# FIBRILACIÓN AURICULAR

## Novedades en el tratamiento

(ESC guidelines 2016)

Francisco Díaz Cortegana

Servicio de Cardiología. Unidad de Arritmias

Hospital Universitario Miguel Servet. Zaragoza

# Potenciales conflictos de interés

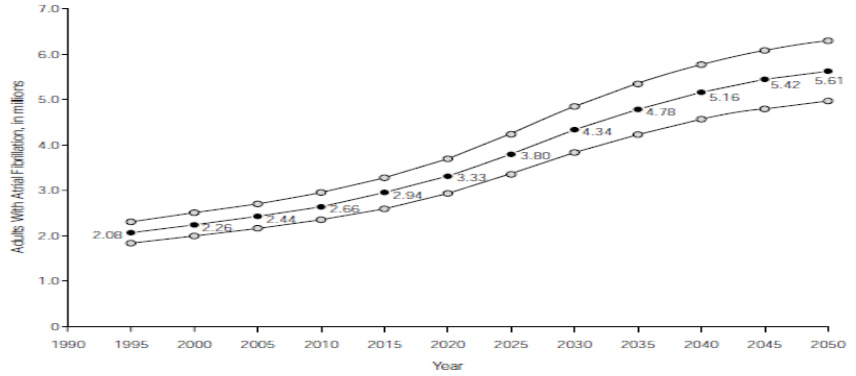
Jonhson & Jonhson. Biosense Webster. Cordis.

Biotronik.

# Fibrilación auricular

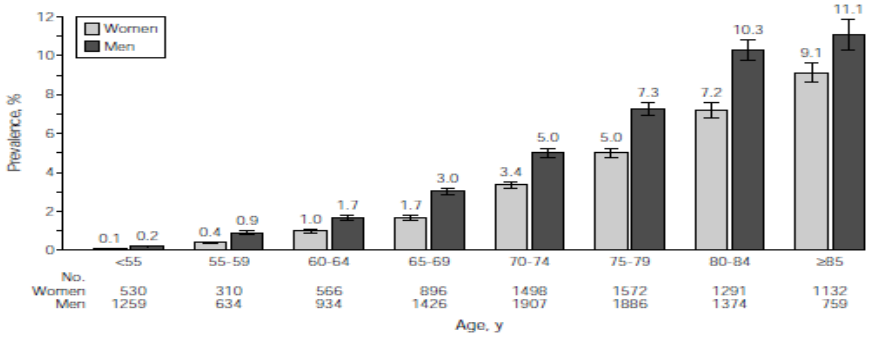
- Prevalencia en 2010, 20,9 millones.
- Incidencia anual 120-215 mil en EU.
- Asociada con edad
- Sexo femenino
- Raza "blanca"

**Figure 3.** Projected Number of Adults With Atrial Fibrillation in the United States Between 1995 and 2050

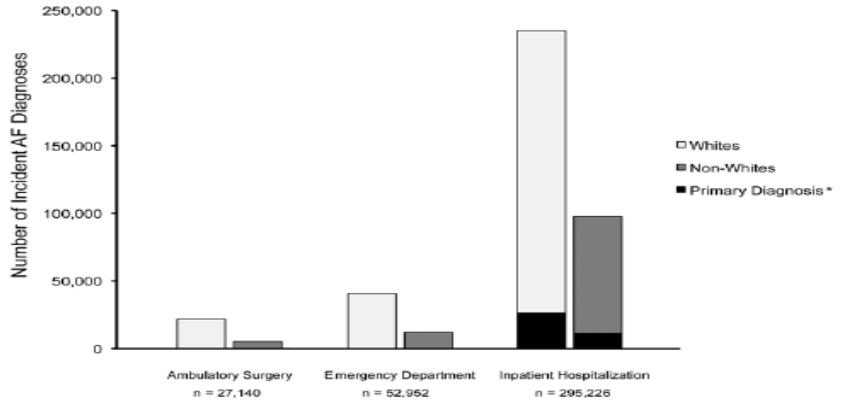



Upper and lower curves represent the upper and lower scenarios based on sensitivity analyses.

**Figure 2.** Prevalence of Diagnosed Atrial Fibrillation Stratified by Age and Sex




Errors bars represent 95% confidence intervals. Numbers represent the number of men and women with atrial fibrillation in each age category.




ATRIA STUDY JAMA 2001;285:2370-2375

# Efecto de FA

- Mortalidad
- Ictus
- Hospitalización
- Calidad de vida
- Disfunción ventricular
- Deterioro cognitivo

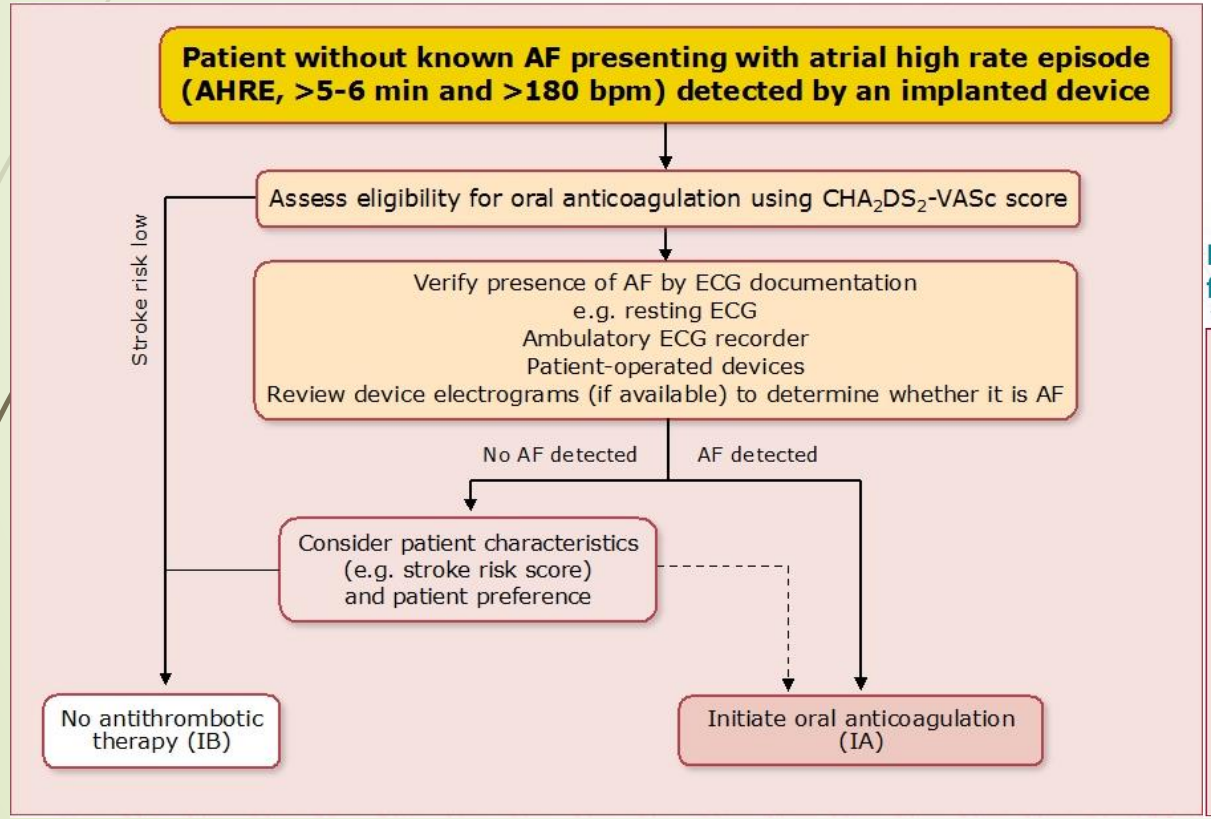
**Table 3 Cardiovascular morbidity and mortality associated with atrial fibrillation**

| Event | Association with AF |
|---|---|
| Death | Increased mortality, especially cardiovascular mortality due to sudden death, heart failure or stroke. |
| Stroke | 20–30% of all strokes are due to AF. A growing number of patients with stroke are diagnosed with 'silent', paroxysmal AF. |
| Hospitalizations | 10–40% of AF patients are hospitalized every year. |
| Quality of life | Quality of life is impaired in AF patients independent of other cardiovascular conditions. |
| Left ventricular dysfunction and heart failure | Left ventricular dysfunction is found in 20–30% of all AF patients. AF causes or aggravates LV dysfunction in many AF patients, while others have completely preserved LV function despite long-standing AF. |
| Cognitive decline and vascular dementia | Cognitive decline and vascular dementia can develop even in anticoagulated AF patients. Brain white matter lesions are more common in AF patients than in patients without AF. |

AF = atrial fibrillation; LV = left ventricular.

# Silent AF

- Screening FA



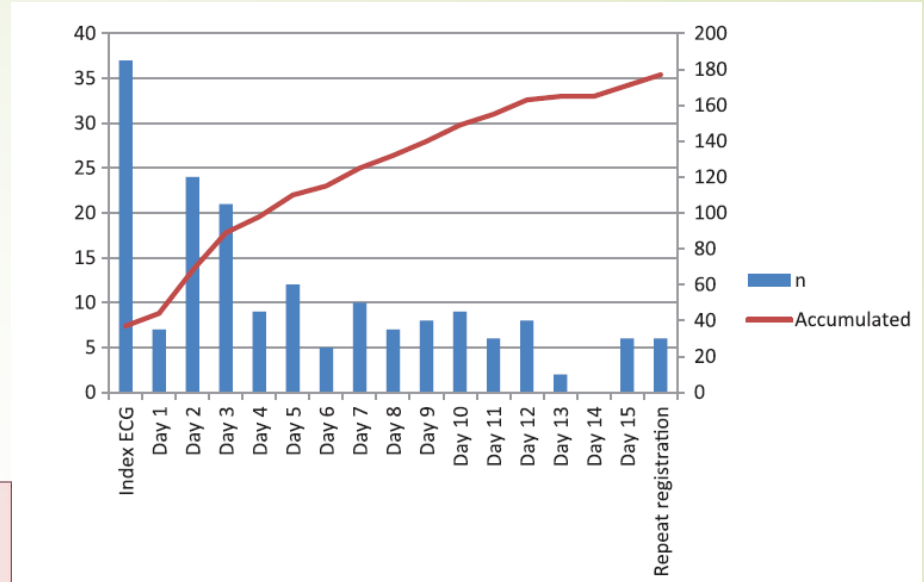
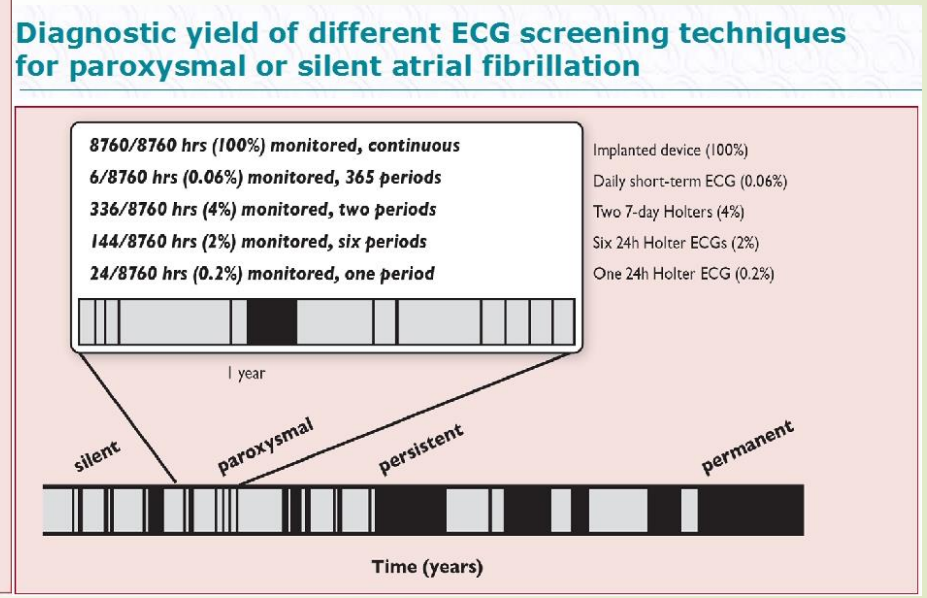




**Figure 3.** Time to first detection of atrial fibrillation among participants undergoing intermittent ECG registrations.




