sinus rhythm before surgery and had no prior history of AF.	**Sympathetic tone**, electrolyte changes, and **volume overload**, Acute factors: inflammation, atrial oxidative stress, high possibly interacting with a pre-existing substrate.
AF in patients with mitral stenosis or prosthetic heart valves	AF in patients with **mitral stenosis**, after **mitral valve surgery** and in some cases other valvular disease.	**Left atrial pressure** (stenosis) and **volume** (regurgitation) **load** are the main drivers of atrial enlargement and structural atrial remodelling in these patients.
AF in athletes	Usually paroxysmal, **related to duration and intensity of training**.	Increased **vagal tone and atrial volume**.
Monogenic AF	AF in patients with **inherited cardiomyopathies**, including channelopathies.	The arrhythmogenic mechanisms responsible for sudden death are likely to contribute

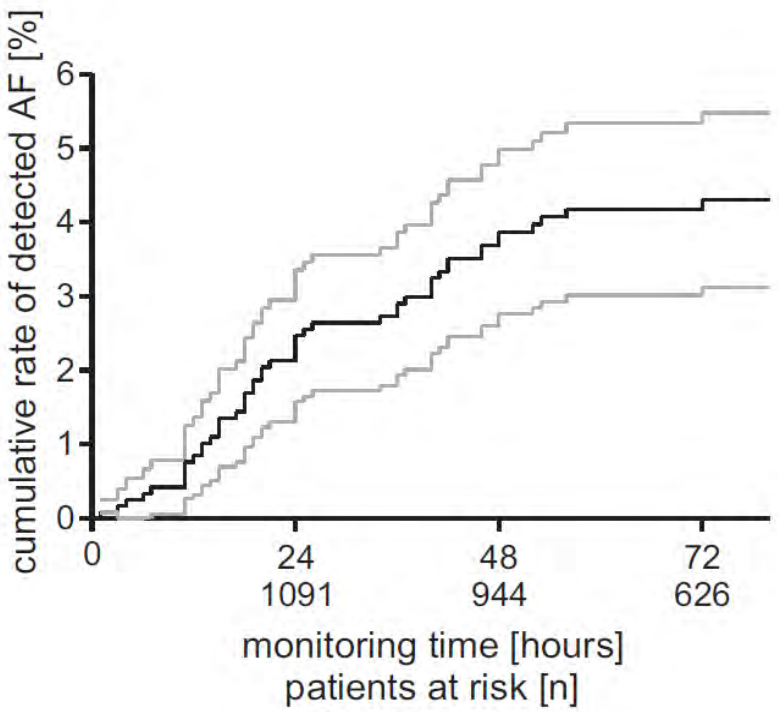
Screening

Screening

- Undiagnosed AF is common, especially in **older** populations and in patients with **heart failure** [1]
- Opportunistic screening for **silent AF seems cost-effective** in elderly populations (e.g. **>65** years)[2]
- Screening of older populations (mean age 64 years) yielded a **prevalence of 2.3% for chronic forms of AF** in 122,571 participants using either **short-term ECG** or **pulse palpation** (followed by ECG in those with an irregular pulse)[3]
- Previously undiagnosed AF was found in **1.4%** of those aged **>65 years**, suggesting a **number needed to screen of 70**[3]
- Paroxysmal AF is often missed and repeated daily ECG recordings increases the detection of silent, asymptomatic paroxysmal AF[4]

1. Davis RC, Hobbs FD, Kenkre JE, Roalfe AK, Iles R, Lip GY, Davies MK. Prevalence of atrial fibrillation in the general population and in high-risk groups: the ECHOES study. Europace 2012;14:1553–1559.
2. Hobbs FD, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, Raftery J, Davies M, Lip G. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. Health Technol Assess 2005;9:iii–iv, ix–x, 1–74.
3. Lowres N, Neubeck L, Redfern J, Freedman SB. Screening to identify unknown atrial fibrillation. A systematic review. Thromb Haemost 2013;110:213–222.
4. Engdahl J, Andersson L, Mirskaya M, Rosenqvist M. Stepwise screening of atrial fibrillation in a 75-year-old population: implications for stroke prevention. Circulation 2013;127:930–937.

Screening



AF detected in **4.3% by 72h** Holter monitor
AF detected in **2.6% by 24h** Holter monitor

The **number needed to screen by 72-hour** ECG was **55 patients** for each additional AF diagnosis

Improved Detection of Silent Atrial Fibrillation Using 72-Hour Holter ECG in Patients With Ischemic Stroke
A Prospective Multicenter Cohort Study

Martin Grond, MD; Marek Jauss, MD; Gerhard Hamann, MD; Erwin Stark, MD; Roland Veltkamp, MD; Darius Nabavi, MD; Markus Horn, MD; Christian Weimar, MD; Martin Köhrmann, MD; Rolf Wachter, MD; Ludger Rosin, MD; Paulus Kirchhof, MD, FESC

Stroke. 2013;44:3357-3364.

Recommendations for screening

- Opportunistic screening for AF is recommended by **pulse taking** or **ECG rhythm strip** in patients **>65 years** of age (**I,B**)
- In patients with **TIA or ischaemic stroke**, screening for AF is recommended by **short-term ECG recording followed by continuous ECG monitoring for at least 72 hours** (**I,B**)
- In stroke patients, additional ECG monitoring by **long-term noninvasive ECG monitors or implanted loop recorders** should be considered to **document silent atrial fibrillation** (**IIa,B**)
- Systematic ECG screening may be considered to detect AF in patients aged >75 years, or those at high stroke risk (**IIb,B**).

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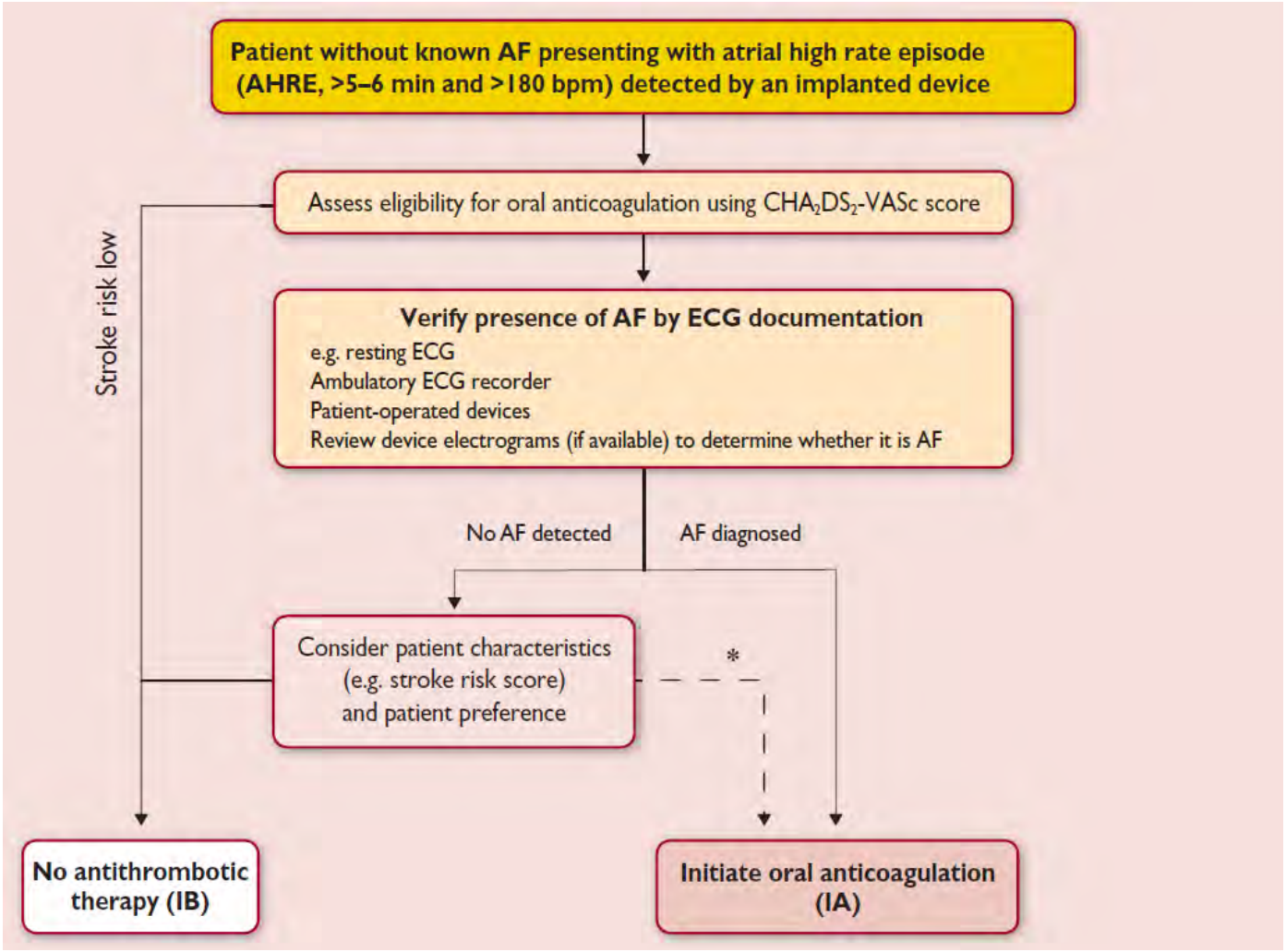
Screening : Patient with implanted devices

5-6minutes of AHRE **>180bpm**



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Symptom burden of Atrial Fibrillation

- Poorer quality of life
- Lethargy
- Palpitations
- Dyspnoea
- Chest tightness
- Sleeping difficulties
- Psychosocial distress
- Cognitive impairment
- None (silent AF)

Modified EHRA score	Symptoms	Description
I	**None**	AF **does not cause any symptoms**
2a	**Mild**	**Normal daily activity not affected** by symptoms related to AF
2b	**Moderate**	Normal daily activity not affected by symptoms related to AF, but **patient troubled by symptoms**
3	**Severe**	**Normal daily activity affected** by symptoms related to AF
4	**Disabling**	**Normal daily activity discontinued**

Wynn GJ, Todd DM,Webber M, Bonnett L, McShane J, Kirchhof P, Gupta D. The European Heart Rhythm Association symptom classification for atrial fibrillation: validation and improvement through a simple modification. Europace 2014;16: 965–972.

Cardiovascular and other conditions independently associated with AF

Characteristic/comorbidity	Association with AF
Genetic predisposition (based on multiple common gene variants associated with AF)[64]	HR range 0.4–3.2
Older age[19]	HR:
50–59 years	1.00 (reference)
60–69 years	4.98 (95% CI 3.49–7.10)
70–79 years	7.35 (95% CI 5.28–10.2)
80–89 years	9.33 (95% CI 6.68–13.0)
Hypertension (treated) vs. none[19]	HR 1.32 (95% CI 1.08–1.60)
Heart failure vs. none[19]	HR 1.43 (95% CI 0.85–2.40)
Valvular heart disease vs. none[205]	RR 2.42 (95% CI 1.62–3.60)
Myocardial infarction vs. none[19]	HR 1.46 (95% CI 1.07–1.98)
Thyroid dysfunction[206,207]	(reference: euthyroid)
Hypothyroidism	HR 1.23 (95% CI 0.77–1.97)
Subclinical hyperthyroidism	RR 1.31 (95% CI 1.19–1.44)
Overt hyperthyroidism	RR 1.42 (95% CI 1.22–1.63)
Obesity[19,208]	HR:
None (BMI <25 kg/m^2)	1.00 (reference)
Overweight (BMI 25–30 kg/m^2)	1.13 (95% CI 0.87–1.46)
Obese (BMI ≥31 kg/m^2)	1.37 (95% CI 1.05–1.78)
Diabetes mellitus vs. none[19]	HR 1.25 (95% CI 0.98–1.60)
Chronic obstructive pulmonary disease[209]	RR:
FEV1 ≥80%	1.00 (reference)
FEV1 60–80%	1.28 (95% CI 0.79–2.06)
FEV1 <60%	2.53 (95% CI 1.45–4.42)

Characteristic/comorbidity	Association with AF
Obstructive sleep apnoea vs. none[210]	HR 2.18 (95% CI 1.34–3.54)
Chronic kidney disease[211]	OR:
None	1.00 (reference)
Stage 1 or 2	2.67 (95% CI 2.04–3.48)
Stage 3	1.68 (95% CI 1.26–2.24)
Stage 4 or 5	3.52 (95% CI 1.73–7.15)
Smoking[212]	HR:
Never	1.00 (reference)
Former	1.32 (95% CI 1.10–1.57)
Current	2.05 (95% CI 1.71–2.47)
Alcohol consumption[213]	RR:
None	1.00 (reference)
1– 6 drinks/week	1.01 (95% CI 0.94–1.09)
7–14 drinks/week	1.07 (95% CI 0.98–1.17)
15–21 drinks/week	1.14 (95% CI 1.01–1.28)
>21 drinks/week	1.39 (95% CI 1.22–1.58)
Habitual vigorous exercise[214]	RR:
Non-exercisers	1.00 (reference)
<1 day/week	0.90 (95% CI 0.68–1.20)
1–2 days/week	1.09 (95% CI 0.95–1.26)
3–4 days/week	1.04 (95% CI 0.91–1.19)
5–7 days/week	1.20 (95% CI 1.02–1.41)

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Prevention of AF in HFrEF patients

- Retrospective analyses from large randomized trials have reported a lower incidence of new-onset AF in patients **treated with ACE inhibitors/ARBs** compared with placebo[1]. The reduced incidence of AF with ACE inhibitors/ARBs is **less evident in patients with HFpEF**[2] and is **lost in patients without heart failure**[3].
- **Beta-blocker** therapy is associated with a **33% reduction in the adjusted odds of incident AF in HFrEF**[4] patients pre-treated with ACE inhibitors/ARBs, reinforcing the importance of beta-blocker therapy in HFrEF patients in sinus rhythm!
- **Eplerenone**, a mineralocorticoid receptor antagonist, **also reduced the risk of new-onset AF** in patients with LVEF ≤35%, New York Heart Association (NYHA) Class II, when added to ACE inhibitors/ARBs and beta-blockers[5]

1. Schneider MP, Hua TA, Bohm M,Wachtell K, Kjeldsen SE, Schmieder RE. Prevention of atrial fibrillation by Renin-Angiotensin system inhibition a meta-analysis. J Am Coll Cardiol 2010;55:2299–2307.
2. Ducharme A, Swedberg K, Pfeffer MA, Cohen-Solal A, Granger CB, Maggioni AP, Michelson EL, McMurray JJ, Olsson L, Rouleau JL, Young JB, Olofsson B, Puu M, Yusuf S, CHARM Investigators. Prevention of atrial fibrillation in patients with symptomatic chronic heart failure by candesartan in the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) program. Am Heart J 2006;152:86–92.
3. GISSI-AF Investigators, Disertori M, Latini R, Barlera S, Franzosi MG, Staszewsky L, Maggioni AP, Lucci D, Di Pasquale G, Tognoni G. Valsartan for prevention of recurrent atrial fibrillation. N Engl J Med 2009;360:1606–1617.
4. Kotecha D, Holmes J, Krum H, Altman DG, Manzano L, Cleland JG, Lip GY, Coats AJ, Andersson B, Kirchhof P, von Lueder TG, Wedel H, Rosano G, Shibata MC, Rigby A, Flather MD, Beta-Blockers in Heart Failure Collaborative Group. Efficacy of beta blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. Lancet 2014;384:2235–2243.
5. Swedberg K, Zannad F, McMurray JJ, Krum H, van Veldhuisen DJ, Shi H, Vincent J, Pitt B. Eplerenone and atrial fibrillation in mild systolic heart failure: results from the EMPHASIS-HF (Eplerenone in Mild Patients Hospitalization And SurvIval Study in Heart Failure) study. J Am Coll Cardiol 2012;59:1598–1603.