STROKE STOP Circulation. 2015;131:2176-2184.

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Subclinical Atrial Fibrillation and the Risk of Stroke

Jeff S. Healey, M.D., Stuart J. Connolly, M.D., Michael R. Gold, M.D., Carsten W. Israel, M.D., Isabelle C. Van Gelder, M.D., Alessandro Capucci, M.D., C.P. Lau, M.D., Eric Fain, M.D., Sean Yang, M.Sc., Christophe Bailleul, M.D., Carlos A. Morillo, M.D., Mark Carlson, M.D., Ellison Themeles, M.Sc., Elizabeth S. Kaufman, M.D., and Stefan H. Hohnloser, M.D., for the ASSERT Investigators*

N Engl J Med 2012;366:120-9.

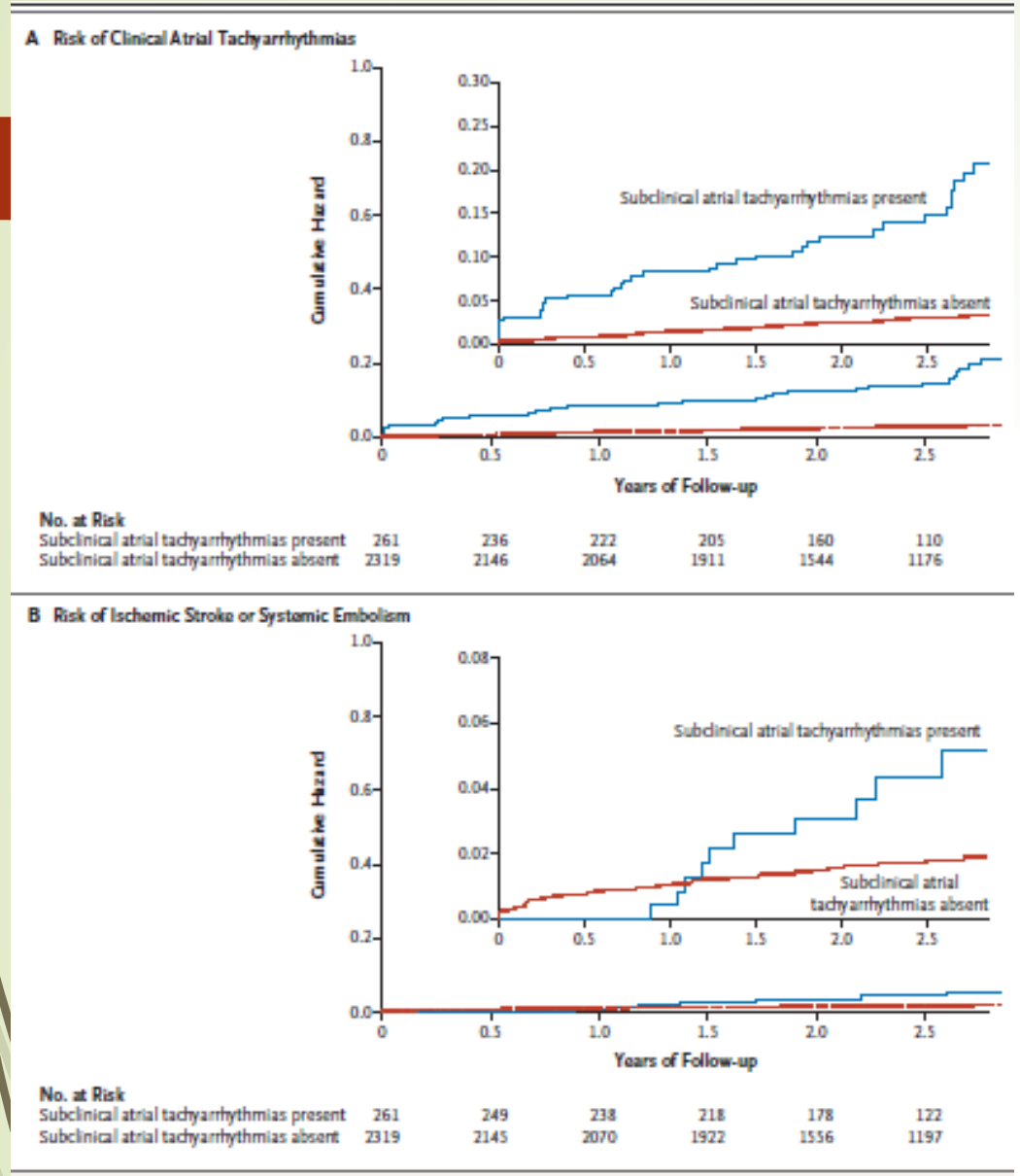


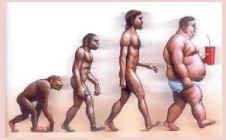

**Figure 1. The Risk of Clinical Atrial Tachyarrhythmias and of Ischemic Stroke or Systemic Embolism, According to the Presence or Absence of Subclinical Atrial Tachyarrhythmias.**

Panel A shows the risk of electrocardiographically documented clinical atrial tachyarrhythmias after the 3-month visit, according to whether subclinical atrial tachyarrhythmias were or were not detected between enrollment and the 3-month visit. Panel B shows the risk of ischemic stroke or systemic embolism after the 3-month visit, according to whether subclinical atrial tachyarrhythmias were or were not detected between enrollment and the 3-month visit. The insets show the same data on an enlarged y axis.

**Table 2. Clinical Outcomes Occurring after the 3-Month Visit, According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.**

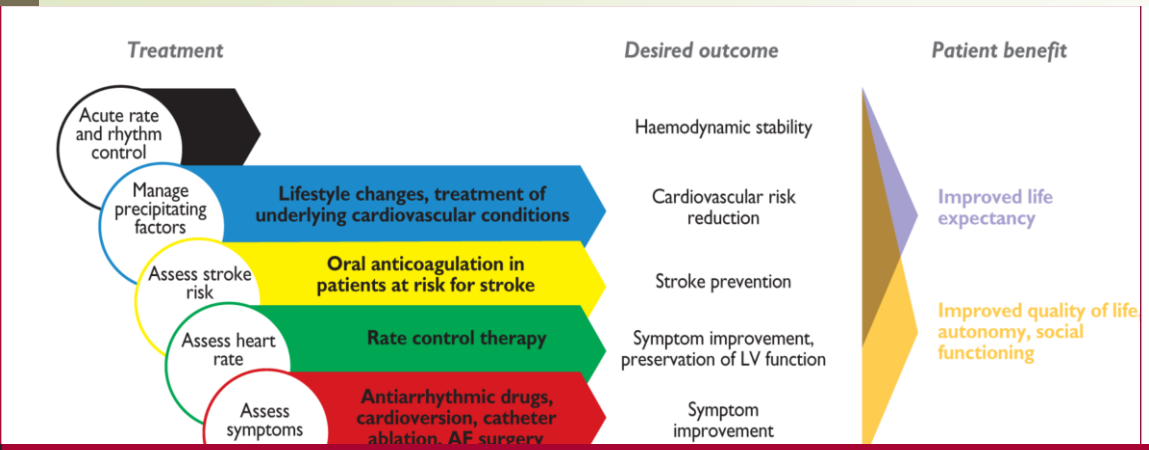
| Clinical Outcome | Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months | | | | Hazard Ratio with Subclinical Atrial Tachyarrhythmias (95% CI) | P Value |
|---|---|---|---|---|---|---|
| | Present (N=261) | | Absent (N=2319) | | | |
| | *no. of events* | %/yr | *no. of events* | %/yr | | |
| Ischemic stroke or systemic embolism* | 11 | 1.69 | 40 | 0.69 | 2.49 (1.28–4.85) | 0.007 |
| Ischemic stroke | 10 | 1.54 | 36 | 0.62 | 2.52 (1.25–5.08) | 0.01 |
| Systemic embolism | 1 | 0.15 | 4 | 0.07 | 2.24 (0.25–20.10) | 0.47 |
| Myocardial infarction | 7 | 1.07 | 39 | 0.67 | 1.52 (0.68–3.42) | 0.31 |
| Death from vascular causes | 19 | 2.92 | 153 | 2.62 | 1.11 (0.69–1.79) | 0.67 |
| Stroke, myocardial infarction, or death from vascular causes | 29 | 4.45 | 206 | 3.53 | 1.25 (0.85–1.84) | 0.27 |
| Hospitalization for heart failure | 20 | 3.07 | 131 | 2.24 | 1.36 (0.85–2.19) | 0.20 |
| Clinical atrial fibrillation or flutter on surface electrocardiogram | 41 | 6.29 | 71 | 1.22 | 5.56 (3.78–8.17) | <0.001 |

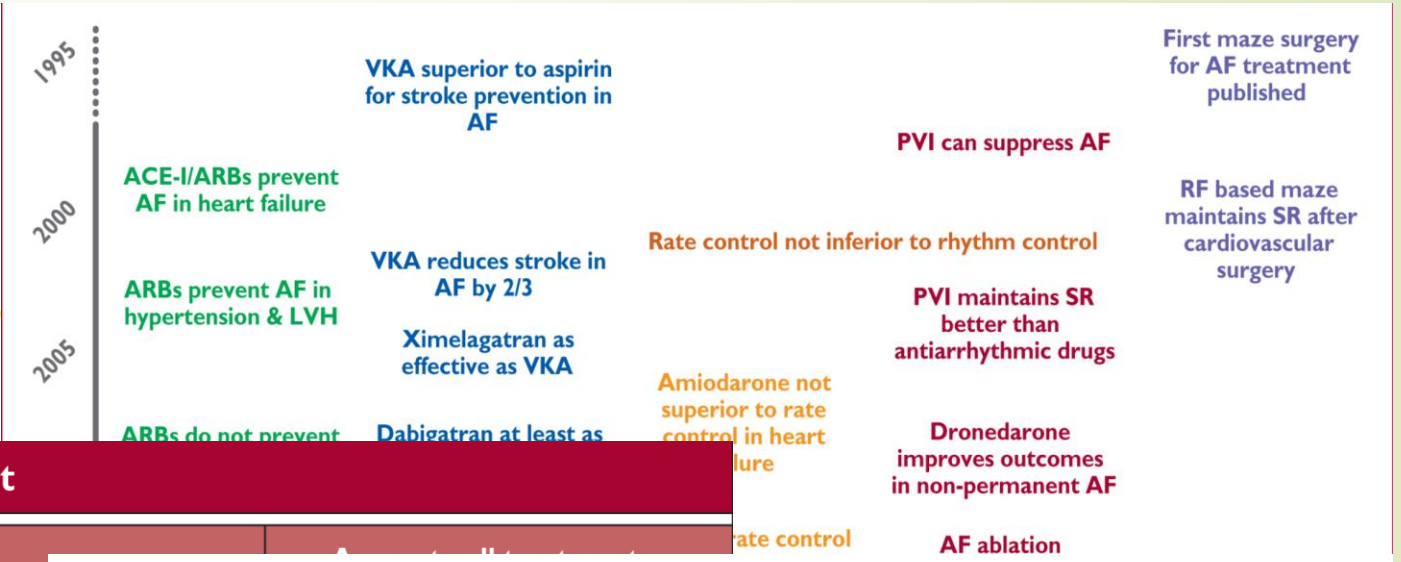
* Five cases of confirmed stroke for which the cause (ischemic or hemorrhagic) was undetermined are included. All five cases occurred in the group of patients who did not have an episode of subclinical atrial tachyarrhythmia between enrollment and 6 months.

| Characteristic/comorbidity | Association with AF |
|---|---|
| Genetic predisposition (based on multiple common gene variants associated with AF) | HR range 0.4–3.2 |
| Older age<br>50-59 years<br>60-69 years<br>70-79 years<br>80-89 years  | HR:<br>1.00 (reference)<br>4.98 (95% CI 3.49–7.10)<br>7.35 (95% CI 5.28–10.2)<br>9.33 (95% CI 6.68–13.0) |
| Hypertension (treated) vs. none  | HR 1.32 (95% CI 1.08–1.60) |
| Heart failure vs. none  | HR 1.43 (95% CI 0.85–2.40) |
| Valvular heart disease vs. none | RR 2.42 (95% CI 1.62–3.60) |
| Myocardial infarction vs. none | HR 1.46 (95% CI 1.07–1.98) |
| Thyroid dysfunction<br>Hypothyroidism<br>Subclinical hyperthyroidism<br>Overt hyperthyroidism | (reference: euthyroid)<br>HR 1.23 (95% CI 0.77–1.97)<br>RR 1.31 (95% CI 1.19–1.44)<br>RR 1.42 (95% CI 1.22–1.63) |
| Obesity (body mass index)<br>None (<25 kg/m²)<br>Overweight (25–30 kg/m²)<br>Obese (≥31 kg/m²)  | HR:<br>1.00 (reference)<br>1.13 (95% CI 0.87–1.46)<br>1.37 (95% CI 1.05–1.78) |
| Diabetes mellitus vs. none | HR 1.25 (95% CI 0.98–1.60) |

| Characteristic/comorbidity | Association with AF |
|---|---|
| Chronic obstructive pulmonary disease<br>FEV1 ≥80%<br>FEV1 60–80%<br>FEV1 <60%  | RR:<br>1.00 (reference)<br>1.28 (95% CI 0.79–2.06)<br>2.53 (95% CI 1.45–4.42) |
| Obstructive sleep apnoea vs. none | HR 2.18 (95% CI 1.34–3.54) |
| Chronic kidney disease<br>None<br>Stage 1 or 2<br>Stage 3<br>Stage 4 or 5 | OR:<br>1.00 (reference)<br>2.67 (95% CI 2.04–3.48)<br>1.68 (95% CI 1.26–2.24)<br>3.52 (95% CI 1.73–7.15) |
| Smoking<br>Never<br>Former<br>Current | HR:<br>1.00 (reference)<br>1.32 (95% CI 1.10–1.57)<br>2.05 (95% CI 1.71–2.47) |
| Alcohol consumption<br>None<br>1– 6 drinks/week<br>7–14 drinks/week<br>15–21 drinks/week<br>>21 drinks/week  | RR:<br>1.00 (reference)<br>1.01 (95% CI 0.94–1.09)<br>1.07 (95% CI 0.98–1.17)<br>1.14 (95% CI 1.01–1.28)<br>1.39 (95% CI 1.22–1.58) |
| Habitual vigorous exercise<br>Non-exercisers<br><1 day/week<br>1–2 days/week<br>3–4 days/week<br>5–7 days/week  | RR:<br>1.00 (reference)<br>0.90 (95% CI 0.68–1.20)<br>1.09 (95% CI 0.95–1.26)<br>1.04 (95% CI 0.91–1.19)<br>1.20 (95% CI 1.02–1.41) |

# Tratamiento FA




## Integrated AF management

| Patient involvement | Multidisciplinary teams | Technolog |
|---|---|---|
| • Central role in care process<br>• Patient education<br>• Encouragement and empowerment for self-management<br>• Advice and education on lifestyle and risk factor management<br>• Shared decision making | • Phycisians (general physicians, cardiology and stroke AF specialists, surgeons) and allied health professionals work in a collaborative practice model<br>• Efficient mix of communication skills, education, and experience | • Information on AF<br>• Clinical decision su<br>• Checklist and com<br>• Used by healthcare and patients<br>• Monitoring of ther and effectiveness |
| • ***Informed, involved, empowered patient*** | • ***Working together in a multidisciplinary chronic AF care team*** | • ***Navigation syster decision making i team*** |

AF = atrial fibrillation; LAA = left atrial appendage.

Outcomes at 12 Months in Unmatched Groups

| Outcome | AF Clinic (n=185) | Usual Care (n=228) | Odds Ratio (95% CI) | *P* Value |
|---|---|---|---|---|
| Death, CV hospitalization, AF-related ED visit | 34 (18.4%) | 65 (28.5%) | 0.57 (0.35, 0.9) | 0.017 |
| Death from any cause | 0 (0%) | 4 (1.8%) | n/a | 0.13[a] |
| CV hospitalization | 11 (6%) | 20 (8.8%) | 0.66 (0.31, 1.41) | 0.28 |
| AF-related ED visit | 25 (13.5%) | 54 (23.7%) | 0.5 (0.3, 0.85) | 0.01 |
| Stroke | 4 (2.2%) | 8 (3.5%) | 0.61 (0.18, 2.05) | 0.42 |
| Major bleeding | 0 (0%) | 3 (1.3%) | n/a | 0.26 |
| Minor bleeding | 4 (2.2%) | 4 (1.8%) | 1.24 (0.31, 5.02) | 0.77 |

AF indicates atrial fibrillation; CV, cardiovascular; ED, emergency department; n/a, .

[a] *P*-value calculated using Fisher's exact test.

J Am Heart Assoc. 2016 Jan; 5(1): e002950.

# Tratamiento farmacológico FA

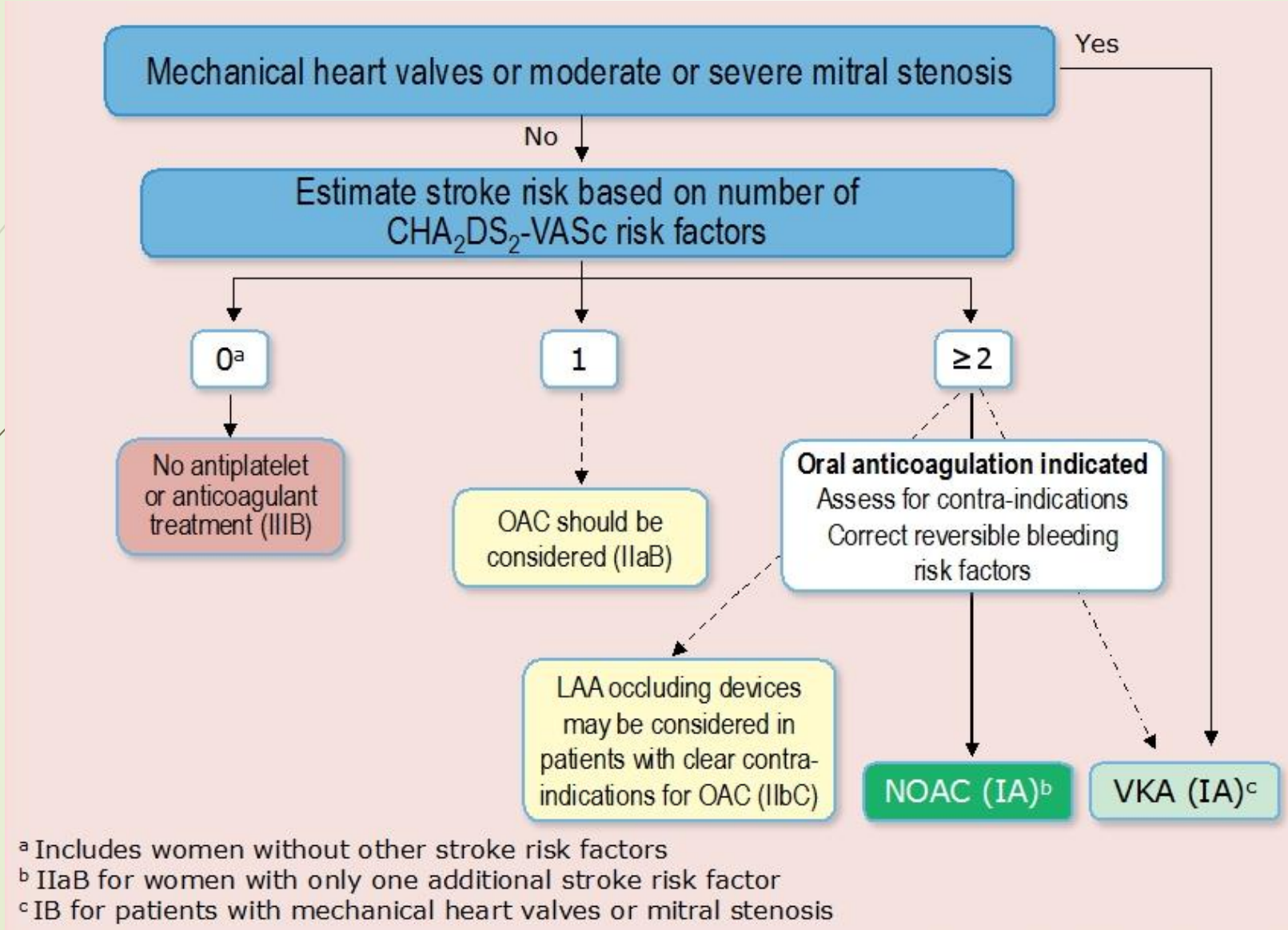
# ANTICOAGULANTES

| Recommendations | Class | Level |
|---|---|---|
| The $CHA_2DS_2$-VASc score is recommended for stroke risk prediction in patients with AF. | I | A |
| Bleeding risk scores should be considered in AF patients on oral anticoagulation to identify modifiable risk factors for major bleeding. | IIa | B |
| Biomarkers such as high-sensitivity troponin and natriuretic peptide may be considered to further refine stroke and bleeding risk in AF patients. | IIb | B |

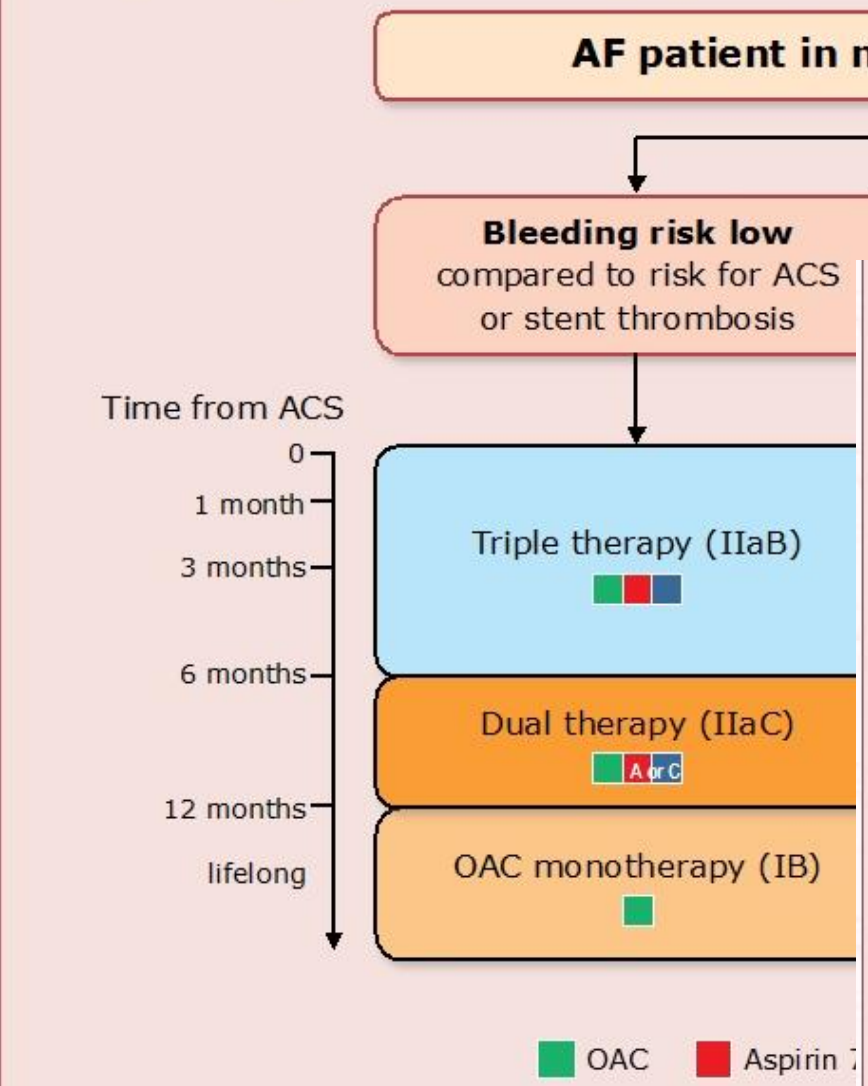
| $CHA_2DS_2$-VASc risk factor | Points |
|---|---|
| **Congestive heart failure**<br>Signs/symptoms of heart failure or objective evidence of reduced left-ventricular ejection fraction | 1 |
| **Hypertension**<br>Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment | 1 |
| **Age 75 years or older** | 2 |
| **Diabetes mellitus**<br>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**<br>Previous myocardial infarction, peripheral artery disease, or aortic plaque | 1 |
| **Age 65–74 years** | 1 |
| **Sex category (female)** | 1 |