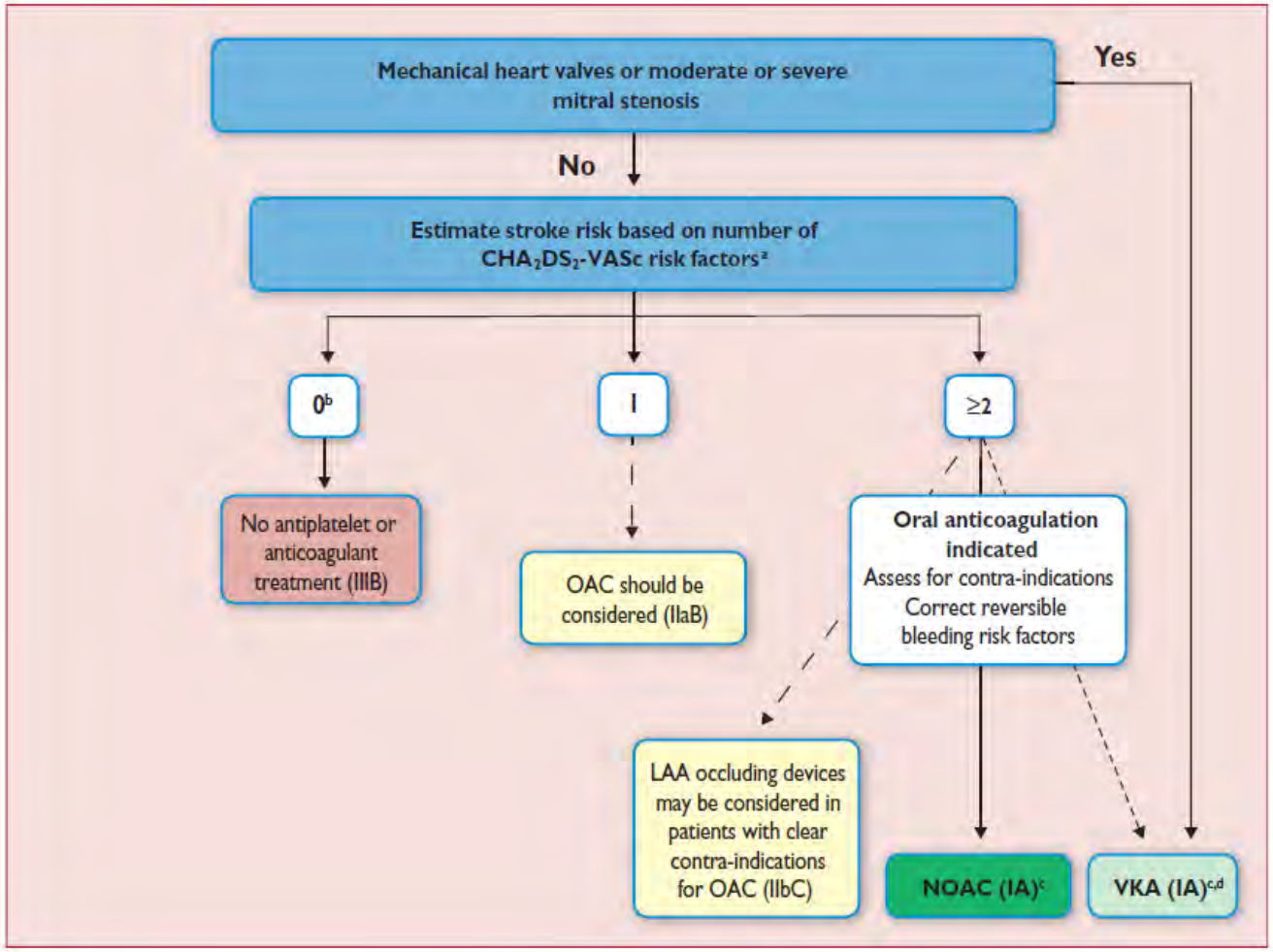
Stroke prevention in AF

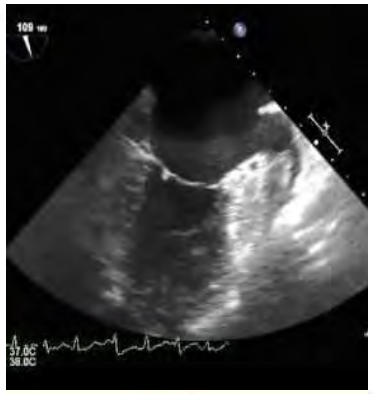
Stroke Prevention in AF

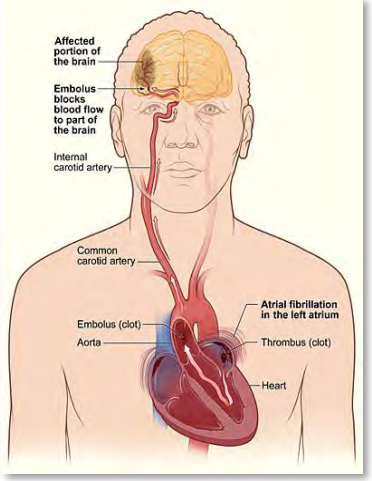
Table 11 Clinical risk factors for stroke, transient ischaemic attack, and systemic embolism in the CHA_2DS_2-VASc score

CHA_2DS_2-VASc risk factor	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left ventricular ejection fraction	+1
Hypertension Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment	+1
Age 75 years or older	+2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin	+1
Previous stroke, transient ischaemic attack, or thromboembolism	+2
Vascular disease Previous myocardial infarction, peripheral artery disease, or aortic plaque	+1
Age 65–74 years	+1
Sex category (female)	+1

CHA_2DS_2-VASc = Congestive Heart failure, hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female).







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European Heart Journal (2016) **37**, 2893–2962
doi:10.1093/eurheartj/ehw210

ESC GUIDELINES

Vitamin K antagonist

- Warfarin and other VKAs were the first anticoagulants used in AF patients
- Both VKAs and NOACs are effective for the prevention of stroke in AF
- VKA therapy **reduces the risk of stroke by 66%** and **mortality by 25%** compared with control (aspirin or no therapy)[1]
- The use of VKAs is **limited by the narrow therapeutic interval**, necessitating frequent monitoring and dose adjustments
- The **only treatment with established safety an AF patients with rheumatic mitral valve disease and/or mechanical heart valve prothesis[2]**

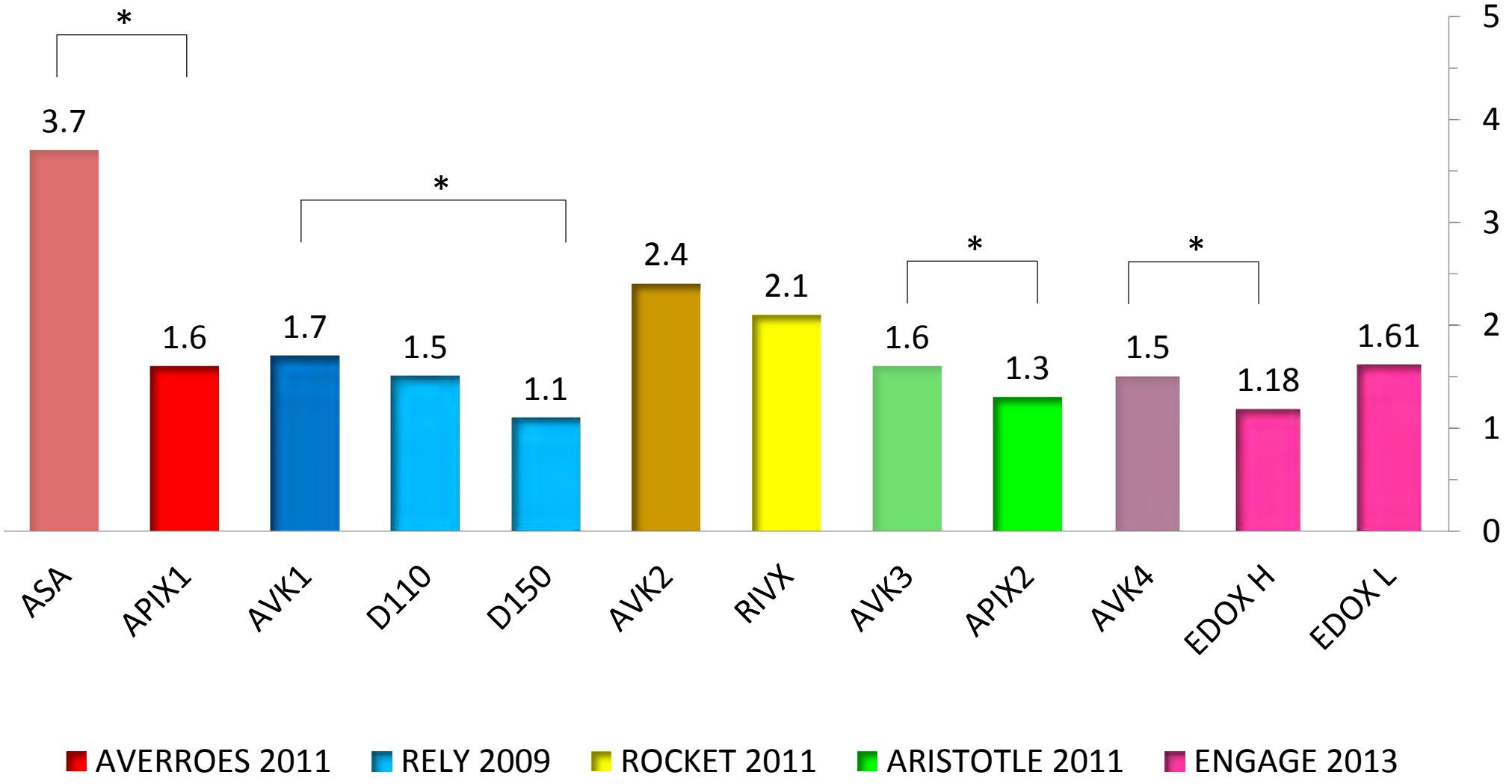
1. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007; 146:857–867
2. Eikelboom JW, Connolly SJ, Brueckmann M, Granger CB, Kappetein AP, Mack MJ, Blatchford J, Devenny K, Friedman J, Guiver K, Harper R, Khder Y, Lobmeyer MT, Maas H, Voigt JU, Simoons ML, Van deWerf F, RE-ALIGN Investigators. Dabigatran versus warfarin in patients with mechanical heart valves. N Engl J Med 2013; 369:1206–1214.

Non-Vitamin K antagonist oral anticoagulants

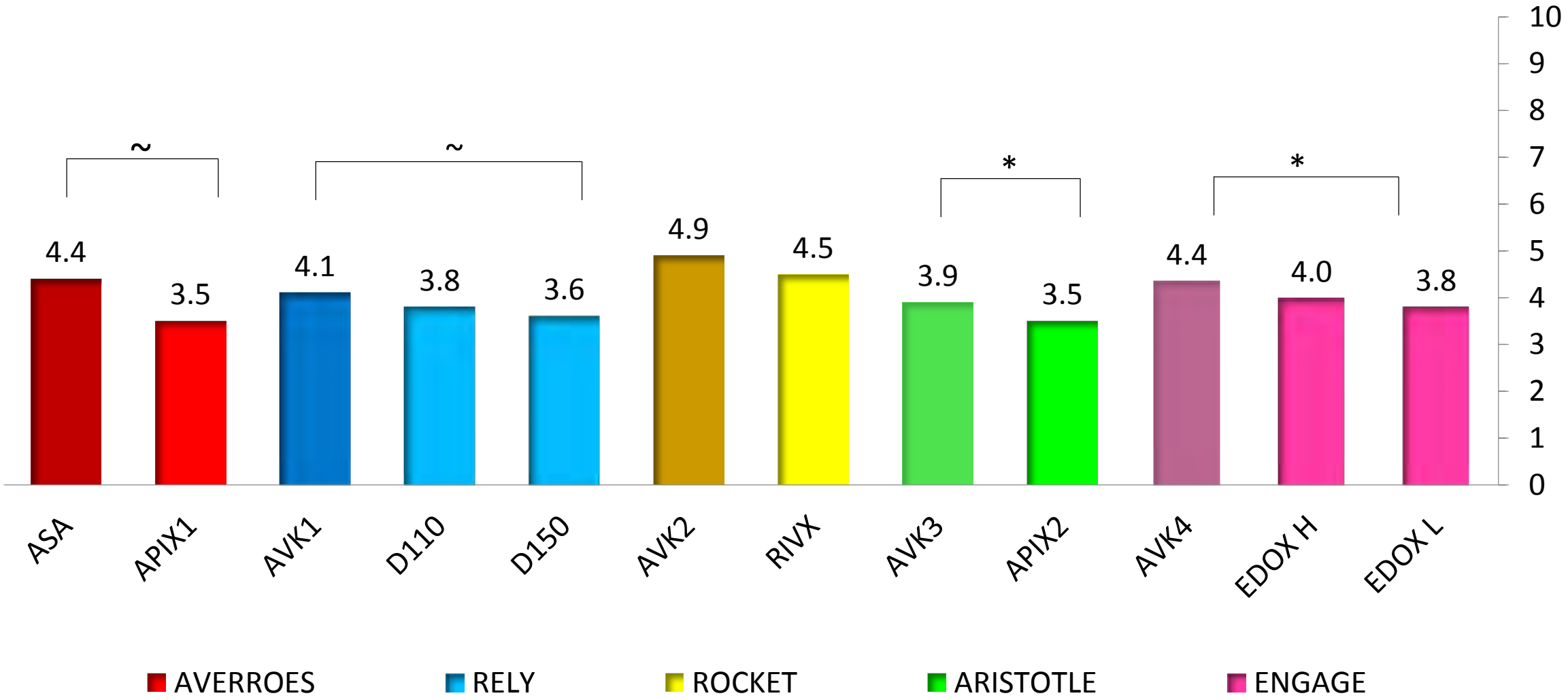
- **Direct thrombin inhibitor** : Dabigatran (Pradaxa®)
- **Factor Xa inhibitors**: Apixaban (Eliquis ®), Edoxaban (Lixiana®), Rivaroxaban (Xarelto®)
- A meta-analysis based on the **high-dose treatment groups** of the pivotal studies of **warfarin vs. NOACs** included 42 411 patients receiving a NOAC and 29 272 receiving warfarin. NOACs in these dosages significantly **reduced stroke or systemic embolic events** by **19% compared with warfarin** (RR 0.81; 95% CI 0.73– 0.91; P<0.0001), **mainly driven by a reduction in haemorrhagic stroke** (RR 0.49; 95% CI 0.38–0.64; P< 0.0001)[1]
- **Mortality is 10% lower** in patients randomized to NOAC therapy (RR 0.90; 95% CI 0.85 – 0.95; P=0.0003)[1]
- **Intracranial haemorrhage is halved** (RR 0.48; 95% CI 0.39 – 0.59; P<0.0001)[1]
- **Gastrointestinal bleeding events are more frequent** (RR 1.25; 95% CI 1.01 – 1.55; P=0.04)[1]

1. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, Camm AJ, Weitz JI, Lewis BS, Parkhomenko A, Yamashita T, Antman EM. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014;383: 955–962.

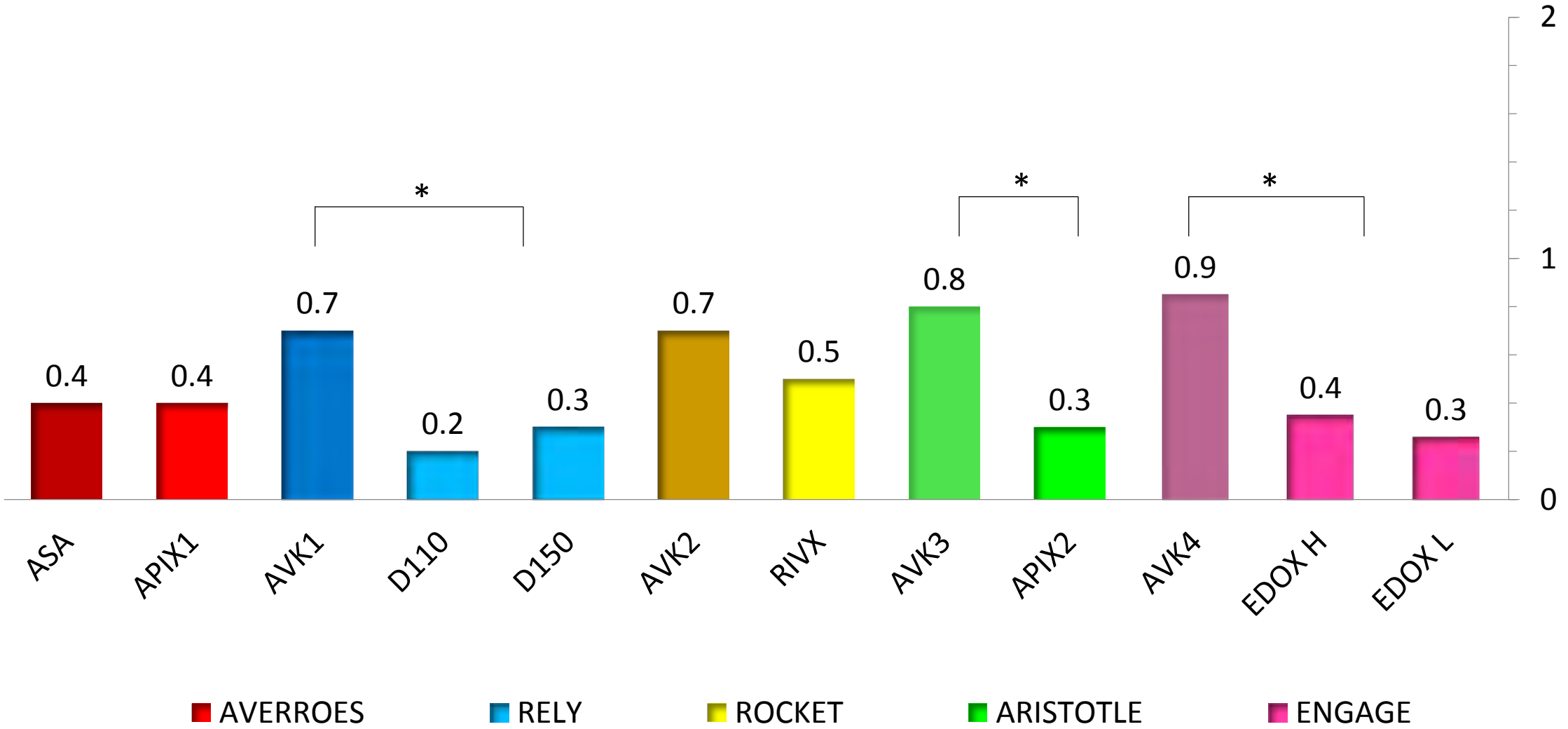
NOACs: Main studies
Thromboembolic events (%/y)