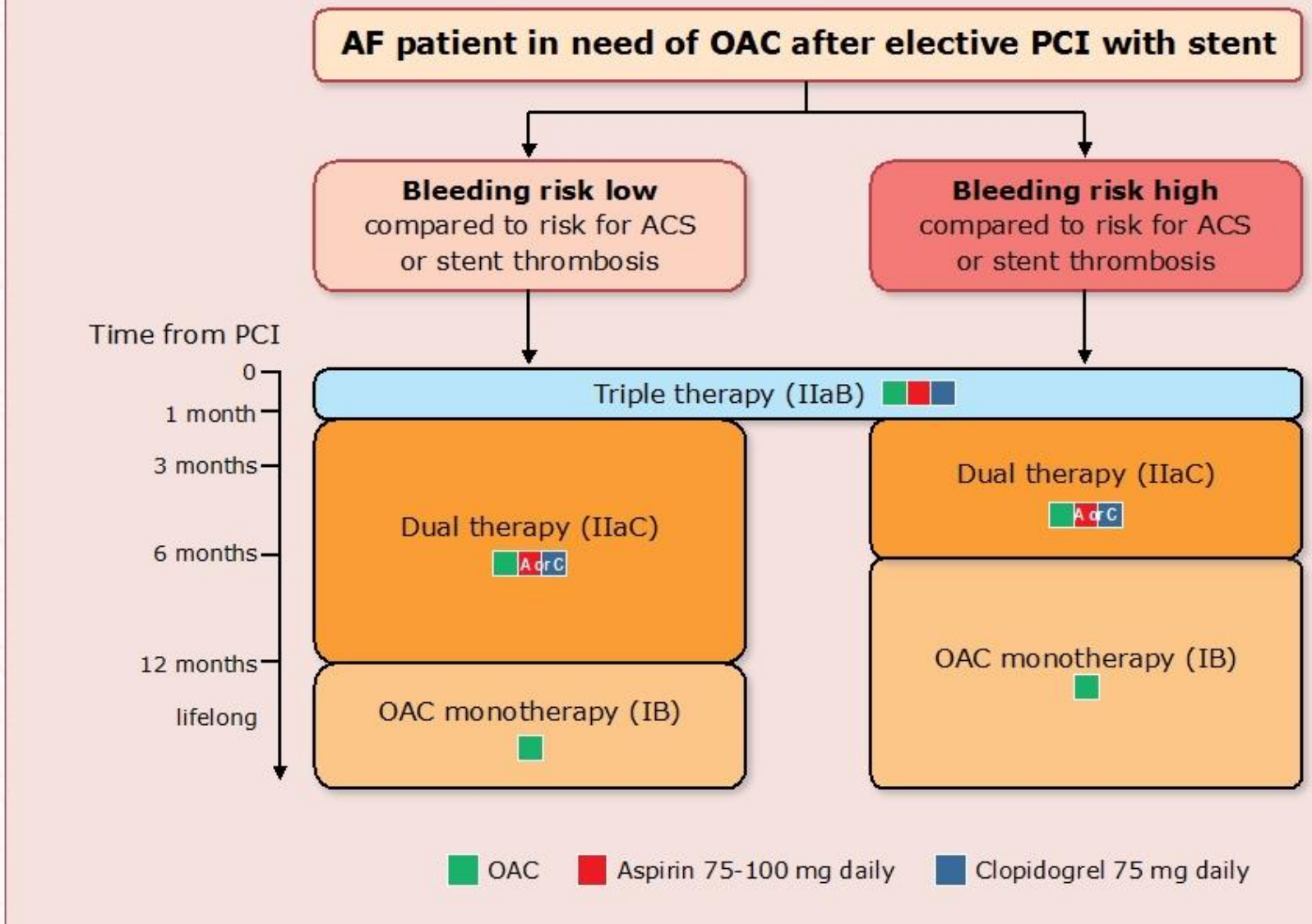
| Modifiable bleeding risk factors: |
|---|
| Hypertension (especially when systolic blood pressure is >160 mmHg) |
| Labile INR or time in therapeutic range <60% in patients on vitamin K antagonists |
| Medication predisposing to bleeding, such as antiplatelet drugs and non-steroidal anti-inflammatory drugs |
| Excess alcohol (≥8 drinks/week) |
| **Potentially modifiable bleeding risk factors:** |
| Anaemia |
| Impaired renal function |
| Impaired liver function |
| Reduced platelet count or function |

| Non-modifiable bleeding risk factors: |
|---|
| Age (>65 years) (≥75 years) |
| History of major bleeding |
| Previous stroke |
| Dialysis-dependent kidney disease or renal transplant |
| Cirrhotic liver disease |
| Malignancy |
| Genetic factors |
| **Biomarker-based bleeding risk factors:** |
| High-sensitivity troponin |
| Growth differentiation factor-15 |
| Serum creatinine/estimated CrCl |




[a] Includes women without other stroke risk factors
[b] IIaB for women with only one additional stroke risk factor
[c] IB for patients with mechanical heart valves or mitral stenosis


AF patient in need of OAC after an ACS
Bleeding risk low
compared to risk for ACS
or stent thrombosis
Bleeding risk high
Time from ACS
0
1 month
3 months
6 months
12 months
lifelong
Triple therapy (IIaB)
Dual therapy (IIaC)
A or C
OAC monotherapy (IB)
OAC
Aspirin


AF patient in need of OAC after elective PCI with stent
Bleeding risk low
compared to risk for ACS
or stent thrombosis
Bleeding risk high
compared to risk for ACS
or stent thrombosis
Time from PCI
0
1 month
3 months
6 months
12 months
lifelong
Triple therapy (IIaB)
Dual therapy (IIaC)
A or C
Dual therapy (IIaC)
A or C
OAC monotherapy (IB)
OAC monotherapy (IB)
OAC
Aspirin 75-100 mg daily
Clopidogrel 75 mg daily

# MANEJO DE SANGRADO EN PACIENTE CON ANTICOAGULACIÓN ORAL

| Recommendations | Class | Level |
|---|---|---|
| Blood pressure control in anticoagulated patients with hypertension should be considered to reduce the risk of bleeding. | IIa | B |
| When dabigatran is used, a reduced dose (110 mg twice daily) may be considered in patients >75 years to reduce the risk of bleeding. | IIb | B |
| In patients at high-risk of gastrointestinal bl NOAC preparation should be preferred over daily, rivaroxaban 20 mg once daily, or edox | | |
| Advice and treatment to avoid alcohol exces AF patients considered for OAC. | | |
| Genetic testing before the initiation of VKA t recommended. | | |
| Reinitiation of OAC after a bleeding event sh eligible patients by a multidisciplinary AF tea anticoagulants and stroke prevention interve management of factors that contributed to b | | |
| In AF patients with severe active bleeding ev interrupt OAC therapy until the cause of blee | | |

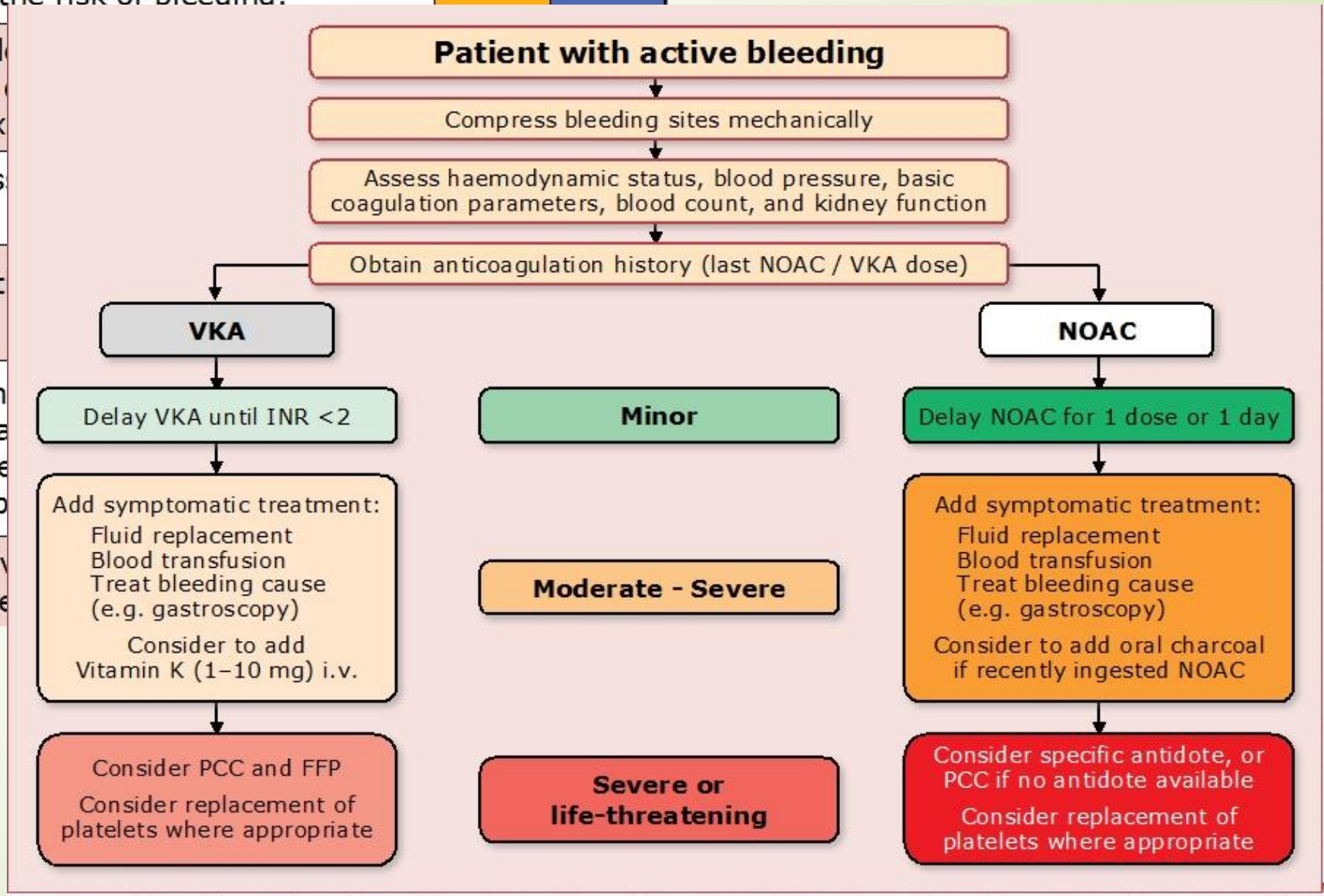


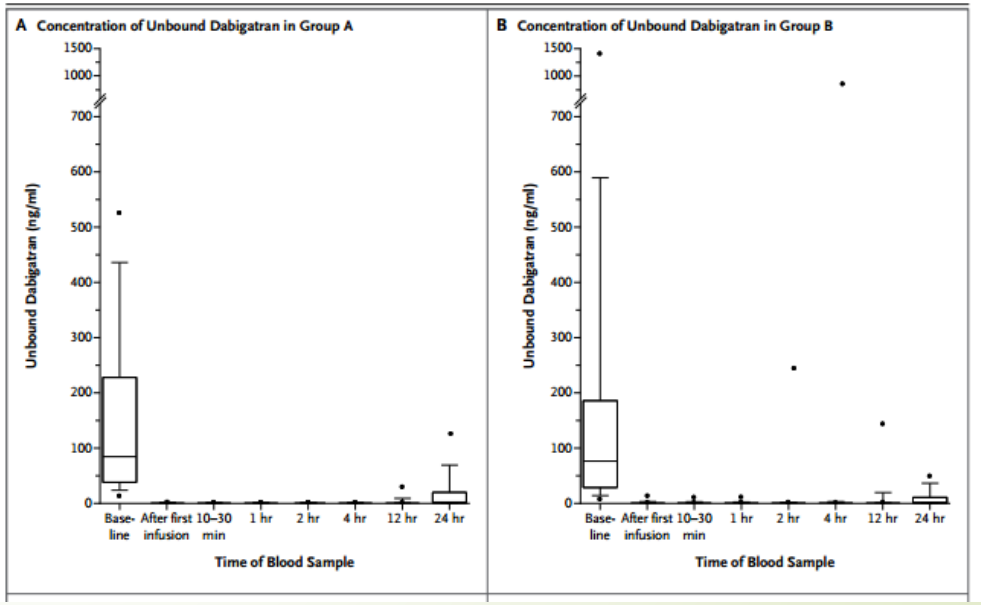
Table 1. Clinical Characteristics of the Patients.*

| Characteristic | Group A (N=51) | Group B (N=39) | Total (N=90) |
|---|---|---|---|
| Age — yr | | | |
| Median | 77.0 | 76.0 | 76.5 |
| Range | 48–93 | 56–93 | 48–93 |
| Male sex — no. (%) | 32 (63) | 18 (46) | 50 (56) |
| Race or ethnic group — no. (%)† | | | |
| Asian | 5 (10) | 1 (3) | 6 (7) |
| Hawaiian or Pacific Islander | 3 (6) | 3 (8) | 6 (7) |
| White | 43 (84) | 35 (90) | 78 (87) |
| Weight — kg | | | |
| Median | 70.5 | 73.0 | 71.9 |
| Range | 42.4–127.5 | 49.5–116.0 | 42.4–127.5 |
| Creatinine clearance‡ | | | |
| Value — ml/min | | | |
| Mean | 59±33 | 65±36 | 62±35 |
| Median | 54 | 60 | 58 |
| Range | 16–187 | 11–171 | 11–187 |
| Distribution — no. (%) | | | |
| <30 ml/min | 5 (10) | 7 (18) | 12 (13) |
| 30 to <50 ml/min | 14 (27) | 6 (15) | 20 (22) |
| 50 to <80 ml/min | 16 (31) | 11 (28) | 27 (30) |
| ≥80 ml/min | 6 (12) | 9 (23) | 15 (17) |
| Missing data | 10 (20) | 6 (15) | 16 (18) |
| Dose of dabigatran — no. (%) | | | |
| 150 mg twice daily | 14 (27) | 15 (38) | 29 (32) |
| 110 mg twice daily | 34 (67) | 24 (62) | 58 (64) |
| 75 mg twice daily | 1 (2) | 0 | 1 (1) |
| Other | 2 (4) | 0 | 2 (2) |
| Indication for dabigatran — no. (%) | | | |
| Atrial fibrillation | 47 (92) | 39 (100) | 86 (96) |
| Venous thromboembolism | 1 (2) | 0 | 1 (1) |
| Other | 3 (6) | 0 | 3 (3) |
| Time since last intake of dabigatran | | | |
| Median — hr | 15.2 | 16.6 | 15.4 |
| Distribution — no. (%) | | | |
| <12 hr | 17 (33) | 15 (38) | 32 (36) |
| 12 to <24 hr | 21 (41) | 10 (26) | 31 (34) |
| 24 to <48 hr | 12 (24) | 10 (26) | 22 (24) |
| ≥48 hr | 1 (2) | 4 (10) | 5 (6) |
| Elevated dilute thrombin time at baseline — no. (%) | 40 (78) | 28 (72) | 68 (76) |
| Elevated ecarin clotting time at baseline — no. (%) | 47 (92) | 34 (87) | 81 (90) |
| Type of bleeding — no. (%)§ | | | |
| Intracranial | 18 (35) | — | 18 (20) |
| Trauma-related | 9 (18) | — | 9 (10) |
| Gastrointestinal | 20 (39) | — | 20 (22) |
| Other | 11 (22) | — | 11 (12) |

ORIGINAL ARTICLE

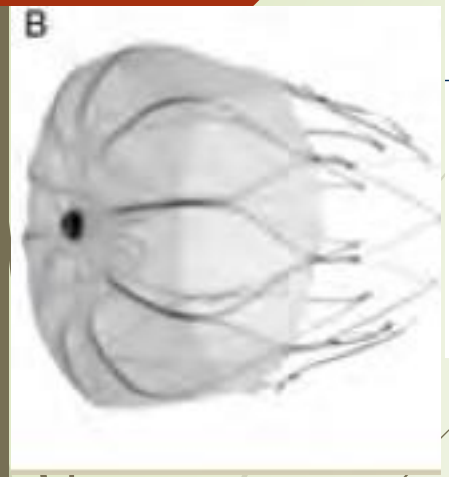
# Idarucizumab for Dabigatran Reversal

Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhamme, M.D., Richard A. Bernstein, M.D., Ph.D., Robert Dubiel, Pharm.D., Menno V. Huisman, M.D., Ph.D., Elaine M. Hylek, M.D., Pieter W. Kamphuisen, M.D., Ph.D., Jörg Kreuzer, M.D., Jerrold H. Levy, M.D., Frank W. Sellke, M.D., Joachim Stangier, Ph.D., Thorsten Steiner, M.D., M.M.E., Bushi Wang, Ph.D., Chak-Wah Kam, M.D., and Jeffrey I. Weitz, M.D.




N Engl J Med 2015;373:511-520

# Prevención de eventos embólicos tratamiento no farmacológico




Stroke

**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**

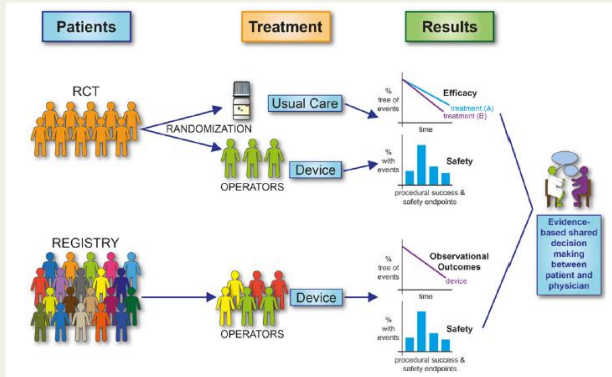
Vivek Y. Reddy, MD; Shephal K. Doshi, MD; Horst Sievert, MD; Maurice Buchbinder, MD; Petr Neuzil, MD, PhD; Kenneth Huber, MD; Jonathan L. Halperin, MD; David Holmes, MD; on behalf of the PROTECT AF Investigators

ORIGINAL INVESTIGATIONS

**Prospective Randomized Evaluation of the Watchman Left Atrial Appendage Closure Device in Patients With Atrial Fibrillation Versus Long-Term Warfarin Therapy**

The PREVAIL Trial

David R. Holmes Jr, MD,* Saibal Kar, MD,† Matthew J. Price, MD,‡ Brian Whisenant, MD,§ Horst Sievert, MD,‖ Shephal K. Doshi, MD,¶ Kenneth Huber, MD,# Vivek Y. Reddy, MD**




European Heart Journal
doi:10.1093/eurheartj/ehv730

AHA FASTTRACK
Atrial fibrillation

**Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry**

**Lucas V.A. Boersma[1]*, Boris Schmidt[2], Timothy R. Betts[3], Horst Sievert[4], Corrado Tamburino[5], Emmanuel Teiger[6], Evgeny Pokushalov[7], Stephan Kische[8], Thomas Schmitz[9], Kenneth M. Stein[10] and Martin W. Bergmann[11], on behalf of the EWOLUTION investigators**

[1]Cardiology Department, St Antonius Hospital, PO 2500, 3430 EM Nieuwegein, the Netherlands; [2]Cardioangiologisches Centrum Bethanien, Frankfurt, Germany; [3]John Radcliffe Hospital, Oxford, UK; [4]Cardio Vasculäres Centrum Sankt Katharinen, Frankfurt, Germany; [5]Ospedale Ferrarotto Alessi, Catania, Italy; [6]CHU Henri Mondor, Créteil, France; [7]State Research Institute of Circulation Pathology, Novosibirsk, Russia; [8]Vivantes Klinikum im Friedrichshain, Berlin, Germany; [9]Elisabeth Krankenhaus Essen, Essen, Germany; [10]Boston Scientific Corp., Minneapolis, MN, USA; and [11]Herzkatheter Asklepios Wandsbek, Hamburg, Germany

Received 30 October 2015; revised 7 December 2015; accepted 10 December 2015

- 91% formación trombo en OI.
  - WATCHMAN : PROTECT-AF y PREVAIL; EWOLUTION. (ASAP)
    - ICTUS 0,1% a 30 días (1,7% al año)
      - ÉXITO DEL PROCEDIMIENTO: 95-98%, LEAKS 0,7%>5MM
      - COMPLICACIONES 2,8% (1,9-4%) (PRIMERA SEMANA) Y MORTALIDAD 0,7% (5% no rel con dispositivo
      - EAS 7,9% a 30 días y 3,6% relacionada con dispositivo.
      - Mejoría ictus en pacientes con contraindicación ACO. 1,7% frente al 5% estimado (similar a Apixaban 1,6%)

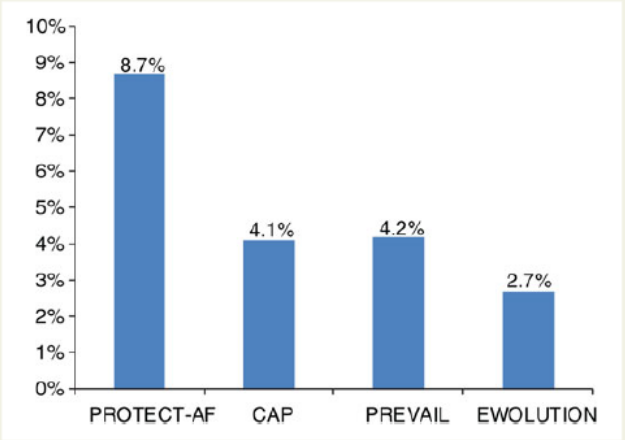


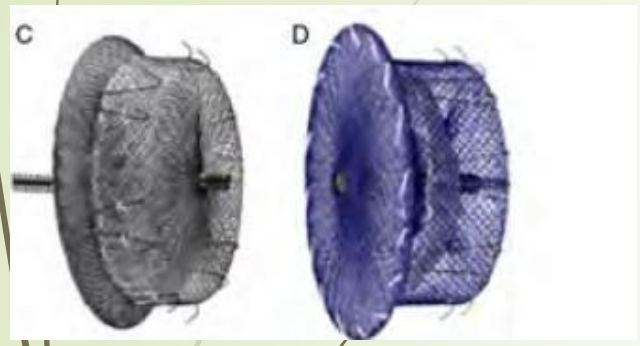

**Figure 2** Serious procedure-/device-related events through 7 days in EWOLUTION when compared with prior WATCHMAN studies.

**Table 2 Procedural results**

| Characteristic | All patients |
|---|---|
| Successful deployment | 98.5% (1004/1019) |
| LAA seal | |
| Complete seal | 91.4% (899/984) |
| Jet size ≤5 mm | 7.9% (78/984) |
| Jet size >5 mm | 0.7% (7/984) |

LAA, left atrial appendage.