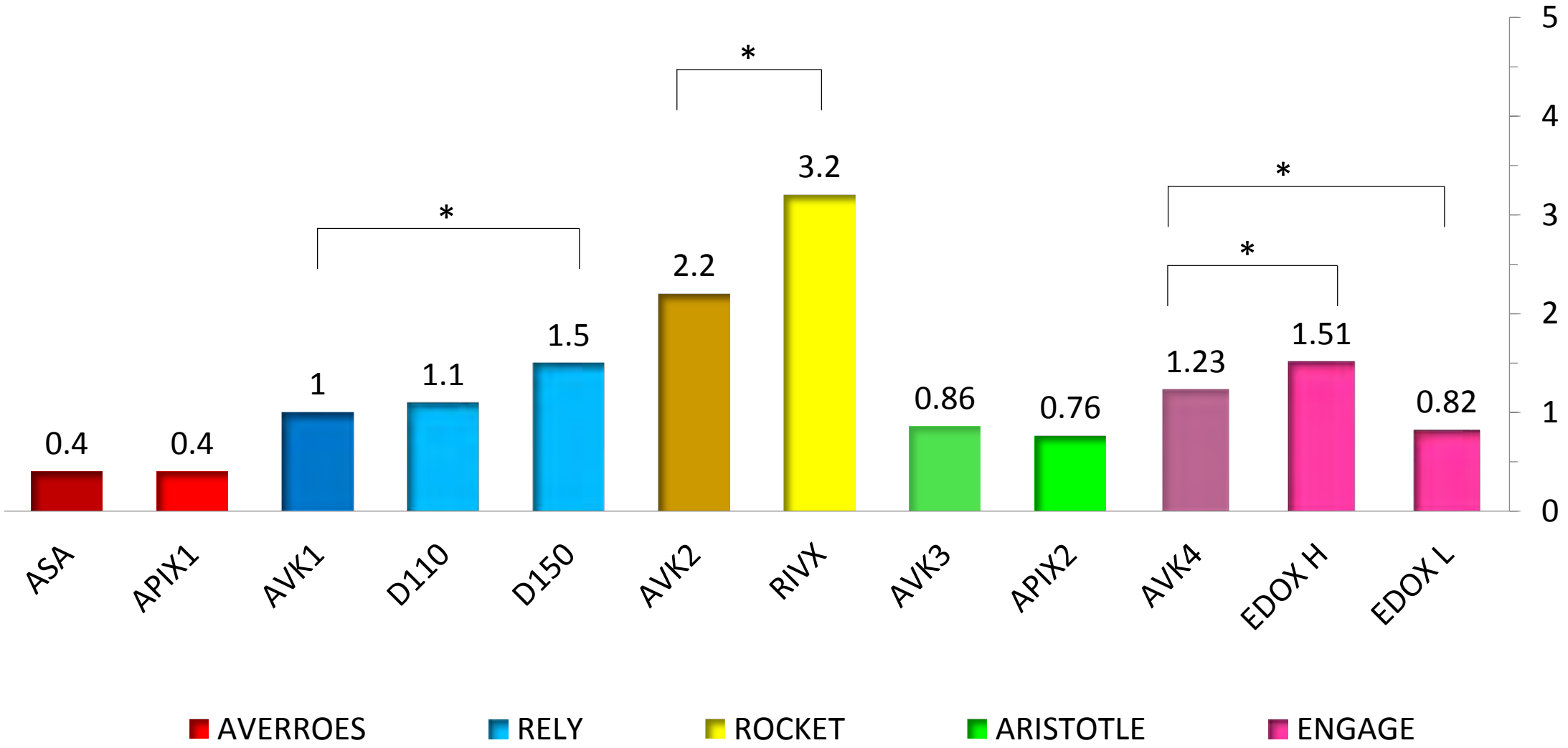
NOACs: Main studies
Total Mortality (%/y)



NOACs: Main studies
Intra cranial haemorrhage (%/y)

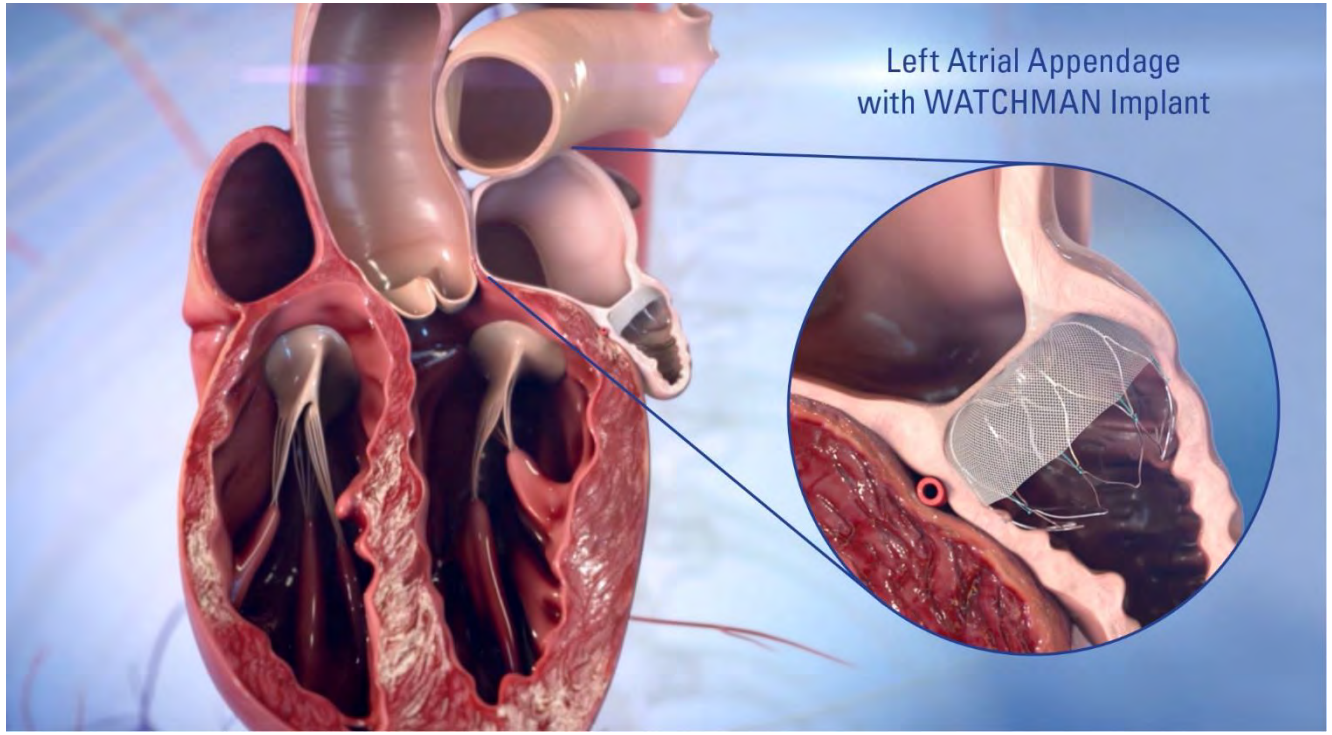


NOACs: Main studies
GI bleeding (%/y)



Left atrial appendage occlusion and exclusion

- Only one device (Watchman®) has been compared with VKA therapy in randomized trials[1]
- **LAA occlusion is non-inferior to VKA treatment for the prevention of stroke in AF patients** with moderate stroke risk, with a possibility of lower bleeding rates in the patients who continued follow-up[1]
- LAA occlusion may also **reduce stroke risk in patients with contraindications to OAC**[2]
- A large recent European registry reported a **high rate of implantation success (98%**), with an acceptable procedure-related complication rate of **4% at 30 days**[3] (device embolization, pericardial effusion with or without tamponade, device thrombus with stroke, femoral hematoma)



1.Reddy VY, Doshi SK, Sievert H, Buchbinder M, Neuzil P, Huber K, Halperin JL, Holmes D. Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) Trial. Circulation 2013;127:720–729.
2.Reddy VY, Mobius-Winkler S, Miller MA, Neuzil P, Schuler G, Wiebe J, Sick P, Sievert H. Left atrial appendage closure with the Watchman device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology). J Am Coll Cardiol 2013;61:2551–2556.
3. Boersma LV, Schmidt B, Betts TR, Sievert H, Tamburino C, Teiger E, Pokushalov E, Kische S, Schmitz T, Stein KM, Bergmann MW, EWOLUTION investigators. Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry. Eur Heart J 2016;37:2465–2474.

Recommendations for stroke prevention in patients with AF

Recommendations	Class	Level
Oral anticoagulation therapy to prevent thromboembolism is recommended for all male AF patients with a CHA2DS2-VASc score of 2 or more.	I	A
Oral anticoagulation therapy to prevent thromboembolism is recommended in all female AF patients with a CHA2DS2-VASc score of 3 or more.	I	A
Oral anticoagulation therapy to prevent thromboembolism should be considered in male AF patients with a CHA2DS2-VASc score of 1, considering individual characteristics and patient preferences.	IIa	B
Oral anticoagulation therapy to prevent thromboembolism should be considered in female AF patients with a CHA2DS2-VASc score of 2, considering individual characteristics and patient preferences.	IIa	B
Vitamin K antagonist therapy (INR 2.0–3.0 or higher) is recommended for stroke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valves.	I	B
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a vitamin K antagonist.	I	A
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III	A
NOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are not recommended in patients with mechanical heart valves (Level of evidence B) or moderate-to-severe mitral stenosis (Level of evidence C).	III	B

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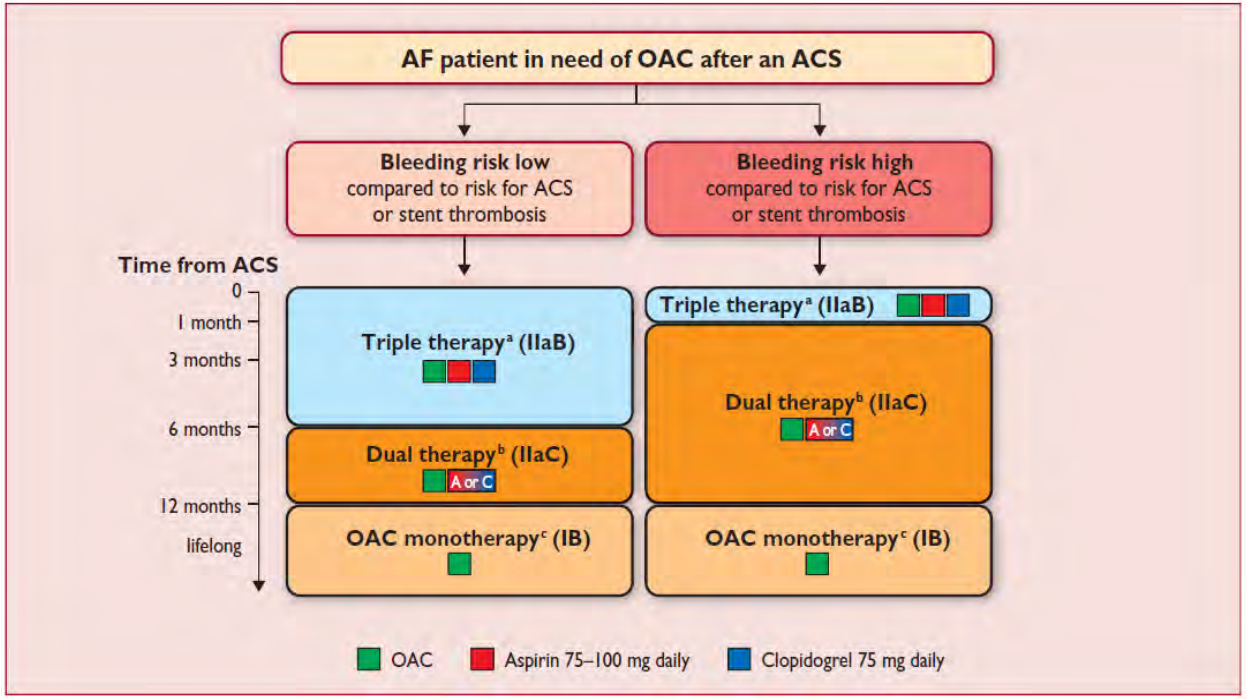
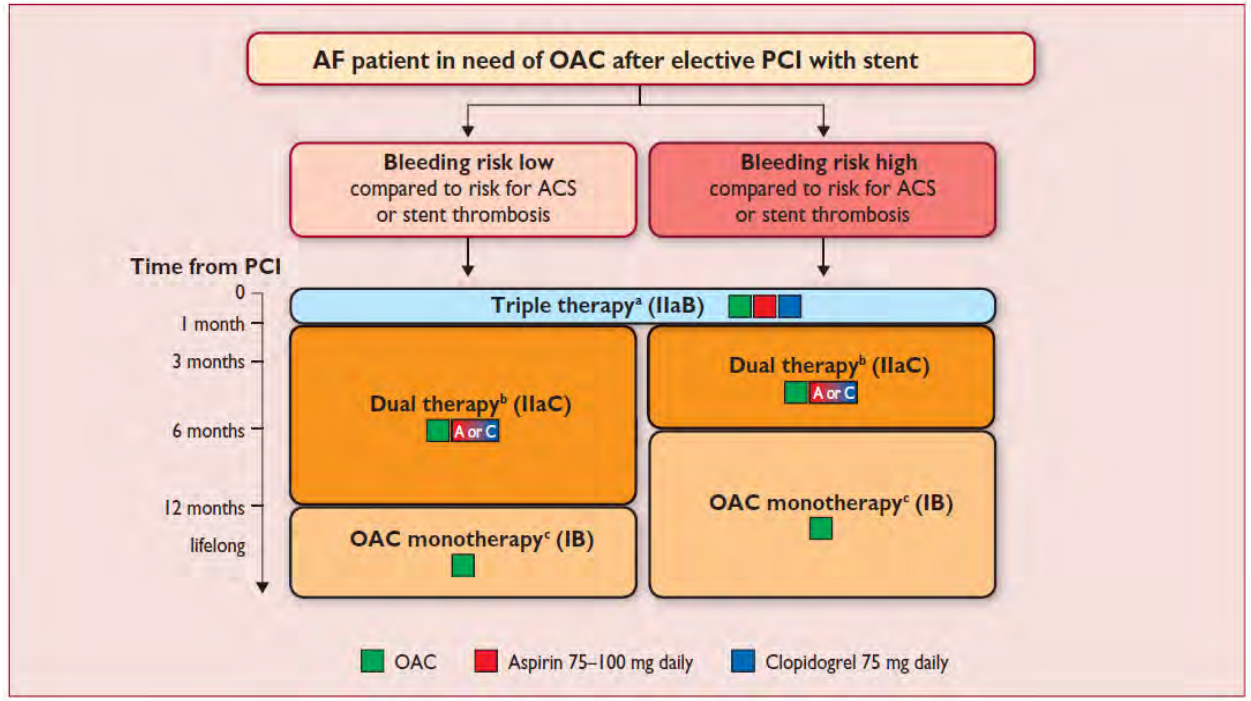
ESC GUIDELINES

Combination therapy with oral anticoagulants and antiplatelets





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ESC GUIDELINES

Rate control

Rate control

- Rate control is an integral part of the management of AF patients, and is **often sufficient to improve AF-related symptoms**
- Pharmacological rate control can be achieved for **acute or long-term** rate control with **beta-blockers**, **digoxin**, the calcium channel blockers **diltiazem and verapamil**, or **combination** therapy
- A number of **antiarrhythmic drugs** also have **rate-limiting properties** (amiodarone, dronedarone, sotalol, and to some extent propafenone), but they should only be used in patients needing rhythm control therapy
- For **acute rate control**, **beta-blockers and diltiazem/verapamil** are **preferred** over digoxin because of their **rapid onset of action** and effectiveness at **high sympathetic tone**
- In patients with **HFrEF, beta-blockers, digitalis** (digoxin or digitoxin), or their **combination** should be used as **diltiazem and verapamil can have negative inotropic effects** in patients with **LVEF 40%.**
- **Digoxin has no effect on mortality compared to placebo in HFrEF** patients in **sinus rhythm** but **reduced hospital admissions**. There have been no head-to-head RCTs of digoxin in AF patients
- In **critically ill** patients and those with **severely impaired LV systolic function**, **intravenous amiodarone** can be used where excess heart rate is leading to haemodynamic instability
- **Urgent cardioversion** should be considered in **unstable patients**
- **Atrioventricular node ablation** should be considered to control heart rate in patients **unresponsive or intolerant** to intensive rate and rhythm control therapy, accepting that these patients will become pacemaker dependent**.**