- ACP/AMULET
- Tasa ictus 0,9% y AIT 0,9%, 2,5% al año.
  - Reducción 66% de ictus  y 61% de sangrados
  - Riesgo de trombos 2% registrados, no asociados a mayor tasa de eventos.




EuroIntervention
Official Journal of EuroPCR and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)
IMPACT FACTOR 3.863
2015 Journal Citation Reports® Science Edition (Thomson Reuters, 2016)
Home / Archives / Volume 11 Number 10 / Left atrial appendage occlusion for stroke prevention in atrial fibrillation: ... /
INTERVENTIONS FOR VALVULAR DISEASE AND HEART FAILURE

## Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicentre experience with the AMPLATZER Cardiac Plug

Published on 19 February 2016

Apostolos Tzikas[1,2*], MD, PhD; Samera Shakir[3], MD; Sameer Gafoor[4], MD; Heyder Omran[5], MD; Sergio Berti[6], MD; Gennaro Santoro[7], MD; Joelle Kefer[8], MD; Ulf Landmesser[9], MD; Jens Erik Nielsen-Kudsk[10], MD; Ignacio Cruz-Gonzalez[11], MD; Horst Sievert[4], MD; Tobias Tichelbäcker[12], MD; Prapa Kanagaratnam[13], MD; Fabian Nietlispach[3,9], MD; Adel Aminian[14], MD; Friederike Kasch[15], MD; Xavier Freixa[16,17], MD; Paolo Danna[18], MD; Marco Rezzaghi[6], MD; Paul Vermeersch[19], MD; Friederike Stock[5], MD; Miroslava Stolcova[7], MD; Marco Costa[20], MD; Reda Ibrahim[17], MD; Wolfgang Schillinger[12], MD; Bernhard Meier[3], MD; Jai-Wun Park[15], MD

KEYWORDS
- bleeding
- Left atrial appendage closure
- stroke risk

| Recommendations | Class | Level |
|---|---|---|
| After surgical occlusion or exclusion of the LAA, it is recommended to continue anticoagulation in at-risk patients with AF for stroke prevention. | I | B |
| LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause). | IIb | B |
| Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery. | IIb | B |
| Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients undergoing thoracoscopic AF surgery. | IIb | B |

- Ablación de FA y Cierre de OI.
  - Posible y seguro.
  - Sólo descripción de series de casos
  - Abordaje transeptal conjunto.

# Cierre quirúrgico de Orejuela izquierda

- Importancia de exclusión incompleta
  - Aumenta riesgo de ictus.
- Asociado a procedimiento quirúrgico

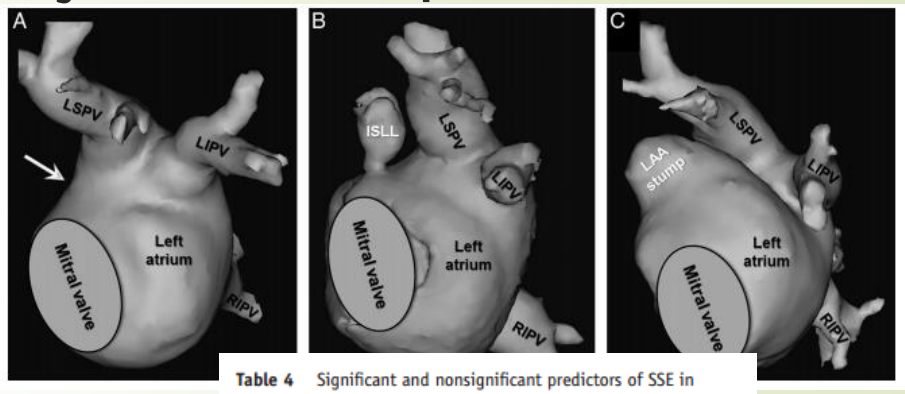
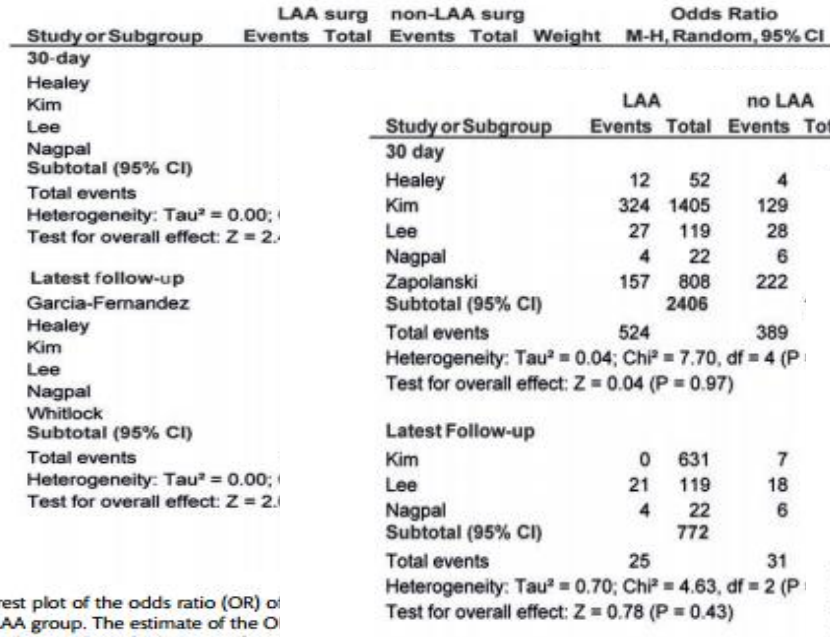



**Table 4** Significant and nonsignificant predictors of SSE in univariate analyses

| Variable | OR (95% CI) | *P* value |
|---|---|---|
| Antiplatelet therapy | 0.68 (0.11–4.38) | .689 |
| $CHADS_2$ score | 2.04 (0.68–6.16) | .204 |
| $CHA_2DS_2$-VASc score | 1.27 (0.75–2.15) | .374 |
| cLAA | 0.12 (0.012–1.16) | .067 |
| ISLL | 16.6 (1.7–161.4) | .015* |

OR = odds ratio.
*Significant *P* value.



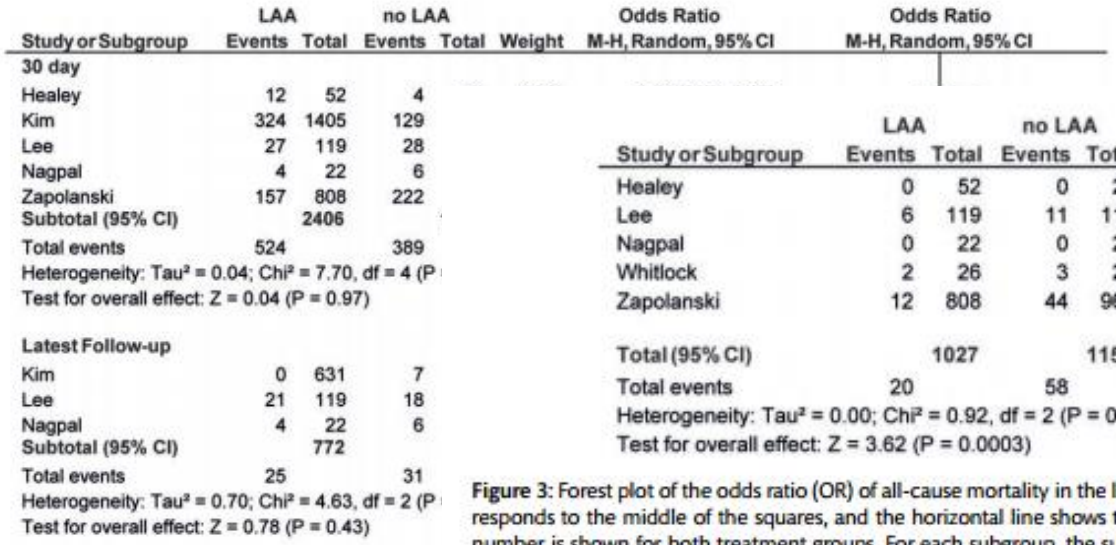




**Figure 1:** Forest plot of the odds ratio (OR) o
versus non-LAA group. The estimate of the O
On each line, the number of events as a fracti
summary OR, is represented by the middle o
M–H: Mantel–Haenszel.

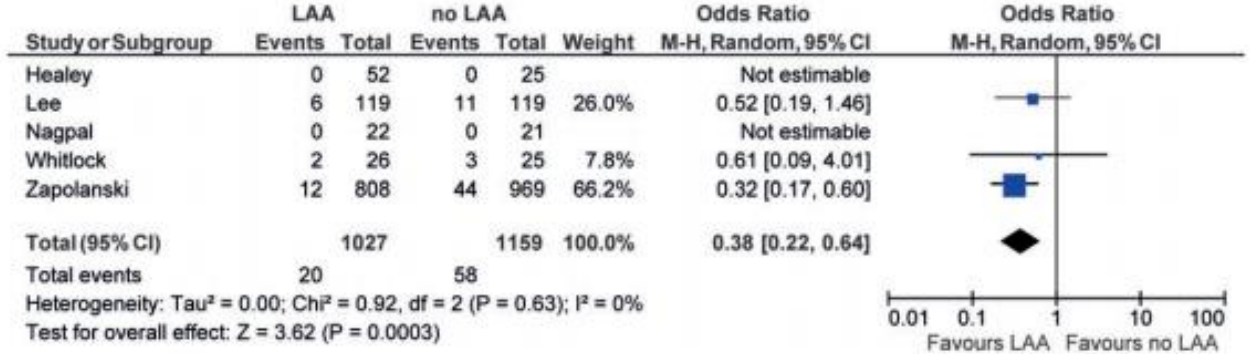
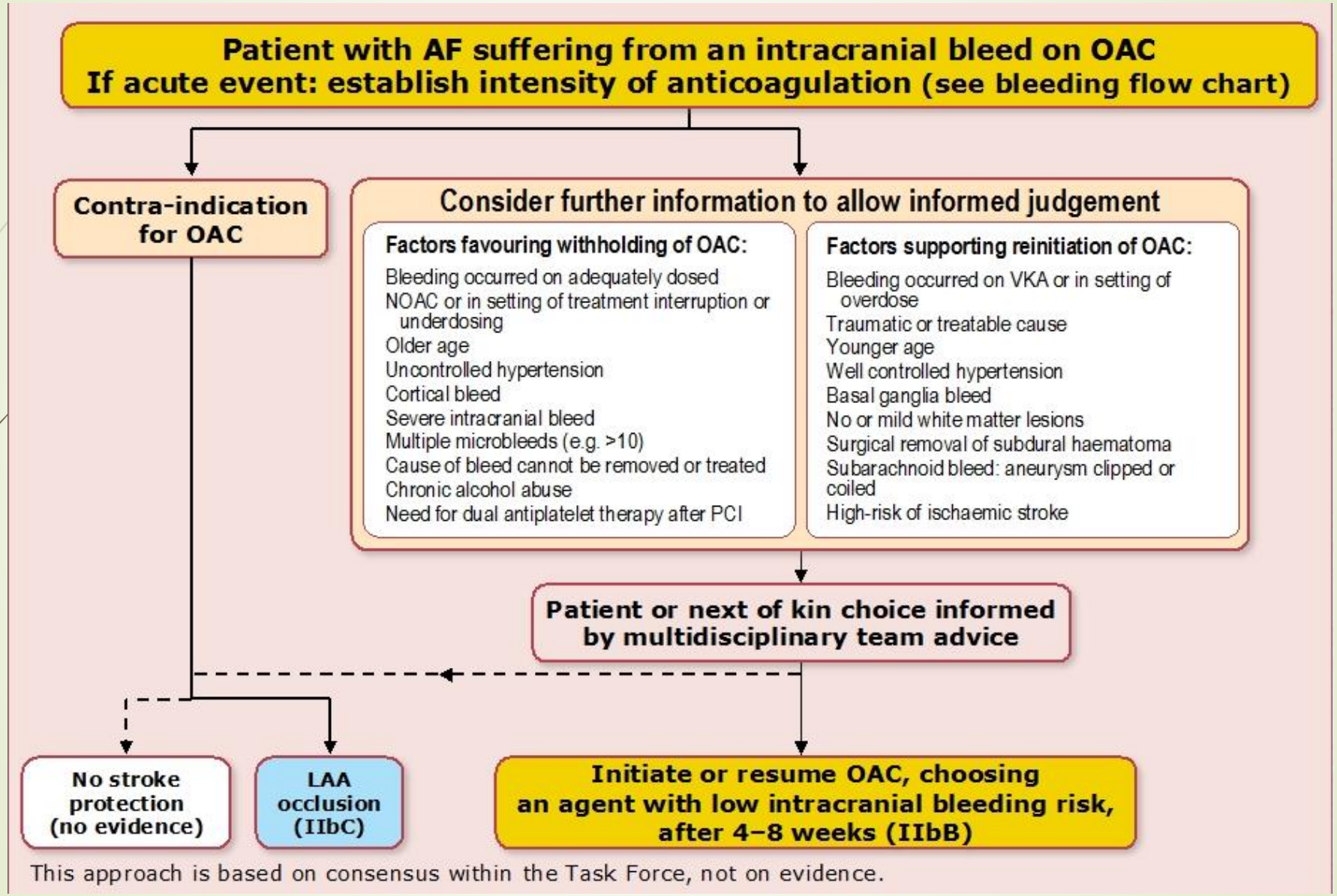



**Figure 3:** Forest plot of the odds ratio (OR) of all-cause mortality in the left atrial occlusion (LAA) group versus non-LAA group. The estimate of the OR of each trial responds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the number of events as a fraction of the number is shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary OR, is represented by the middle of the solid monds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics. M–H: Mantel–Haenszel.