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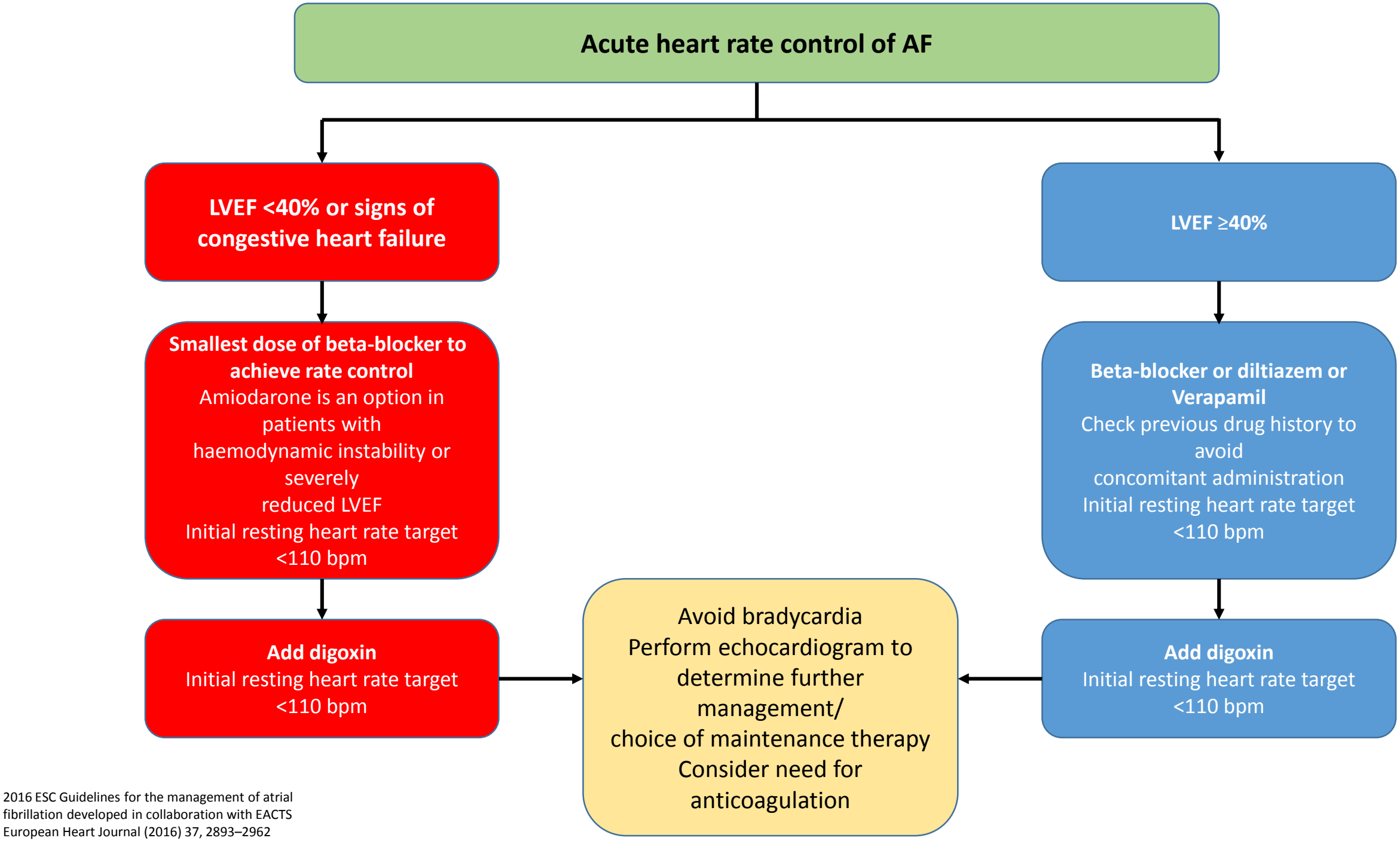

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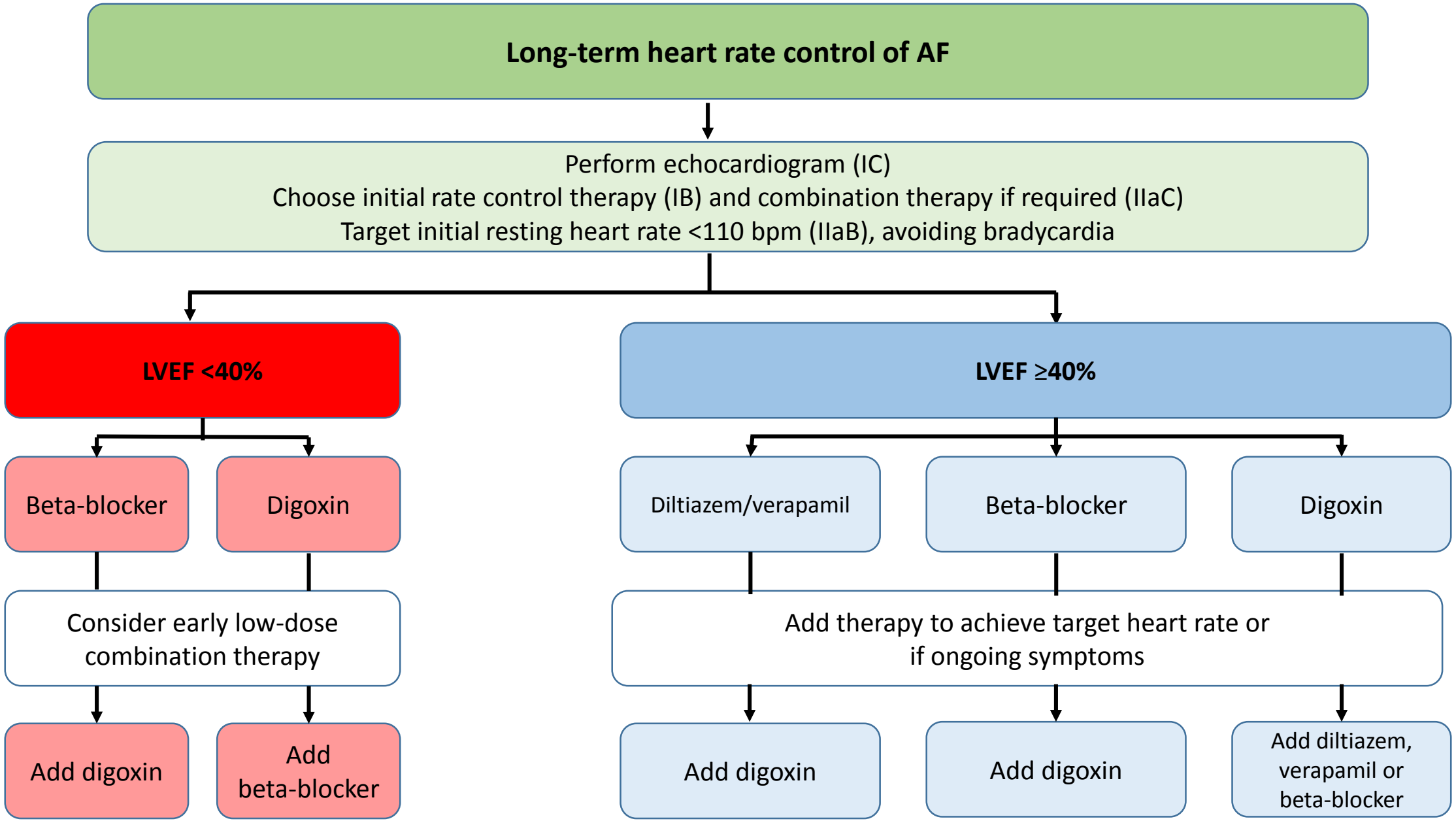

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Beta-Blockers in long term rate control

- **Beta-adrenoreceptor blocker monotherapy** is often the **first-line long term rate-controlling agent**, largely based on observations of better acute heart rate control than digoxin
- The **prognostic benefit** of beta-blockers seen in HFrEF patients with sinus rhythm is **lost in those with AF** *(Kotecha D et al.Beta-Blockers in Heart Failure Collaborative Group. Efficacy of beta blockers in patients with heart failure plus atrial fibrillation:an individual-patient data meta-analysis. Lancet 2014;384:2235–2243)*
- **Despite this lack of benefit in HFrEF, betablockers** are **recommended as a useful first-line rate control agent** across **all AF patients**, based on the potential for symptomatic and functional improvement as a result of rate control, the lack of harm from published studies, and the **good tolerability** profile across all ages in sinus rhythm and in AF

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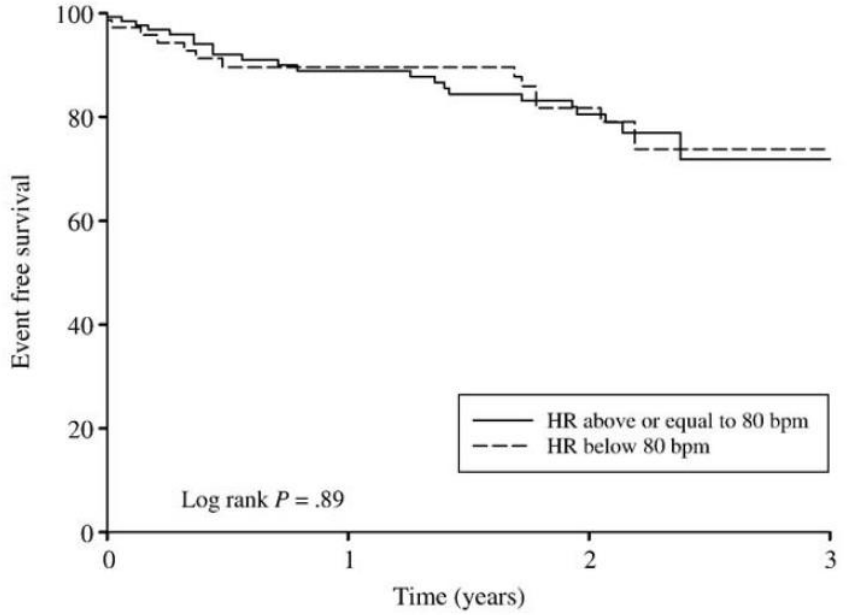
ESC GUIDELINES

Rate control

HR **<80bpm vs ≥80bpm**

No significant **difference** in **CV morbidity and mortality** and **quality of life** between patients having **a higher or lower HR during AF**. **Prognosis** seems **determined by the underlying cardiovascular disease**, the use of **digoxin**, and **interrupted use of oral anticoagulation**. No difference in QoL and changes in left ventricular function nor atrial sizes between both levels of rate control were observed

Cardiovascular mortality



Heart rate <80 bpm (n):			
75	58	39	0
Heart rate ≥80 bpm (n):			
139	86	62	40

Electrophysiology

Does intensity of rate control influence outcome in persistent atrial fibrillation?: Data of the RACE study

Hessel F. Groenveld, MD,[a] Harry J.G.M. Crijns, MD, PhD,[b] Michiel Rienstra, MD, PhD,[a] Maarten P. Van den Berg, MD, PhD,[a] Dirk J. Van Veldhuisen, MD, PhD, FACC,[a] and Isabelle C. Van Gelder, MD, PhD[a,c] for the RACE investigators[d] *Groningen, The Netherlands*

Am Heart J 2009;158:785-91

Rate control

Resting HR **<110bpm** (lenient rate control) **vs <80bpm** (strict rate control) (or 110bpm during moderate exercise)

Lenient rate control is noninferior to strict rate control in the **prevention of major cardiovascular events** in patients with **permanent** atrial fibrillation.

Incidence of **HF similar** in the two groups

Rate of adverse effects of drugs, syncope and pacemaker implantation was **similar** between the two groups

No significant differences in the prevalence of symptoms associated with atrial fibrillation.

Lenient rate control is easier to achieve and **more convenient**, since fewer outpatient visits and examinations are needed.

Cardiovascular mortality

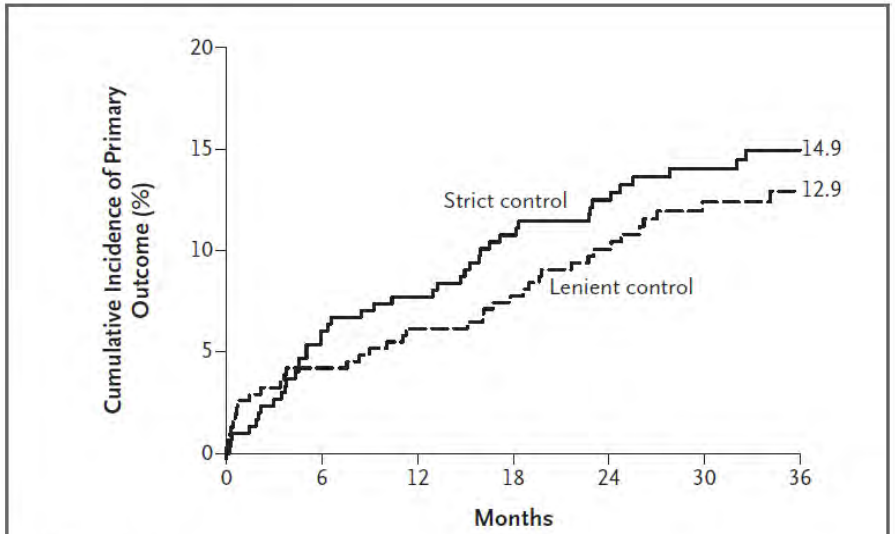


Figure 2. Kaplan–Meier Estimates of the Cumulative Incidence of the Primary Outcome, According to Treatment Group.
The numbers at the end of the Kaplan–Meier curves are the estimated cumulative incidence of the primary outcome at 3 years.

The NEW ENGLAND JOURNAL of MEDICINE
APRIL 15, 2010

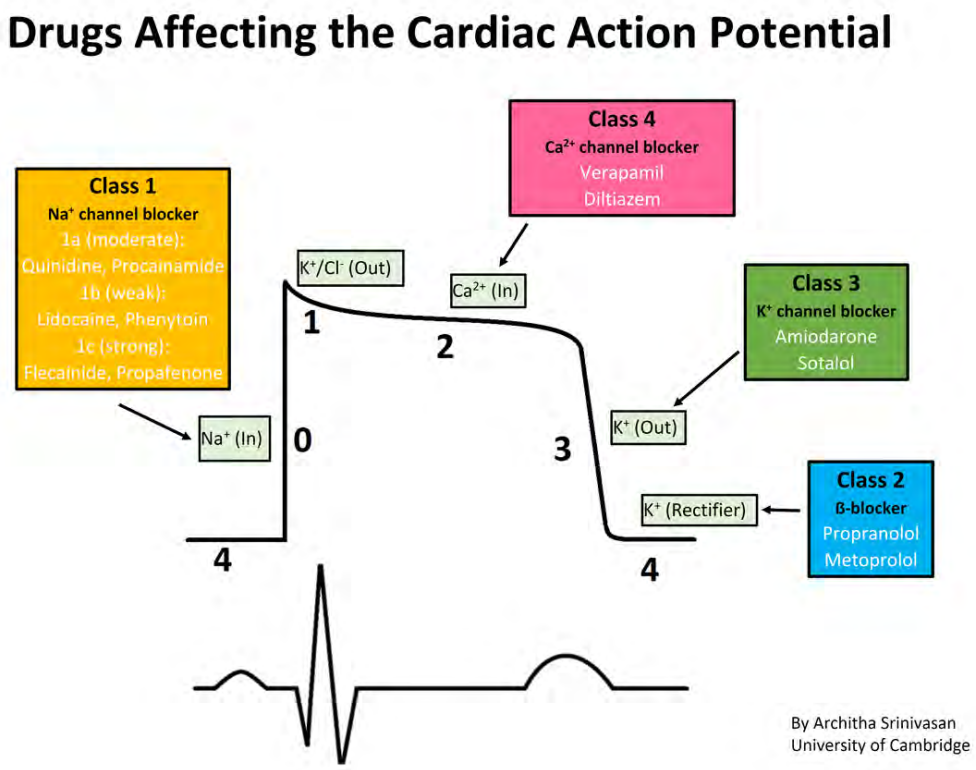
Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

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*

Rhythm control

Rhythm Control

- Flecainide (Tambocor®), Ic
- Amiodarone (Cordarone®), III
- Propafenone (Rytmonorm®), Ic
- Ibutilide (Corvert®), III
- Vernakalant (Brinavess®), III



Class I : Block Na+ channels
Class II: B-adrenoreceptor antagonists
Class III: Prolong action potential and prolong refractory period
Class IV: Ca+ channel antagonists

Drug	Dose	Main Contra-indications and precautions	Warning signs warranting discontinuation	AV nodal slowing	Suggested ECG monitoring during initiation
Amiodarone	600mg in divided doses for 4 weeks, 400mg for 4 weeks, then 200mg once daily	Caution when using concomitant therapy with QT-prolonging drugs and in patients with SAN or AV nodeand conduction disease. The dose of VKAs and of digitalis should be reduced. Increased risk of myopathy with statins. Caution in patients with pre-existing liver disease.	**QT prolongation >500 ms**	10–12 bpm in AF	**Baseline, 1 week, 4 weeks**
Flecainide	100-150mg twice daily	Contra-indicated if CrCl <50 mg/mL, liver disease, IHD or reduced LV ejection fraction Caution in the presence of SAN or AV node or conduction disease. CYP2D6 inhibitors (e.g. fluoxetine or tricyclic antidepressants) increase plasma concentration.	**QRS duration increases >25%** above baseline	None	**Baseline, day 1, day 2–3**
Propafenone	150mg-300mg three times daily	Contra-indicated in IHD or reduced LV ejection fraction. Caution in the presence of SAN or AV node and conduction disease, renal or liver impairment, and asthma. Increases concentration of digitalis and warfarin.	**QRS duration increase >25%** above baseline	Slight	**Baseline, day 1, day 2–3**
Sotalol	80-160mg twice daily	Contra-indicated in the presence of significant LV hypertrophy, systolic heart failure, asthma, pre-existing QT prolongation, hypokalaemia, CrCl<50 mg/mL. Moderate renal dysfunction requires careful adaptation of dose.	**QT interval >500 ms**, QT prolongation by >60 ms upon therapy initiation	Similar to high dose blockers	**Baseline, day 1, day 2–3**

Rhythm control

- **Catheter ablation or combination therapy** is often **effective** when **antiarrhythmic drugs fail**
- Although many clinicians believe that maintaining sinus rhythm can improve outcomes in AF patients, all trials that have **compared rhythm control and rate control** to rate control alone (with appropriate anticoagulation) have resulted in **neutral outcomes**.
- **Pharmacological cardioversion** restores sinus rhythm in approximately **50% of patients with recent-onset AF**
- **In the short-term**, **electrical cardioversion** restores sinus rhythm **quicker and more effectively** than pharmacological cardioversion and is associated with shorter hospitalization.
- **Flecainide and propafenone** are effective for pharmacological cardioversion, but their use is restricted to patients **without structural heart disease**. High ventricular rates resulting from the **conversion of AF into atrial flutter with 1:1 conduction** by flecainide or propafenone **can be prevented by pre-administering a beta-blocker, verapamil, or diltiazem**
- **Amiodarone** can be used in patients with heart failure and in patients with **ischaemic heart disease**
- **Both amiodarone and flecainide** appear **more effective** than sotalol in restoring sinus rhythm.