European Journal of Cardio-Thoracic Surgery (2014) 1–8


Patient with AF suffering from an intracranial bleed on OAC
If acute event: establish intensity of anticoagulation (see bleeding flow chart)
Contra-indication for OAC
Consider further information to allow informed judgement
Factors favouring withholding of OAC:
Bleeding occurred on adequately dosed NOAC or in setting of treatment interruption or underdosing
Older age
Uncontrolled hypertension
Cortical bleed
Severe intracranial bleed
Multiple microbleeds (e.g. >10)
Cause of bleed cannot be removed or treated
Chronic alcohol abuse
Need for dual antiplatelet therapy after PCI
Factors supporting reinitiation of OAC:
Bleeding occurred on VKA or in setting of overdose
Traumatic or treatable cause
Younger age
Well controlled hypertension
Basal ganglia bleed
No or mild white matter lesions
Surgical removal of subdural haematoma
Subarachnoid bleed: aneurysm clipped or coiled
High-risk of ischaemic stroke
Patient or next of kin choice informed by multidisciplinary team advice
No stroke protection (no evidence)
LAA occlusion (IIbC)
Initiate or resume OAC, choosing an agent with low intracranial bleeding risk, after 4–8 weeks (IIbB)
This approach is based on consensus within the Task Force, not on evidence.

# CONTROL DE FRECUENCIA
# tratamiento farmacológico

## Efficacy of β blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis

Dipak Kotecha, Jane Holmes, Henry Krum, Douglas G Altman, Luis Manzano, John G F Cleland, Gregory Y H Lip, Andrew J S Coats, Bert Andersson, Paulus Kirchhof, Thomas G von Lueder, Hans Wedel, Giuseppe Rosano, Marcelo C Shibata, Alan Rigby, Marcus D Flather, on behalf of the Beta-Blockers in Heart Failure Collaborative Group

Lancet. 2014;384(9961):2235-43

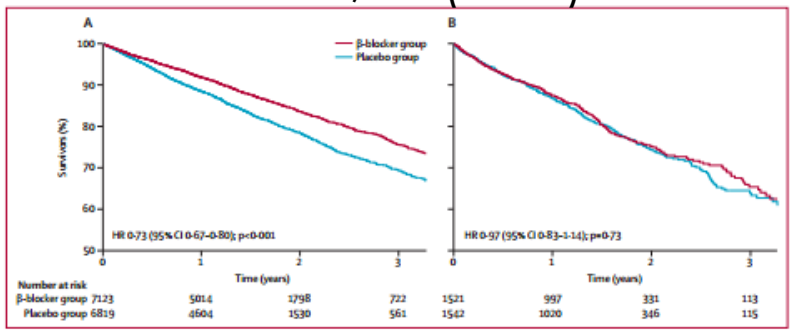
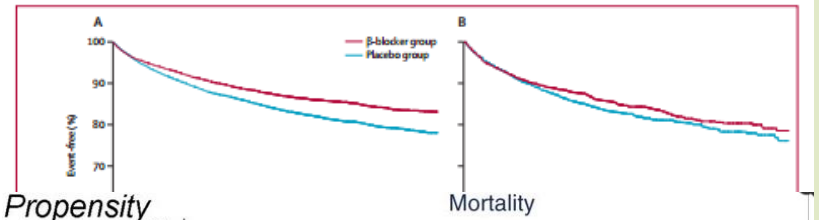



Figure 1: Kaplan-Meier survival curve for patients with sinus rhythm (A) and atrial fibrillation (B) in the β-blocker and placebo groups
Data are unadjusted survival curves for all reported deaths. HRs are derived from the adjusted one-stage Cox regression model and stratified by study. HR=hazard ratio.



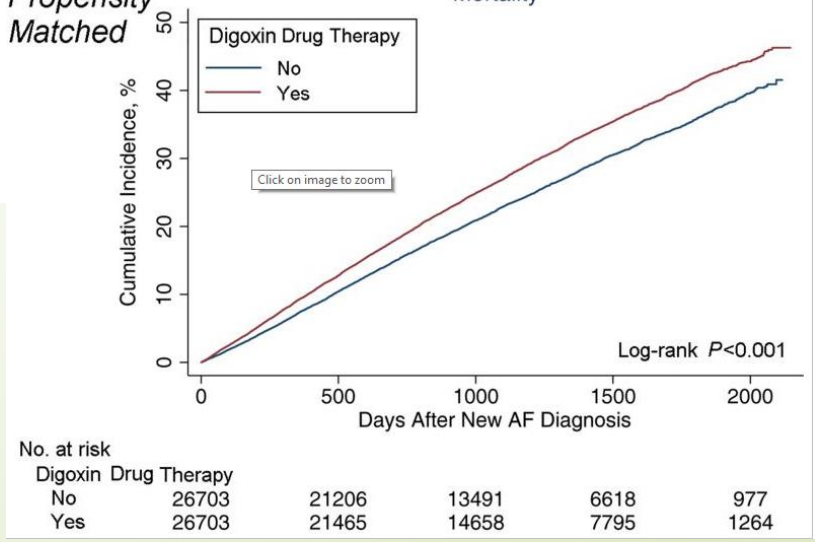

- 18000 p (76% FA)
- BB no afectan a mortalidad en FA, sí en RS
- Digoxina+ BB/ACA
- Digoxina FA y Carvedilol.

- DIG trial -> no efecto en Mortalid
- Aumento digoxina
- Amiodar agudo, e
- FC<80 o aumento o RACE.

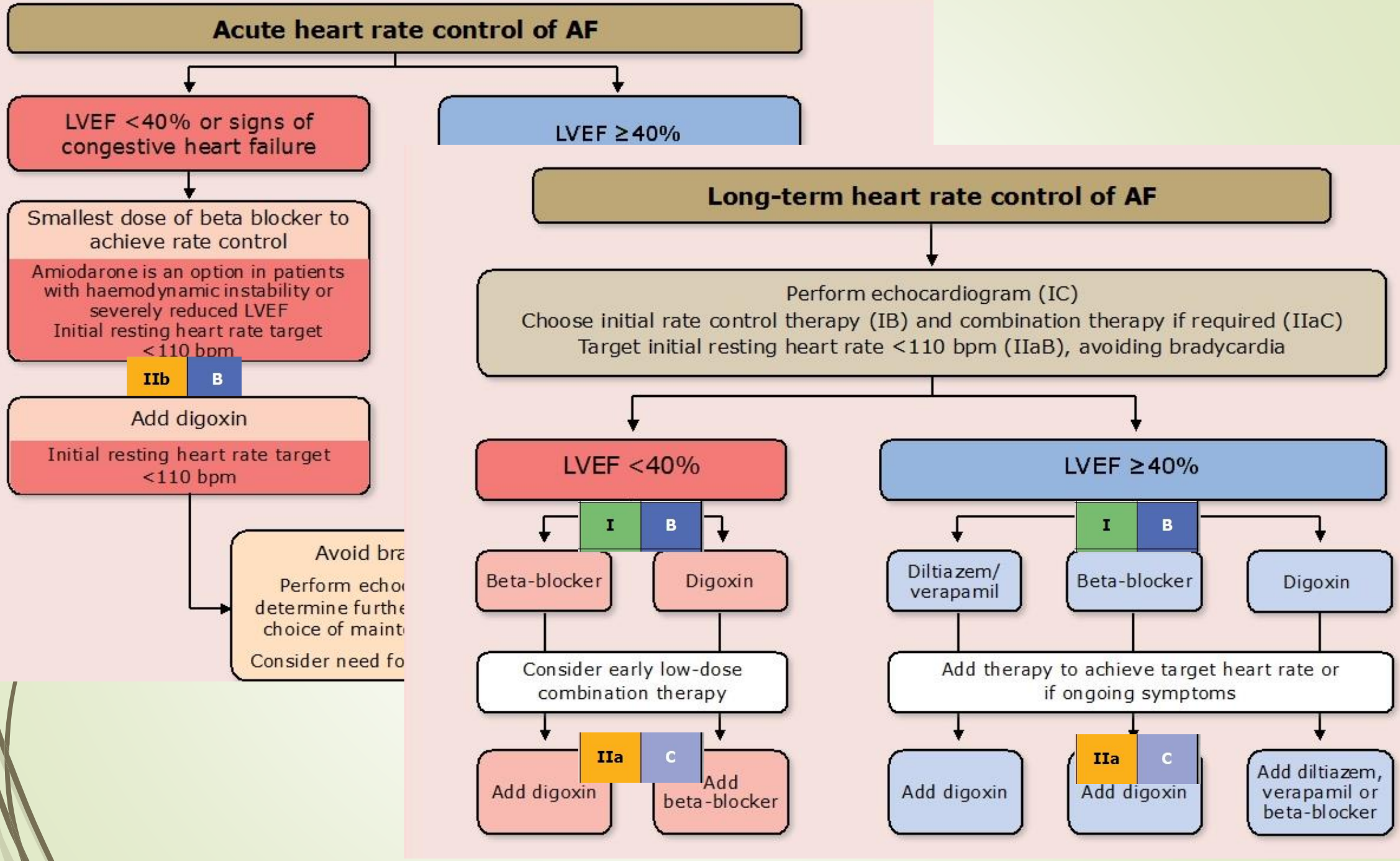
| Model | *Full Cohort* HR (95% CI) N=122,465 | *P* | *Propensity-Matched* Cohort HR (95% CI) N=53,406 | *P* |
|---|---|---|---|---|
| **Unadjusted** | 1.37 (1.33-1.40) | <0.001 | — | — |
| **Age, sex, race** | 1.40 (1.37-1.44) | <0.001 | — | — |
| **Full model**[*] | | | | |
| **All patients** | 1.26 (1.23-1.29) | <0.001 | 1.21 (1.17-1.25) | <0.001 |
| **Adherence (MPR)-adjusted** [†] | 1.31 (1.27-1.36) | <0.001 | 1.18 (1.10-1.27) | <0.001 |