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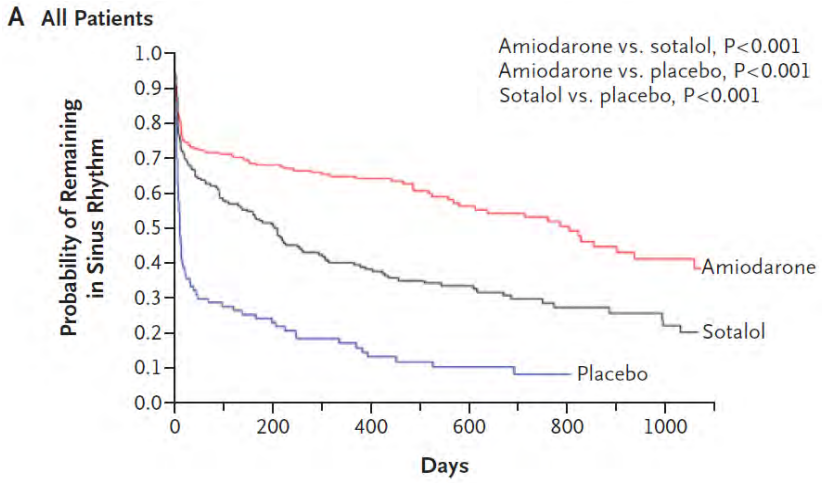
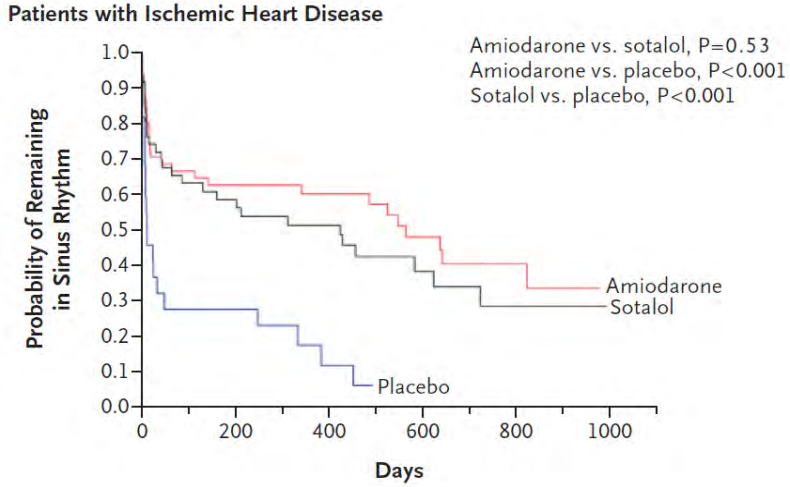
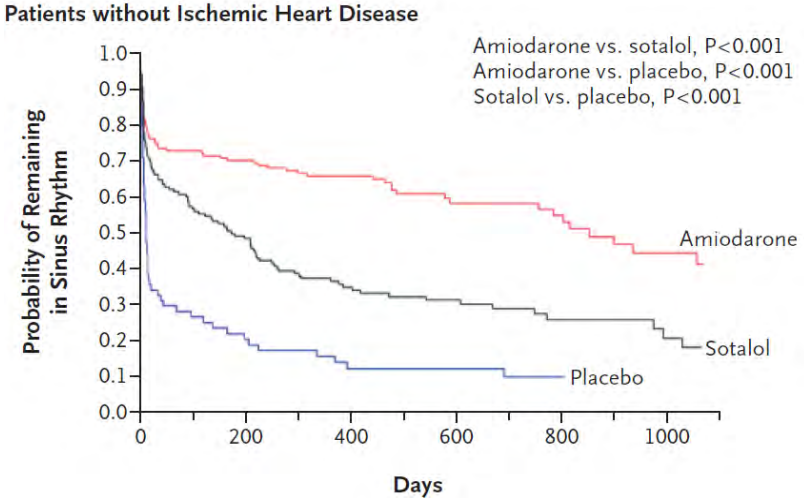
ESC GUIDELINES

Amiodarone vs Sotalol







Amiodarone and sotalol are equally efficacious in converting atrial fibrillation to sinus rhythm. **Amiodarone is superior** for **maintaining sinus rhythm**, but both drugs have similar efficacy in patients with ischemic heart disease.

ORIGINAL ARTICLE

Amiodarone versus Sotalol for Atrial Fibrillation

Bramah N. Singh, M.D., D.Sc., Steven N. Singh, M.D., Domenic J. Reda, Ph.D., X. Charlene Tang, M.D., Ph.D., Becky Lopez, R.N., Crystal L. Harris, Pharm.D., Ross D. Fletcher, M.D., Satish C. Sharma, M.D., J. Edwin Atwood, M.D., Alan K. Jacobson, M.D., H. Daniel Lewis, Jr., M.D., Dennis W. Raisch, Ph.D., and Michael D. Ezekowitz, M.B., Ch.B., Ph.D., for the Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T) Investigators*

N Engl J Med 2005;352:1861-72.

“Pill in the pocket” rhythm control

- In selected patients with **infrequent symptomatic episodes** of **paroxysmal AF**, a single bolus of **oral flecainide (200–300 mg)** or **propafenone (450–600 mg)** can be self-administered by the patient at home
- This approach seems marginally **less effective than hospital-based cardioversion**, but is **practical** and provides control and reassurance to selected patients.

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Long-term antiarrhythmic drug therapy

- The **decision to initiate long term antiarrhythmic drug therapy** needs to **balance symptom** burden, **possible adverse drug reactions**, and **patient preferences.**
- The **principles of antiarrhythmic drug therapy**:
  1. *Treatment is aimed at **reducing AF-related symptoms***
  2. *Efficacy of antiarrhythmic drugs to **maintain sinus rhythm** is **modest***
  3. *Clinically successful antiarrhythmic drug therapy may **reduce rather than eliminate** the recurrence of AF*
  4. *If one antiarrhythmic drug 'fails', a clinically acceptable response may be achieved with another agent*
  5. *Drug-induced **pro-arrhythmia or extracardiac side-effects are frequent***
  6. *Safety rather than **efficacy** considerations should primarily guide the choice of antiarrhythmic drug.*
- Antiarrhythmic drug therapy approximately **doubles sinus rhythm maintenance compared with no therapy.**
- To **reduce the risk of side effects**, a shorter duration of antiarrhythmic drug therapy seems desirable.
- **Short-term antiarrhythmic** drug therapy is also used to **avoid early AF recurrences after catheter ablation**
- **Management of concomitant** cardiovascular **conditions** can **reduce symptom burden** in AF and facilitate the maintenance of sinus rhythm (weight reduction,blood pressure control, heart failure treatment, increasing cardiorespiratory fitness, and other measures)

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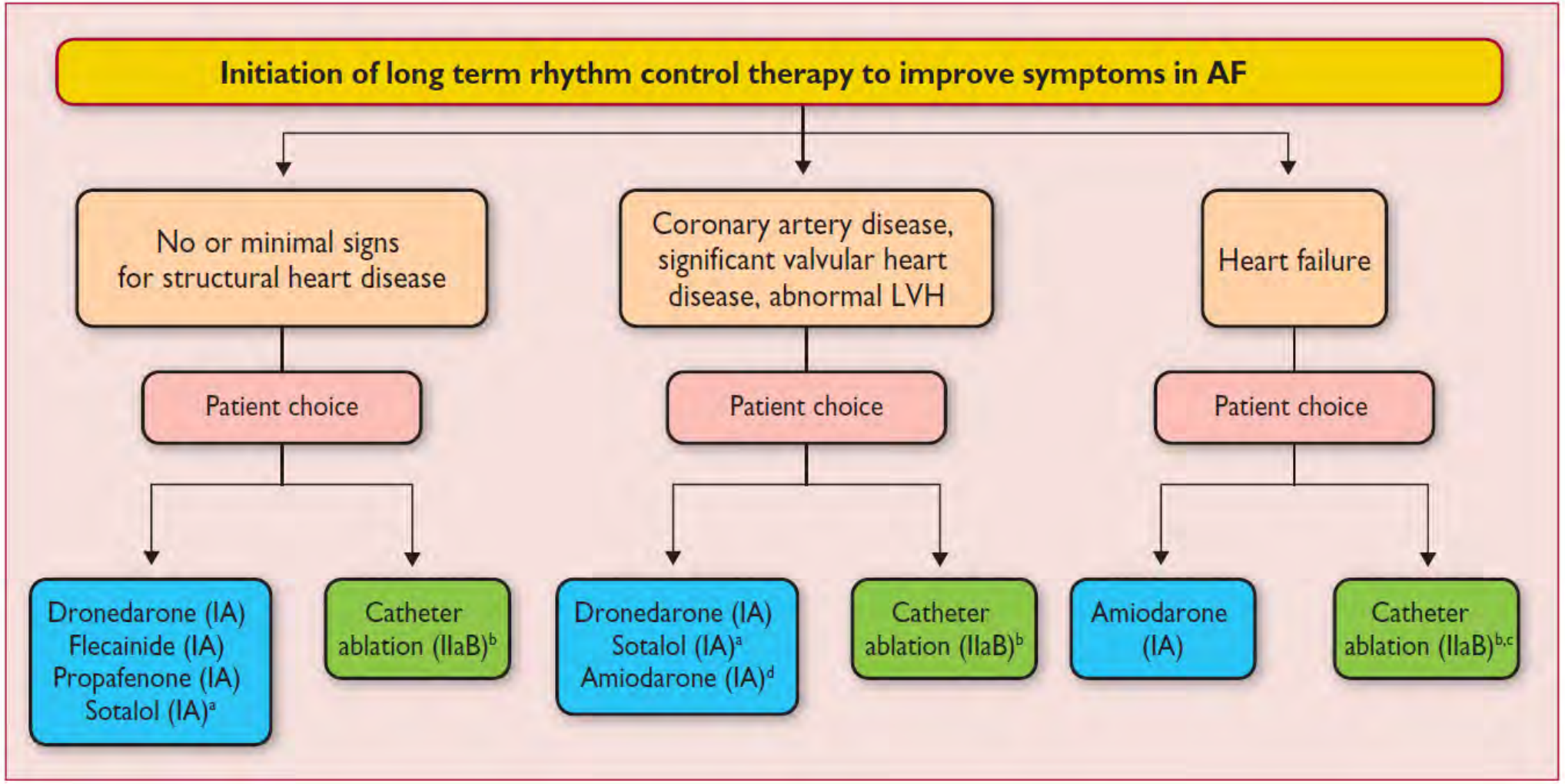
Long term rhythm control strategy



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Rhythm control Recommendations

Recommendations	Class	Level
Rhythm control therapy is indicated for **symptom** improvement in patients with AF.	I	B
Management of cardiovascular risk factors and avoidance of AF triggers should be pursued in patients on rhythm control therapy to facilitate maintenance of sinus rhythm.	IIa	B
With the exception of AF associated with haemodynamic instability, **the choice between electrical and pharmacological cardioversion should be guided by patient and physician** preferences.	IIa	C

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Cardioversion

Cardioversion Recommendations

Recommendations	Class	Level
Electrical cardioversion of AF is recommended in patients with **acute haemodynamic instability** to restore cardiac output.	I	B
Cardioversion of AF (either electrical or pharmacological) is recommended in symptomatic patients with persistent or long-standing persistent AF as part of rhythm control therapy.	I	B
Pre-treatment with amiodarone, flecainide, ibutilide, or propafenone should be considered to enhance success of electrical cardioversion and prevent recurrent AF	IIa	B
In patients with **no history of ischaemic or structural heart disease**, **flecainide, propafenone**, or vernakalant are recommended for pharmacological cardioversion of new-onset AF	I	A
In selected patients with recent-onset AF and no significant structural or ischaemic heart disease, a single oral dose of flecainide or propafenone (the '**pill in the pocket**' approach) should be considered for patient-led cardioversion, following safety assessment.	IIa	B
In patients with **ischaemic and/or structural heart disease, amiodarone** is recommended for cardioversion of AF.	I	A
Vernakalant may be considered as an alternative to amiodarone for pharmacological conversion of AF in patients without hypotension, severe heart failure or severe structural heart disease (especially aortic stenosis).	IIb	B

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

European Heart Journal (2016) **37**, 2893–2962
doi:10.1093/eurheartj/ehw210

ESC GUIDELINES

Anticoagulation in patients undergoing cardioversion

- Cardioversion carries an inherent risk of stroke in non-anticoagulated patients, which is reduced substantially by the administration of anticoagulation.
- **Immediate** initiation of anticoagulation is important in **all patients scheduled for cardioversion.**
- Patients who have been in **AF for longer than 48h** should start OAC at **least 3 weeks before cardioversion and continue it for 4 weeks afterwards** (in patients without a need for long-term anticoagulation)
- OAC should be continued **indefinitely in patients at risk of stroke**. This practice has never been evaluated in controlled trials, but seemed safe in a large observational data set from Finland *(Nuotio I, Hartikainen JE, Gronberg T, Biancari F, Airaksinen KE. Time to cardioversion for acute atrial fibrillation and thromboembolic complications. JAMA 2014;312:647–649)*
- When **early cardioversion is desired**, **TOE can exclude the majority of left atrial thrombi**, allowing immediate cardioversion.

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ESC GUIDELINES

Stroke prevention in patients designated for cardioversion of AF Recommendations

Recommendations	Class	Level
Anticoagulation with heparin or a NOAC should be initiated **as soon as possible before every cardioversion** of AF or atrial flutter.	IIa	B
For cardioversion of AF/atrial flutter, effective anticoagulation is recommended for a **minimum of 3 weeks before** cardioversion.	I	B
Transoesophageal echocardiography (**TOE**) is recommended to exclude cardiac thrombus as an **alternative to preprocedural** anticoagulation when early cardioversion is planned.	I	B
Early cardioversion can be performed **without TOE** in patients with a definite duration of **AF <48 hours.**	IIa	B
In patients at risk for stroke, anticoagulant therapy should be continued **long-term** after cardioversion according to the long-term anticoagulation recommendations, irrespective of the method of cardioversion or the apparent maintenance of sinus rhythm. In patients **without stroke risk factors, anticoagulation is recommended for 4 weeks after cardioversion.**	I	B
In patients where thrombus is identified on TOE, effective anticoagulation is recommended for at least 3 weeks.	I	C
A repeat TOE to ensure thrombus resolution should be considered before cardioversion.	IIa	C

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ESC GUIDELINES

Rate control vs rhythm control

Rate vs rhythm control

Rhythm control	Rate control
Advantages • Fewer symptoms • Better exercise tolerance • Improved haemodynamic function • Less need for anticoagulation	**Advantages** • Avoidance of antiarrhythmic drugs • Good efficacy of rate control drugs • Fewer admissions to hospital • More cost effective • Risk of stroke similar to rhythm control • Mortality similar to rhythm control
Disadvantages • Side effects of antiarrhythmic drugs • Poor efficacy of antiarrhythmic drugs • Expensive • High rates of recurrence • Increased admissions to hospital	**Disadvantages** • Risks of anticoagulation • Risk of tachycardiomyopathy • Symptoms of persisting arrhythmia • Atrial remodelling (permanent)

Iqbal et al. BMJ 2005

Rate vs rhythm control

The strategy of restoring and maintaining sinus rhythm had **no clear advantage** over the strategy of controlling the ventricular rate and allowing atrial fibrillation to persist.

Trend toward increased mortality in association with the **rhythm-control** strategy (P=0.08)

The rates of the **composite end point** of *death*, *disabling stroke*, *disabling anoxic encephalopathy*, *major bleeding*, and *cardiac arrest* were also **similar in the two groups** (P=0.33).

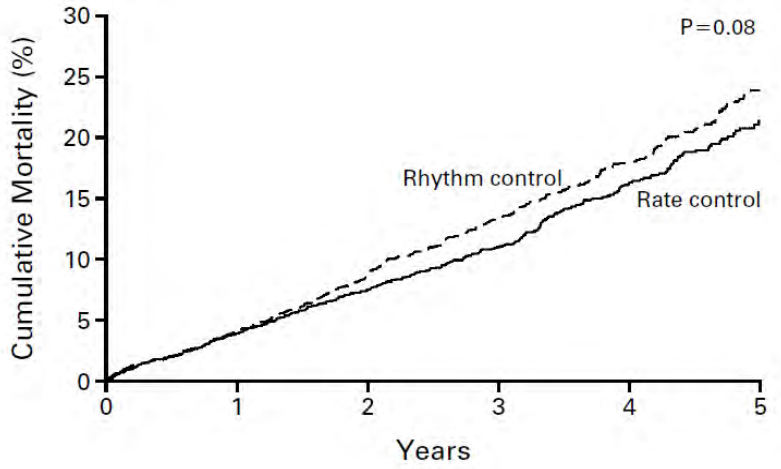
The majority of strokes in both groups occurred in patients who had **stopped taking warfarin or whose INR was subtherapeutic** at the time of the stroke, in general agreement with previously reported observations.

Torsade de pointes or **bradycardic arrest** occurred **more often in the rhythm-control group** than in the rate-control group.

The patients in the **rhythm-control group** were significantly **more likely to be hospitalized and have adverse drug effects** than those in the rate-control group

This study also suggest **that continuous anticoagulation is warranted in all patients** with atrial fibrillation and **risk factors for stroke**, **even when sinus rhythm appears to be restored** and **maintained.**

Mortality (any cause)



No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

Figure 1. Cumulative Mortality from Any Cause in the Rhythm-Control Group and the Rate-Control Group.

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

The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators*

The New England Journal of Medicine

VOLUME 347 DECEMBER 5, 2002 NUMBER 23

Rate vs rhythm control

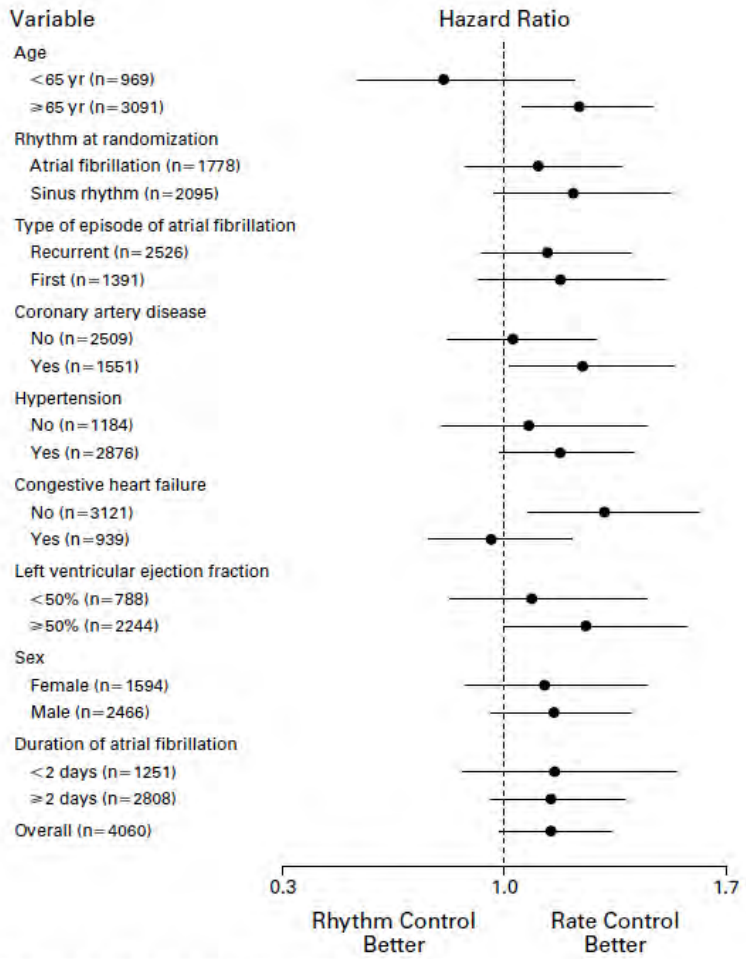


Figure 2. Hazard Ratios for Death in Prespecified Subgroups.

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

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

The New England Journal of Medicine

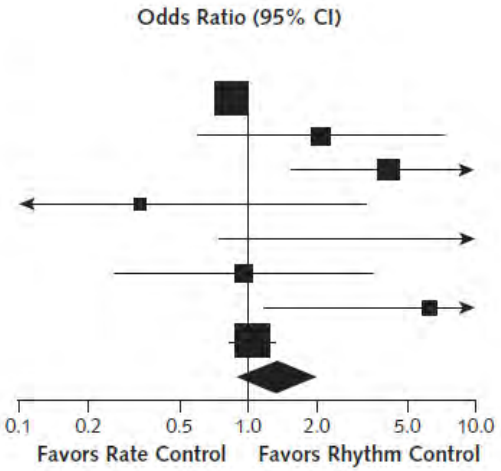
VOLUME 347 DECEMBER 5, 2002 NUMBER 23

Rate vs rhythm control

Overall death

A.

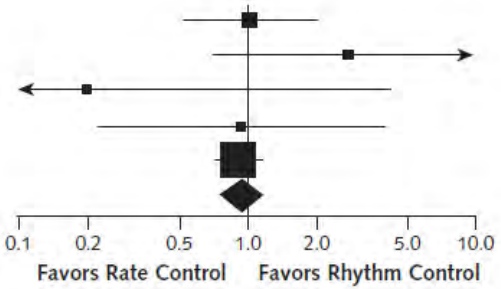
Study, Year (Reference)	Odds Ratio (95% CI)	Deaths/Total, *n/N*	
		Rate Control	Rhythm Control
Wyse et al, 2002 (27)	0.851 (0.720–1.005)	310/2027	356/2033
Carlsson et al, 2003 (18)	2.087 (0.608–7.167)	8/100	4/100
Okçün et al, 2004 (20)	4.125 (1.562–10.895)	36/84	6/39
Opolski et al, 2004 (21)	0.337 (0.034–3.291)	1/101	3/104
Vora et al, 2004 (26)	14.099 (0.754–263.543)	5/40	0/45
Petrac et al, 2005 (22)	0.957 (0.260–3.532)	5/52	5/50
Yildiz et al, 2008 (28)	6.270 (1.185–33.192)	5/66	2/155
Talajic et al, 2010 (24)	1.048 (0.836–1.314)	228/694	217/682
Overall	1.343 (0.893–2.020)		



CV death

B.

		Cardiovascular Deaths/Total, *n/N*	
		Rate Control	Rhythm Control
Van Gelder et al, 2002 (25)	1.042 (0.529–2.051)	18/256	18/266
Carlsson et al, 2003 (18)	2.812 (0.724–10.924)	8/100	3/100
Opolski et al, 2004 (21)	0.202 (0.010–4.259)	0/101	2/104
Petrac et al, 2005 (22)	0.958 (0.226–4.060)	4/52	4/50
Talajic et al, 2010 (24)	0.926 (0.728–1.179)	175/694	182/682
Overall	0.959 (0.769–1.196)		



REVIEW | Annals of Internal Medicine

Rate- and Rhythm-Control Therapies in Patients With Atrial Fibrillation

A Systematic Review

Sana M. Al-Khatib, MD, MHS; Nancy M. Allen LaPointe, PharmD; Ranee Chatterjee, MD, MPH; Matthew J. Crowley, MD; Matthew E. Dupre, PhD; David F. Kong, MD; Renato D. Lopes, MD, PhD; Thomas J. Povsic, MD, PhD; Shveta S. Raju, MD; Bimal Shah, MD; Andrzej S. Kosinski, PhD; Amanda J. McBroom, PhD; and Gillian D. Sanders, PhD

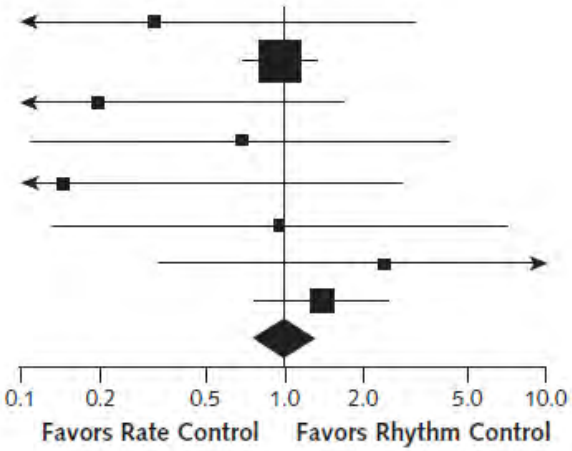
Ann Intern Med. 2014;160:760-773.

Rate vs rhythm control

Stroke

C.

		Stroke/Total, *n/N*	
		Rate Control	Rhythm Control
Brignole et al, 2002 (17)	0.319 (0.032–3.142)	1/69	3/68
Wyse et al, 2002 (27)	0.964 (0.701–1.326)	77/2027	80/2033
Carlsson et al, 2003 (18)	0.192 (0.022–1.673)	1/100	5/100
Okçün et al, 2004 (20)	0.685 (0.110–4.276)	3/84	2/39
Opolski et al, 2004 (21)	0.143 (0.007–2.801)	0/101	3/104
Petrac et al, 2005 (22)	0.960 (0.130–7.091)	2/52	2/50
Yildiz et al, 2008 (28)	2.391 (0.330–17.342)	2/66	2/155
Talajic et al, 2010 (24)	1.392 (0.776–2.495)	28/694	20/682
Overall	0.994 (0.759–1.302)		



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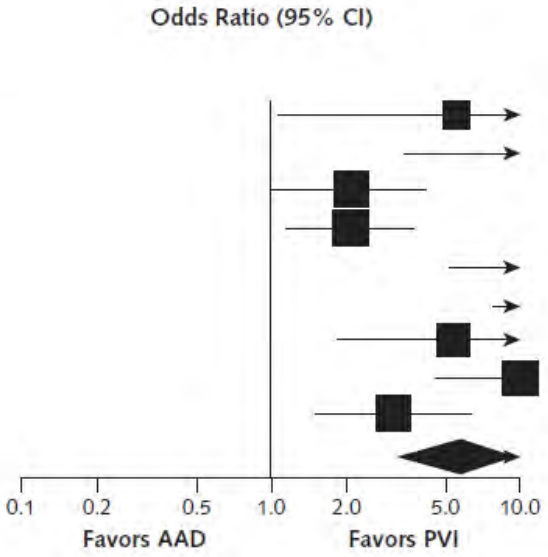
Ann Intern Med. 2014;160:760-773.

Rate vs rhythm control

Maintenance of SR AAD vs PVI

E.

Study, Year (Reference)	Odds Ratio (95% CI)	Maintenance of Sinus Rhythm/Total, *n/N*	
		PVI	AAD
Krittayaphong et al, 2003 (147)	5.500 (1.065–28.416)	11/14	6/15
Wazni et al, 2005 (157)	11.846 (3.387–41.433)	28/32	13/35
Oral et al, 2006 (114)	2.066 (1.028–4.155)	57/77	40/69
Pappone et al, 2006 (115)	2.048 (1.130–3.711)	72/99	56/99
Stabile et al, 2006 (119)	13.300 (5.069–34.894)	38/68	6/69
Jaïs et al, 2008 (143)	24.769 (8.634–71.059)	46/52	13/55
Forleo et al, 2009 (112)	5.333 (1.839–15.471)	28/35	15/35
Wilber et al, 2010 (126)	9.917 (4.509–21.808)	70/106	10/61
Mont et al, 2014 (132)	3.059 (1.494–6.263)	69/98	21/48
Overall	5.874 (3.180–10.849)		



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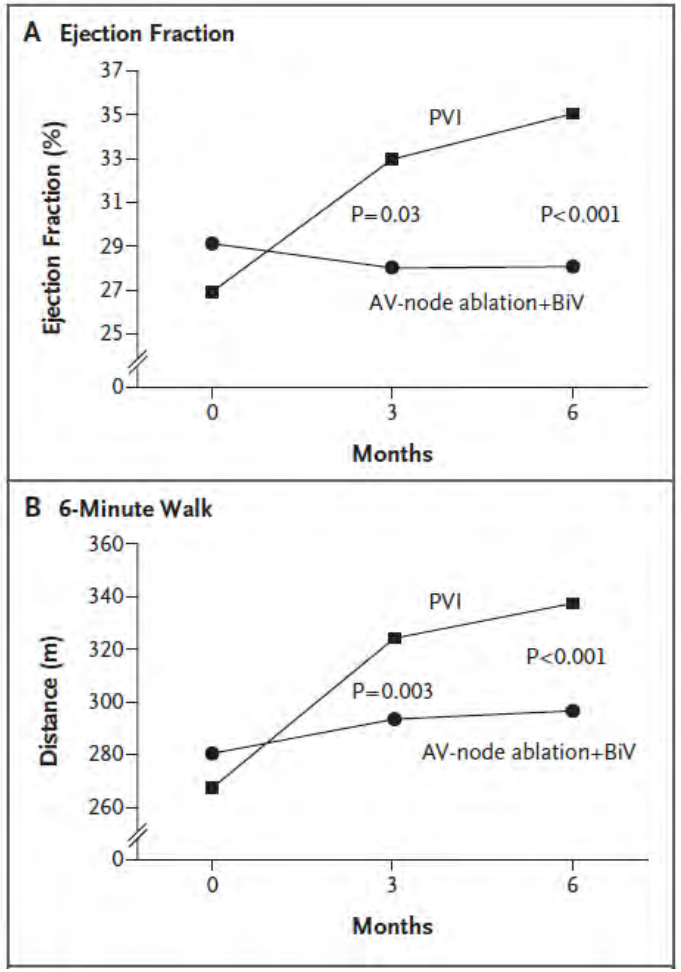
Ann Intern Med. 2014;160:760-773.

Rhythm control in Heart Failure

- 41 patients with drug resistant AF (paroxysmal, persistent)
- LVEF<40%
- NYHA II-III
- Pulmonary vein isolation vs CRT-P + AV node ablation

Pulmonary-vein isolation (=**rhythm control strategy**) is **superior** to atrioventricular-node ablation with biventricular pacing (= **rate control strategy) in patients with heart failure who had drug-refractory atrial fibrillation**



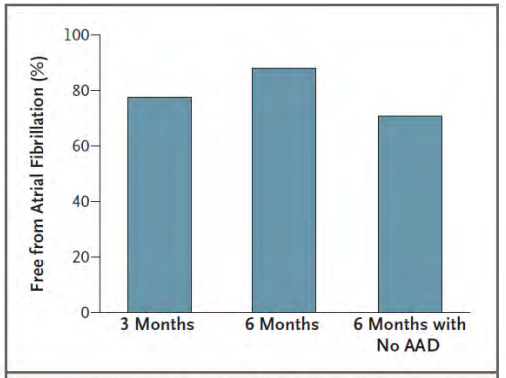


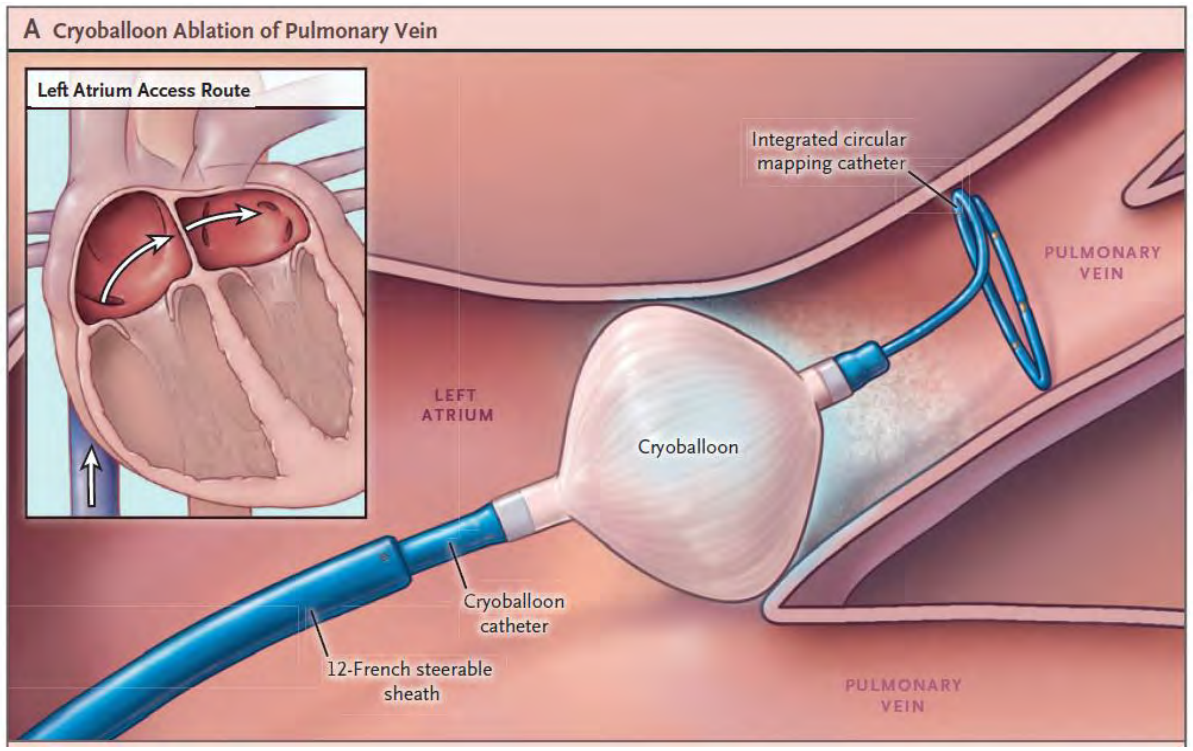
Figure 2. Freedom from Atrial Fibrillation in Patients Undergoing Pulmonary-Vein Isolation with or without Antiarrhythmic Drugs (AAD).

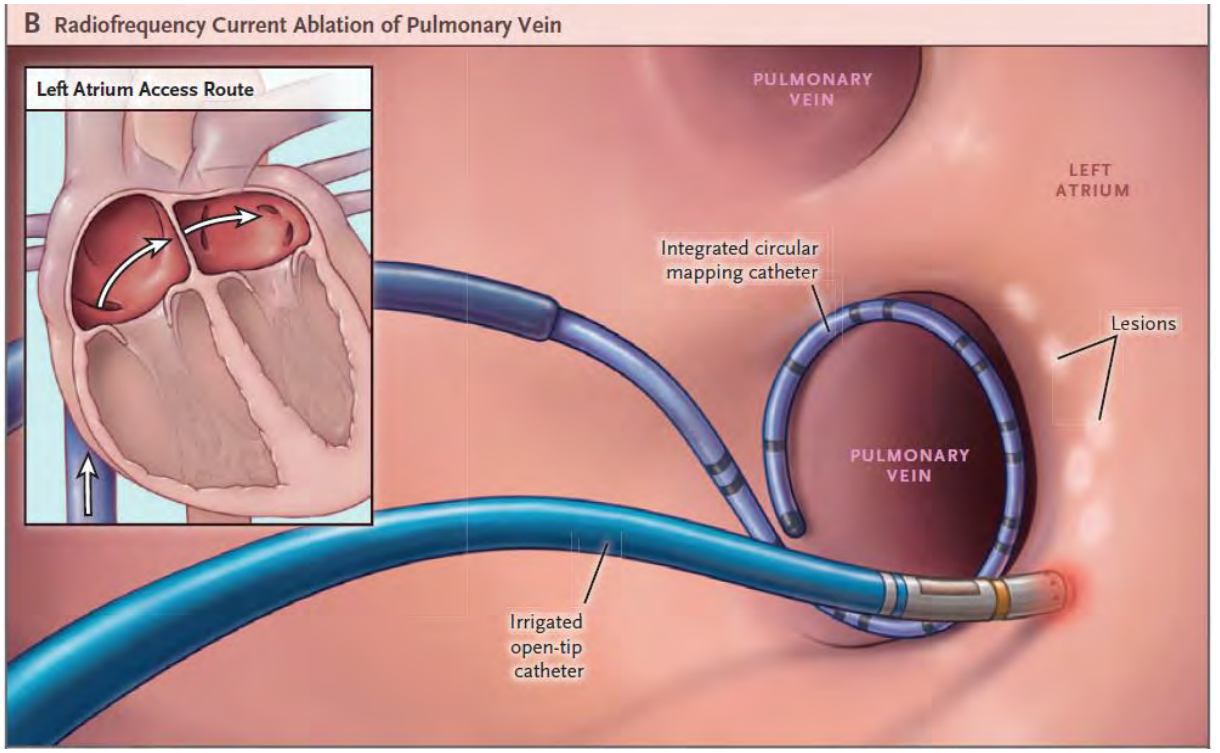
ORIGINAL ARTICLE

Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure

Catheter Ablation vs Medical Therapy

Catheter Ablation of AF





ORIGINAL ARTICLE

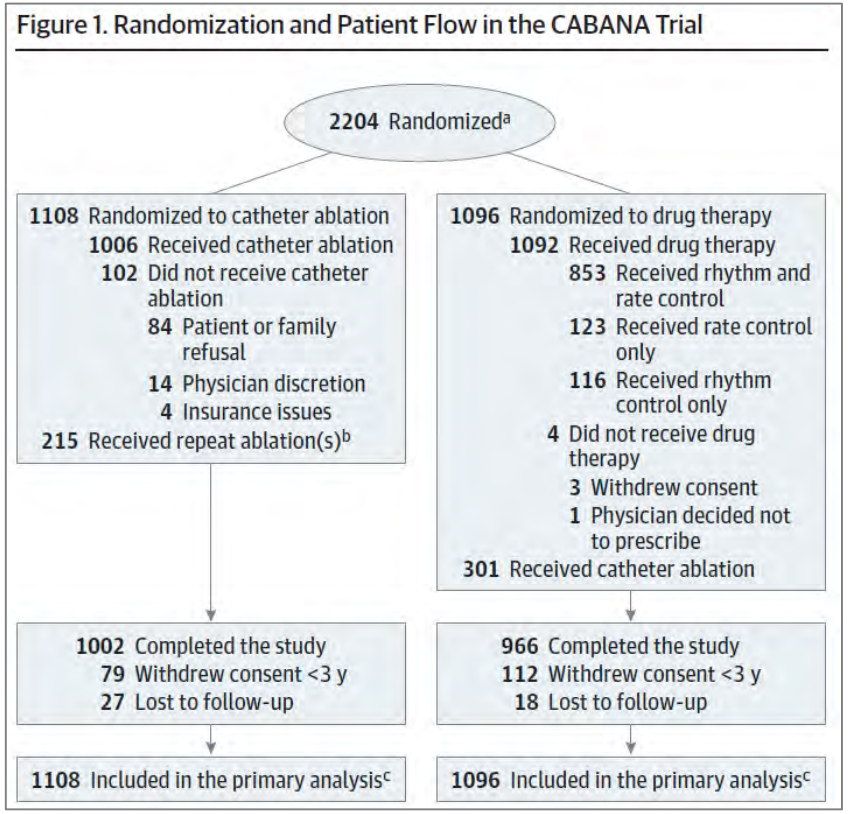
Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Karl-Heinz Kuck, M.D., Josep Brugada, M.D., Alexander Fürnkranz, M.D., Andreas Metzner, M.D., Feifan Ouyang, M.D., K.R. Julian Chun, M.D., Arif Elvan, M.D., Ph.D, Thomas Arentz, M.D., Kurt Bestehorn, M.D., Stuart J. Pocock, Ph.D., Jean-Paul Albenque, M.D., Ph.D., and Claudio Tondo, M.D., Ph.D., for the FIRE AND ICE Investigators*

N Engl J Med 2016;374:2235-45.

Catheter Ablation vs Medical Therapy

- **2204** symptomatic patients
- **Paroxysmal**, **persistent** or **longstanding persistent** AF
- **Catheter ablation** group (n= 1108) vs **standard rhythm** and/or rate-control drugs (n= 1096)
- **At least 1 risk factor** for stroke
- Randomized from November 2009 to April 2016
- 126 centers in 10 countries
- Primary study outcome: Composite measure of death, disabling stroke, serious bleeding, or cardiac arrest
- Secondary objective: Long term QOL outcomes



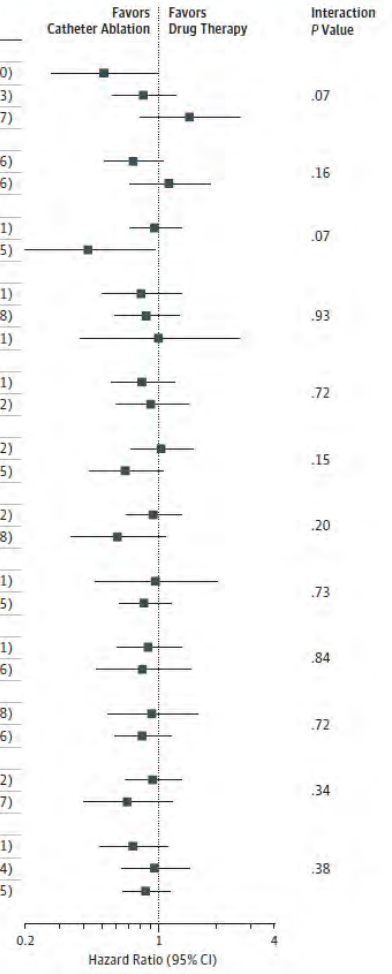
JAMA | Original Investigation
Effect of Catheter Ablation vs Medical Therapy on Quality of Life Among Patients With Atrial Fibrillation
The CABANA Randomized Clinical Trial

Daniel B. Mark, MD, MPH; Kevin J. Anstrom, PhD; Shubin Sheng, PhD; Jonathan P. Piccini, MD, MHS; Khaula N. Baloch, MPH; Kristi H. Monahan, RN; Melanie R. Daniels, BA; Tristram D. Bahnson, MD; Jeanne E. Poole, MD; Yves Rosenberg, MD, MPH; Kerry L. Lee, PhD; Douglas L. Packer, MD; for the CABANA Investigators

Catheter Ablation vs Medical Therapy

Figure 4. Primary End Point Subgroup Analysis (Intention to Treat)

Source	No. of Events/Patients (Person-Years)		Hazard Ratio (95% CI)	Interaction *P* Value
	Catheter Ablation	Drug Therapy		
Age, y				
<65	14/375 (1483)	27/391 (1498)	0.52 (0.27-1.00)	
≥65 and <75	50/577 (2159)	56/553 (2019)	0.84 (0.57-1.23)	.07
≥75	25/156 (514)	18/152 (529)	1.46 (0.80-2.67)	
Sex				
Male	54/695 (2670)	71/690 (2591)	0.74 (0.52-1.06)	.16
Female	35/413 (1485)	30/406 (1456)	1.14 (0.70-1.86)	
Minority status				
White	80/995 (3721)	82/984 (3654)	0.96 (0.71-1.31)	.07
Minority[a]	9/113 (434)	19/112 (393)	0.43 (0.20-0.95)	
Atrial fibrillation type[b]				
Paroxysmal	31/470 (1756)	38/476 (1761)	0.82 (0.51-1.31)	.93
Persistent	49/524 (1922)	55/518 (1860)	0.87 (0.59-1.28)	
Long-standing persistent	9/114 (477)	8/101 (426)	1.01 (0.39-2.61)	
Time since onset of atrial fibrillation, y				
≤1	50/540 (1922)	58/523 (1835)	0.83 (0.57-1.21)	.72
>1	39/560 (2207)	42/562 (2177)	0.92 (0.59-1.42)	
Baseline NYHA class[c]				
No heart failure or class I	55/719 (2735)	52/689 (2657)	1.04 (0.71-1.52)	.15
≥ Class II	34/378 (1396)	49/400 (1372)	0.68 (0.44-1.05)	
History of congestive heart failure				
No	68/934 (3506)	72/931 (3500)	0.95 (0.68-1.32)	.20
Yes	21/174 (650)	29/163 (547)	0.61 (0.35-1.08)	
Hypertension				
Absent	15/232 (857)	14/195 (761)	0.97 (0.47-2.01)	.73
Present	74/876 (3298)	87/900 (3287)	0.85 (0.62-1.15)	
Hypertension with LVH				
Absent	53/632 (2391)	51/544 (2022)	0.89 (0.61-1.31)	.84
Present	22/286 (1126)	27/301 (1152)	0.83 (0.47-1.46)	
CHA_2DS_2-VASc score[d]				
≤2 (Less risk)	26/481 (1861)	28/478 (1859)	0.93 (0.54-1.58)	.72
>2 (More risk)	63/627 (2295)	73/618 (2188)	0.83 (0.59-1.16)	
Sleep apnea				
Absent	65/846 (3129)	69/849 (3106)	0.94 (0.67-1.32)	.34
Present	24/262 (1027)	32/246 (941)	0.69 (0.41-1.17)	
Body mass index[e]				
<30 (Not obese)	42/541 (2012)	53/523 (1886)	0.74 (0.49-1.11)	.38
≥30 (Obese)	45/545 (2088)	48/561 (2122)	0.96 (0.64-1.44)	
All patients	89/1108 (4155)	101/1096 (4047)	0.86 (0.65-1.15)	



JAMA | Original Investigation

Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation
The CABANA Randomized Clinical Trial

Douglas L. Packer, MD; Daniel B. Mark, MD, MPH; Richard A. Robb, PhD; Kristi H. Monahan, RN; Tristram D. Bahnson, MD; Jeanne E. Poole, MD; Peter A. Noseworthy, MD; Yves D. Rosenberg, MD, MPH; Neal Jeffries, PhD; L. Brent Mitchell, MD; Greg C. Flaker, MD; Evgeny Pokushalov, MD; Alexander Romanov, MD; T. Jared Bunch, MD; Georg Noelker, MD; Andrey Ardashev, MD; Amiran Revishvili, MD; David J. Wilber, MD; Riccardo Cappato, MD; Karl-Heinz Kuck, MD; Gerhard Hindricks, MD; D. Wyn Davies, MD; Peter R. Kowey, MD; Gerald V. Naccarelli, MD; James A. Reiffel, MD; Jonathan P. Piccini, MD, MHS; Adam P. Silverstein, MS; Hussein R. Al-Khalidi, PhD; Kerry L. Lee, PhD; for the CABANA Investigators

Catheter Ablation vs Medical Therapy

Baseline Characteristic	Catheter Ablation (n = 1108)	Drug Therapy (n = 1096)
Comorbidities		
CHA_2DS_2-VASc[f]		
Median (Q1, Q3)	3.0 (2.0, 4.0)	3.0 (2.0, 4.0)
0-1 (Lowest risk)	208 (18.8)	187 (17.1)
2	273 (24.6)	291 (26.6)
3	308 (27.8)	329 (30.0)
4	178 (16.1)	151 (13.8)
≥5 (Highest risk)	141 (12.7)	138 (12.6)

Table 1. Baseline Demographics and Clinical Characteristics (continued)

	No. (%)	
Baseline Characteristic	Catheter Ablation (n = 1108)	Drug Therapy (n = 1096)
Arrhythmia History		
Time since onset of AF, y		
Median (Q1, Q3)	1.1 (0.3, 4.1)	1.1 (0.3, 3.7)
Type of AF at enrollment[g]		
Persistent	524 (47.3)	518 (47.3)
Paroxysmal	470 (42.4)	476 (43.5)
Long-standing persistent	114 (10.3)	101 (9.2)
Prior hospitalization for AF	449 (40.6)	425 (38.8)
Prior direct cardioversion	398 (36.0)	411 (37.5)
History of atrial flutter	140 (12.9)	158 (14.6)
Prior ablation for atrial flutter	48 (4.3)	60 (5.5)
Rhythm control therapy[h]		
1 Rhythm control drug	398 (81.6)	452 (82.2)
≥2 Rhythm control drugs	90 (18.4)	98 (17.8)

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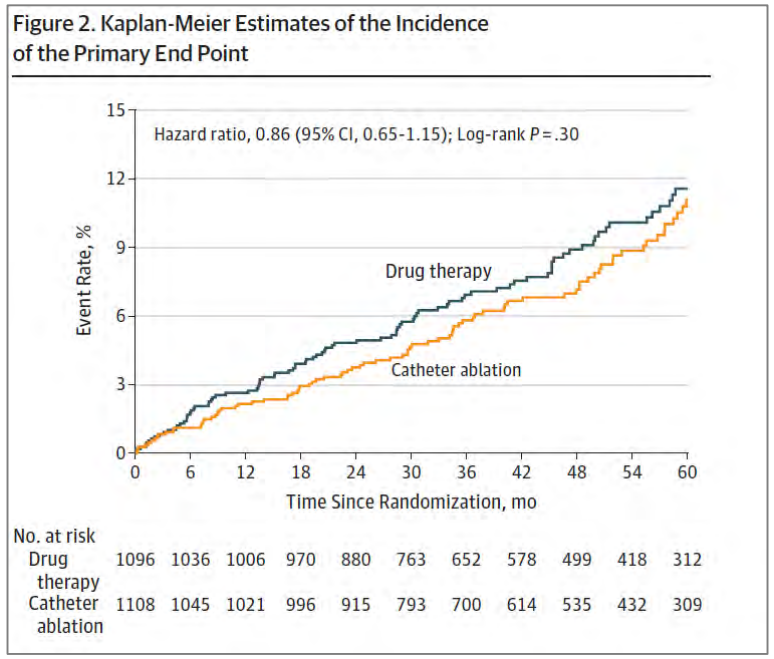
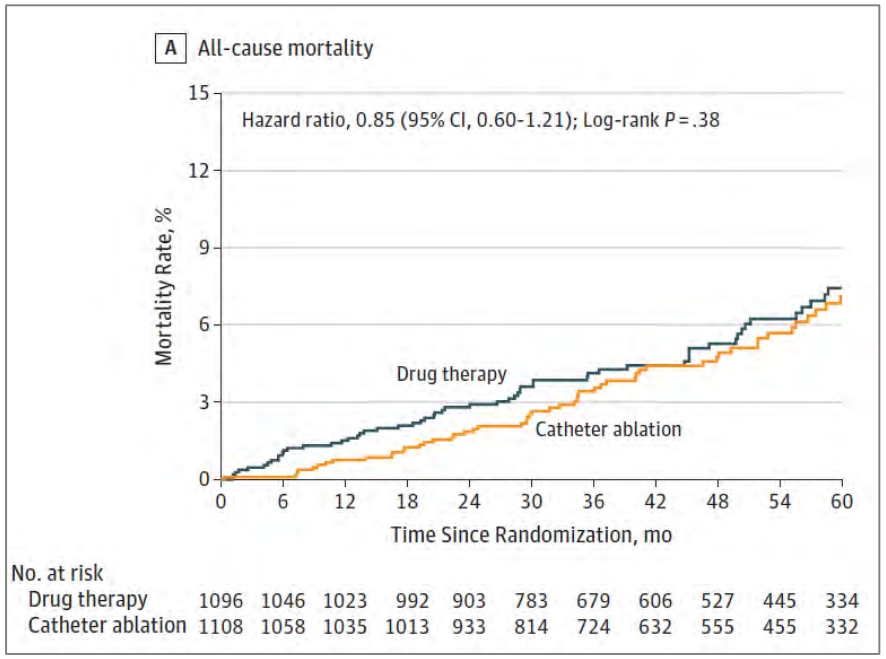
Catheter Ablation vs Medical Therapy

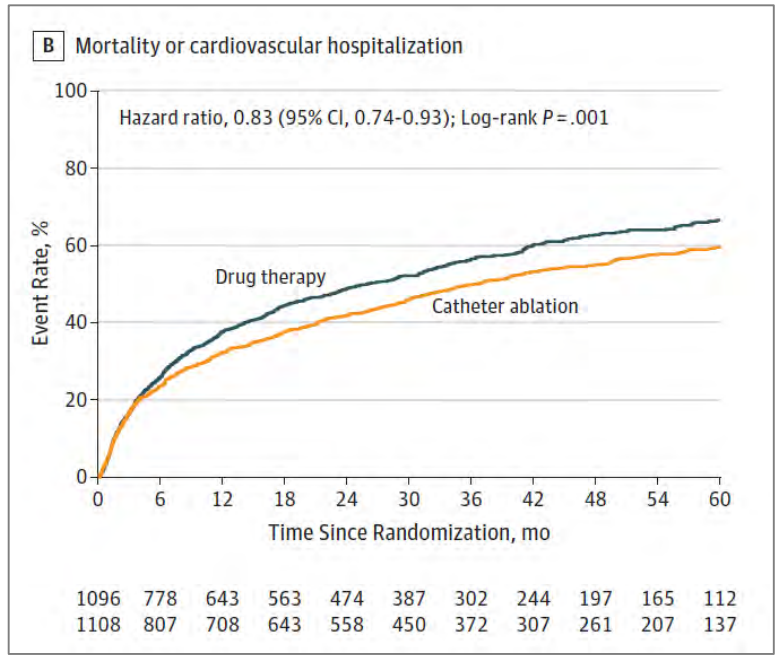
Cumulative risk of **death**, **disabling stroke**, serious **bleeding** or **cardiac arrest**



All cause mortality



Mortality or Cardiovascular Hospitalization



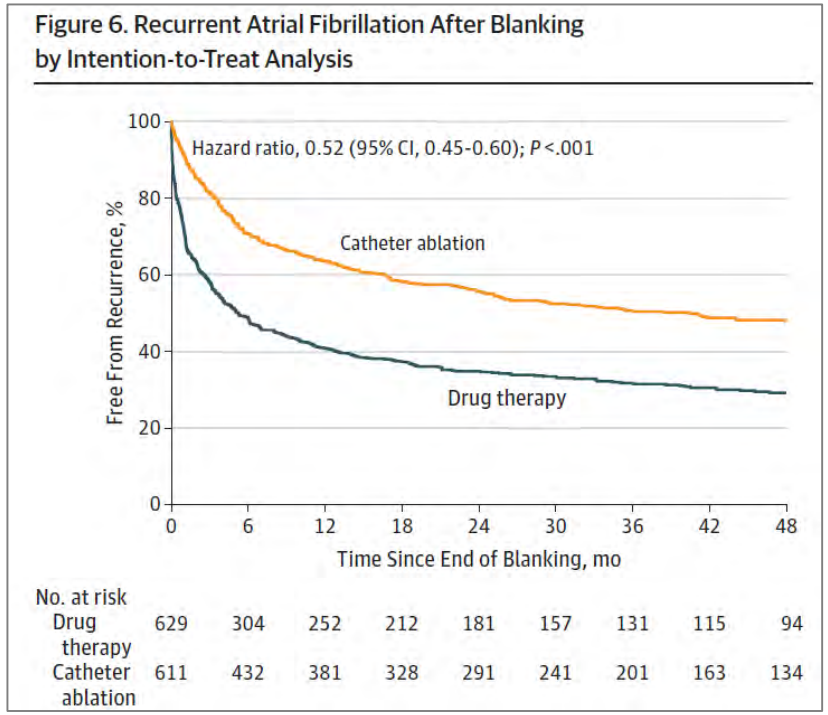
Among patients with **AF,** the strategy of **catheter ablation**, compared with medical therapy**, does not significantly reduce the primary composite end point of death, disabling stroke, serious bleeding, or cardiac arrest.**

JAMA | Original Investigation

Effect of Catheter Ablation vs Medical Therapy on Quality of Life Among Patients With Atrial Fibrillation
The CABANA Randomized Clinical Trial

Daniel B. Mark, MD, MPH; Kevin J. Anstrom, PhD; Shubin Sheng, PhD; Jonathan P. Piccini, MD, MHS; Khaula N. Baloch, MPH; Kristi H. Monahan, RN; Melanie R. Daniels, BA; Tristram D. Bahnson, MD; Jeanne E. Poole, MD; Yves Rosenberg, MD, MPH; Kerry L. Lee, PhD; Douglas L. Packer, MD; for the CABANA Investigators

Catheter Ablation vs Medical Therapy



Catheter ablation is associated with a lower AF recurrence rate than drug therapy (50% vs 69% at 3years post blanking follow-up).

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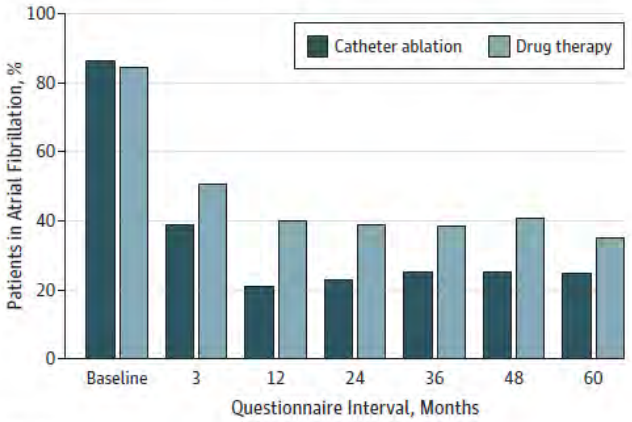
Catheter Ablation vs Medical Therapy

Figure 1. Patients Who Reported Being in Atrial Fibrillation Currently or Within the Past Month



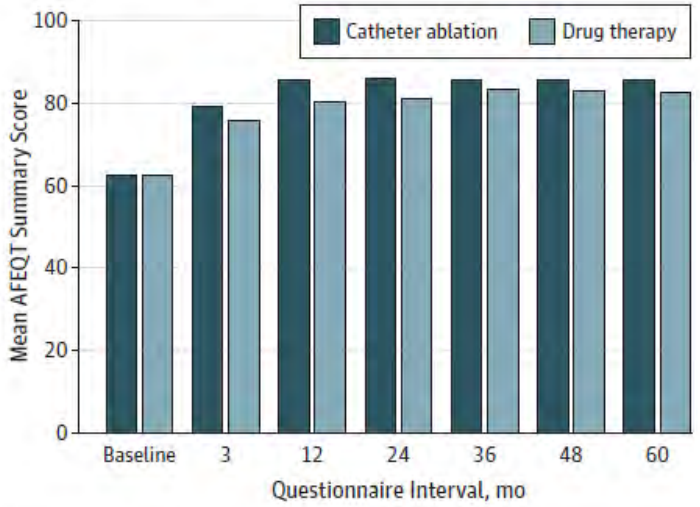
No. of patients

Catheter ablation	915	374	195	198	164	127	85
Drug therapy	885	493	362	314	239	199	117

Responses to the first item in the Atrial Fibrillation Effect on Quality of Life instrument.

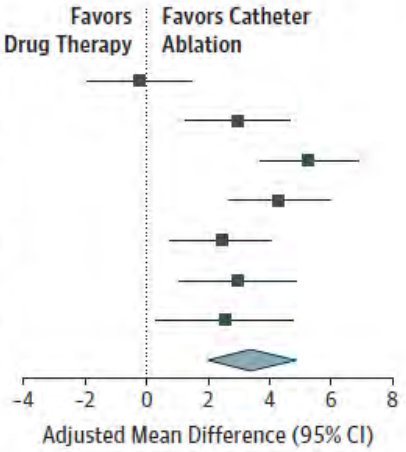
Figure 2. Atrial Fibrillation Effect on Quality of Life (AFEQT) Summary Scores

A Mean AFEQT summary score



B Between-group AFEQT summary score difference

Interval, mo	No. of Patients Ablation (n = 1108)	No. of Patients Drug Rx (n = 1096)	Adjusted Mean Difference (95% CI)
Baseline	1084	1078	-0.2 (-1.9 to 1.5)
3	971	983	3.0 (1.3 to 4.7)
12	915	903	5.3 (3.7 to 6.9
24	856	798	4.3 (2.7 to 6.0)
36	645	605	2.5 (0.8 to 4.1)
48	476	473	3.0 (1.1 to 4.9)
60	329	320	2.6 (0.3 to 4.8)
All	4192	4082	3.4 (2.1 to 4.8)



Catheter **ablation** provides **incremental symptomatic and QOL benefits over drug therapy** that is clinically important and statistically significant for patients with AF

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Catheter Ablation of AF

- AF ablation, when performed in experienced centers by adequately trained teams, is **more effective than antiarrhythmic drug therapy** in **maintaining sinus rhythm**, and the **complication rate**, though not negligible, is **similar** to the complication rate for antiarrhythmic drugs
- Effective in restoring and maintaining sinus rhythm in patients with symptomatic **paroxysmal**, **persistent**, and probably **long-standing persistent AF**, in general as **second-line treatment** after failure of or intolerance to antiarrhythmic drug therapy
- **As first-line treatment** for paroxysmal AF, randomized trials showed only **modestly improved rhythm outcome** with catheter ablation compared to antiarrhythmic drug therapy.
- In patients who experience **symptomatic recurrences of AF despite antiarrhythmic drug therapy, all RCTs showed better sinus rhythm maintenance with catheter ablation** than on antiarrhythmic drugs.
- **Fewer data** are available reporting the effectiveness and safety of catheter ablation in patients with **persistent or longstanding persistent AF**, but **all point to lower recurrence rates** after catheter ablation compared to antiarrhythmic drug therapy with or without cardioversion
- There is **no current indication for catheter ablation to prevent cardiovascular outcomes** (or desired withdrawal of anticoagulation), or to **reduce hospitalization**.

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

European Heart Journal (2016) **37**, 2893–2962
doi:10.1093/eurheartj/ehw210

ESC GUIDELINES

Recommendations for catheter ablation

Recommendations	Class	Level
Catheter ablation of symptomatic **paroxysmal AF** is recommended to **improve AF symptoms** in patients who have **symptomatic recurrences on antiarrhythmic drug therapy** (amiodarone, dronedarone, flecainide, propafenone, sotalol), and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.	I	A
Ablation of common atrial flutter should be considered to prevent recurrent flutter as part of an AF ablation procedure if documented or occurring during the AF ablation.	IIa	B
Catheter ablation of AF should be considered as first-line therapy to prevent recurrent AF and to improve symptoms in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.	IIa	B
All patients should receive oral anticoagulation for at least **8 weeks after** catheter (IIaB) or surgical (IIaC) ablation.	IIa	B
Anticoagulation for stroke prevention should **be continued indefinitely after apparently successful catheter or surgical ablation** of AF in patients at high-risk of stroke.	IIa	B
AF ablation should be considered in symptomatic patients with AF and heart failure with reduced ejection fraction to improve symptoms and cardiac function when tachycardiomyopathy is suspected.	IIa	C
AF ablation should be considered as a **strategy to avoid pacemaker implantation** in patients with **AF-related bradycardia**.	IIa	C
Catheter or surgical ablation should be considered in patients with symptomatic persistent or long-standing persistent AF refractory to AAD therapy to improve symptoms, considering patient choice, benefit and risk, supported by an AF Heart	IIa	C

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ESC GUIDELINES

Complications of catheter ablation

Complication severity	Complication type	Rate [727, 748, 750, 754-759]
Life-threatening complications	Periprocedural death	<0.2%
	Oesophageal injury (perforation/fistula)[a]	<0.5%
	Periprocedural stroke (including TIA/air embolism)	<1%
	Cardiac tamponade	1–2%
Severe complications	Pulmonary vein stenosis	<1%
	Persistent phrenic nerve palsy	1–2%
	Vascular complications	2–4%
	Other severe complications	≈1%
Other moderate or minor complications		1–2%
Unknown significance	Asymptomatic cerebral embolism (silent stroke)[b]	5–20%
	Radiation exposure	

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Conclusions

- **Opportunistic screening** for AF is recommended by pulse taking or ECG rhythm strip in **patients >65 years of age.**
- In patients with **TIA or ischaemic stroke**, screening for AF is recommended by short-term ECG recording followed by continuous ECG monitoring for at least **72 hours.**
- **Transthoracic echocardiography is recommended in all AF patients** to guide management.
- The **CHA_2DS_2-VASc score is recommended for stroke risk prediction** in patients with AF.
- Oral anticoagulation therapy to prevent thromboembolism is recommended for all **male** AF patients with a **CHA_2DS_2-VASc score of 2 or more.**
- Oral anticoagulation therapy to prevent thromboembolism is recommended in all **female** AF patients with a **CHA_2DS_2-VASc score of 3 or more**.
- When oral anticoagulation is initiated in a patient with AF who is eligible for a non vitamin-K-antagonist oral anticoagulant (apixaban, dabigatran, edoxaban, or rivaroxaban), a **NOAC is recommended in preference to a vitamin K antagonist.**
- **NOACs** (apixaban, dabigatran, edoxaban, and rivaroxaban) are **not recommended in patients with mechanical heart valves or moderate-to-severe mitral stenosis**

Conclusion (2)

- **Beta-blockers, digoxin, diltiazem, or verapamil** are recommended to **control heart rate in AF patients with LVEF ≥40%.**
- **Beta-blockers and/or digoxin** are recommended to control heart rate in AF patients with **LVEF <40%.**
- **Rhythm control therapy** is indicated for **symptom improvement** in patients with AF.
- In patients with **no history of ischaemic or structural heart disease, flecainide, propafenone**, or vernakalant are recommended for pharmacological cardioversion of new-onset AF.
- In patients with **ischaemic and/or structural heart disease, amiodarone is recommended for cardioversion of AF.**
- **For cardioversion of AF/atrial flutter**, **effective anticoagulation is recommended for a minimum of 3 weeks before** cardioversion.
- Dronedarone, flecainide, propafenone, or sotalol are recommended for prevention of recurrent symptomatic AF in patients with normal left ventricular function and without pathological left ventricular hypertrophy.
- **Amiodarone is recommended** for prevention of recurrent symptomatic AF in patients with **heart failure.**
- **Catheter ablation of symptomatic paroxysmal AF is recommended to improve AF symptoms** in patients who have symptomatic further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer the procedure in an experienced centre.

Fin