Mortality

*Propensity Matched*

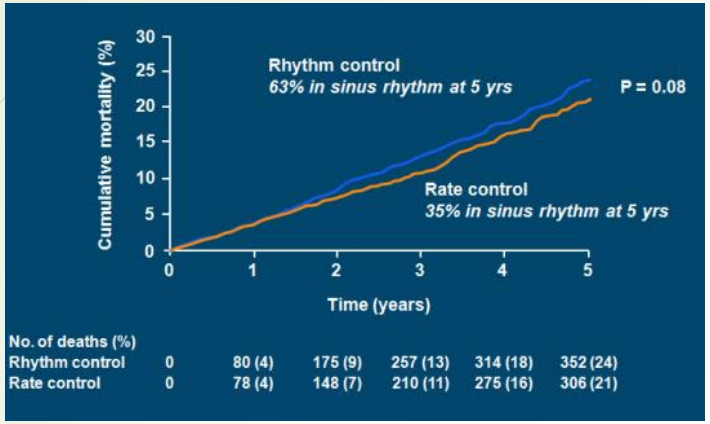



J Am Coll Cardiol. 2014;64(7):660-8


Acute heart rate control of AF
LVEF <40% or signs of congestive heart failure
LVEF ≥40%
Smallest dose of beta blocker to achieve rate control
Amiodarone is an option in patients with haemodynamic instability or severely reduced LVEF
Initial resting heart rate target <110 bpm
IIb
B
Add digoxin
Initial resting heart rate target <110 bpm
Avoid bra
Perform echo
determine furthe
choice of maint
Consider need fo
Long-term heart rate control of AF
Perform echocardiogram (IC)
Choose initial rate control therapy (IB) and combination therapy if required (IIaC)
Target initial resting heart rate <110 bpm (IIaB), avoiding bradycardia
LVEF <40%
LVEF ≥40%
I
B
Beta-blocker
Digoxin
Diltiazem/ verapamil
Beta-blocker
Digoxin
Consider early low-dose combination therapy
Add therapy to achieve target heart rate or if ongoing symptoms
IIa
C
Add digoxin
Add beta-blocker
Add digoxin
Add digoxin
Add diltiazem, verapamil or beta-blocker

# Control de ritmo en FA

# ESTRATEGIAS DE CONTROL FAA



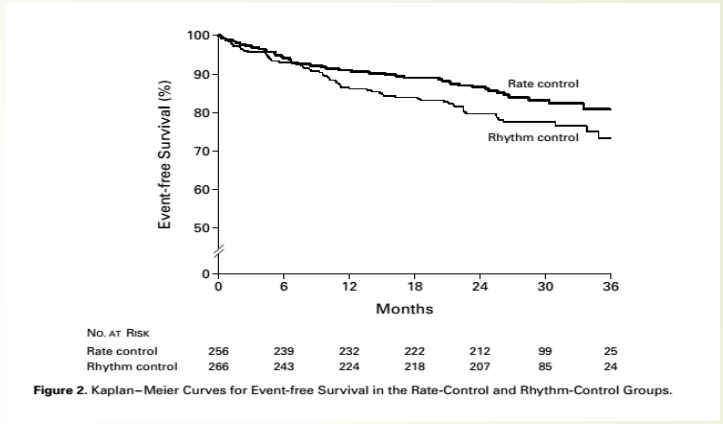
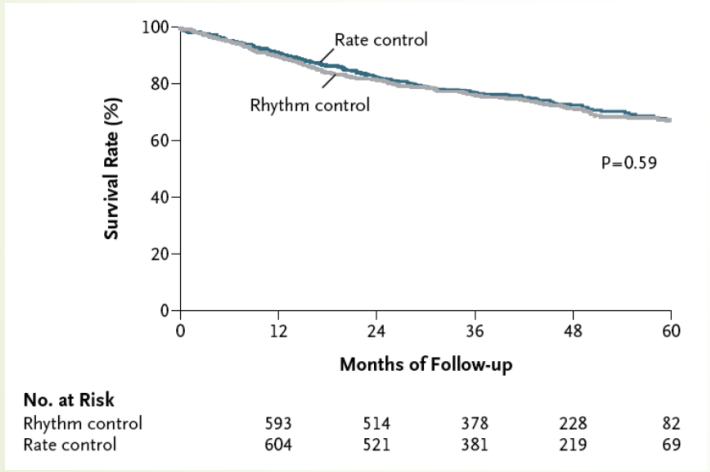
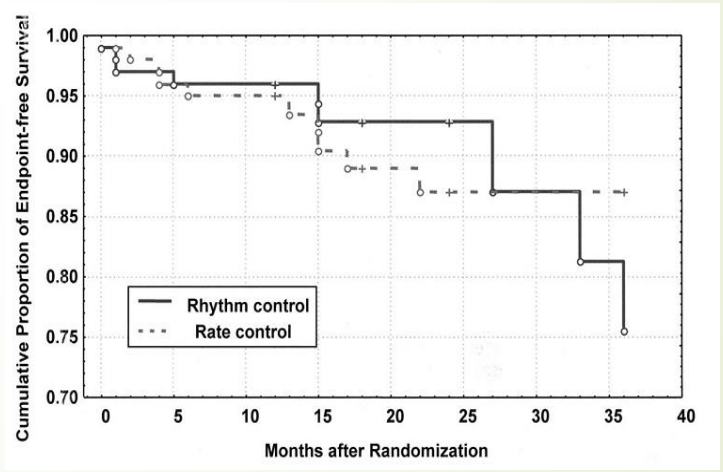



**Figure 2.** Kaplan–Meier Curves for Event-free Survival in the Rate-Control and Rhythm-Control Groups.




J Am Coll Cardiol. May 21 2003;41(10):1690–1696.

N Engl J Med.Dec 5 2002;347(23):1825 –1833

J Am Coll Cardiol. Aug15 2006;48(4):721– 730.

Circulation.Jul 17 2001;104(3):292–296

N Engl JMed.Dec 5 2002;347(23):1834 – 1840.

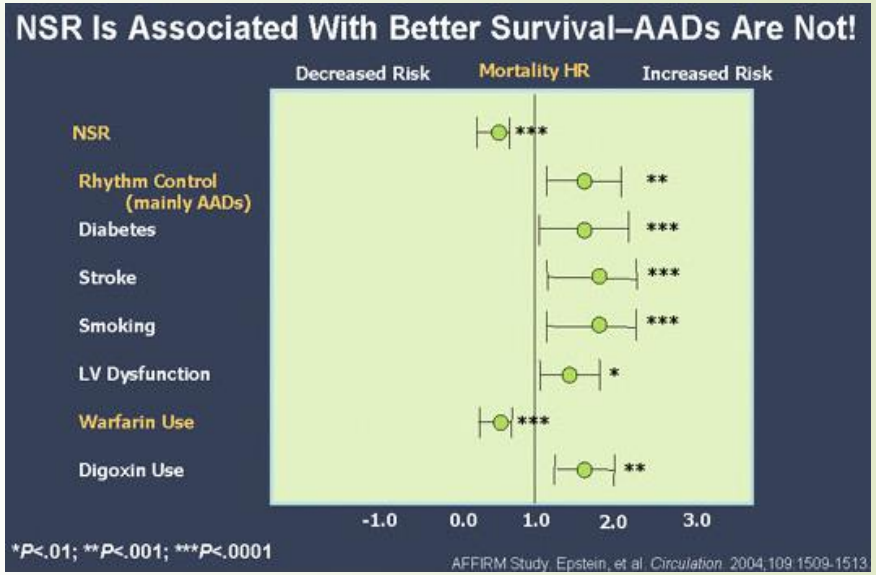
Lancet.Nov 25 2000;356(9244):1789 –1794.

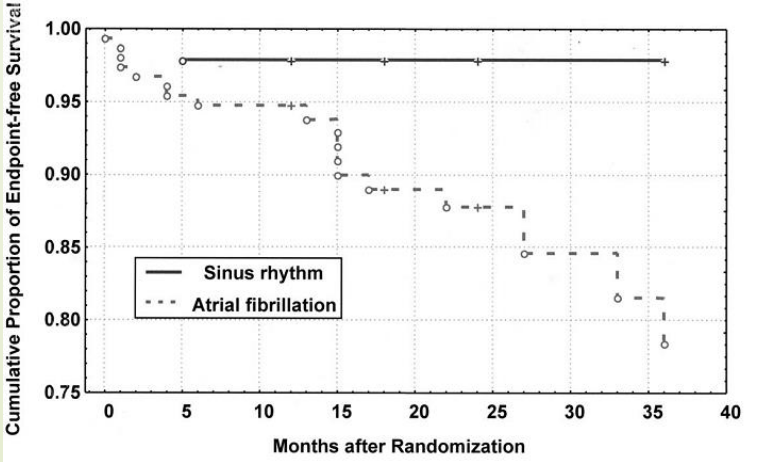
Circulation. Mar 30 2004;109(12):1509–1513.

# CONTROL DE RITMO

**ESTRATEGIA DE CONTROL RITMO/CONTROL FRECUENCIA**

- NO MEJORÍA SUPERVIVENCIA (STAF, AFFIRM, RACE)
- CONTROL RITMO NO INFERIOR EN CALIDAD DE VIDA Y EFERCICIO.
- NO MEJORA LA IC (AF CHF)




**ANÁLISIS POR CONTROL DEL RITMO**

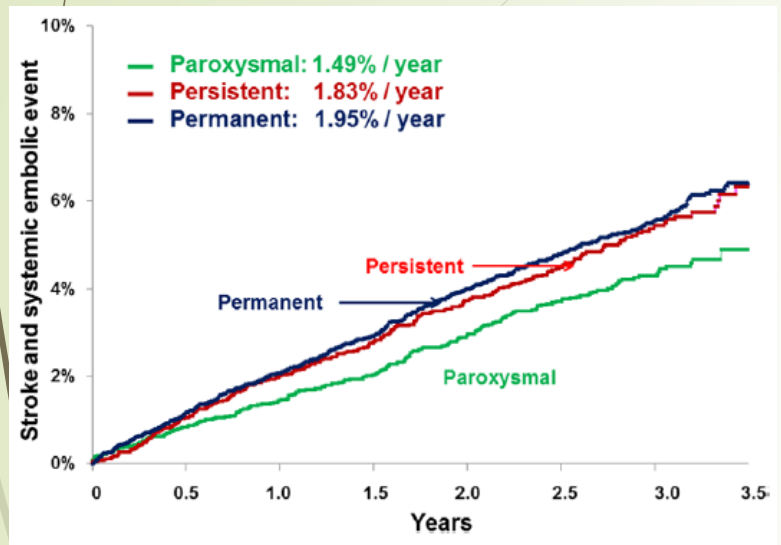
- AFFIRM:
  - RS aumento de supervivencia (47%; HR 0,53 )
  - Aumento de mortalidad con FAA (49%, HR 1.49)
- DIAMOND
  - RS 56% de recucción de mortalidad vs FA (HR 0,43 y 0,38 dofetilide y placebo respec)

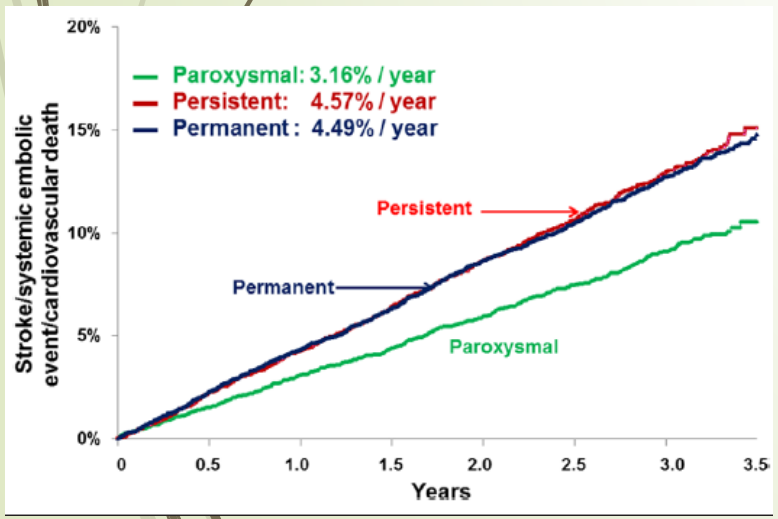
ún tipo

**Original Article**

## Stroke and Mortality Risk in Patients With Various Patterns of Atrial Fibrillation

### Results From the ENGAGE AF-TIMI 48 Trial (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48)



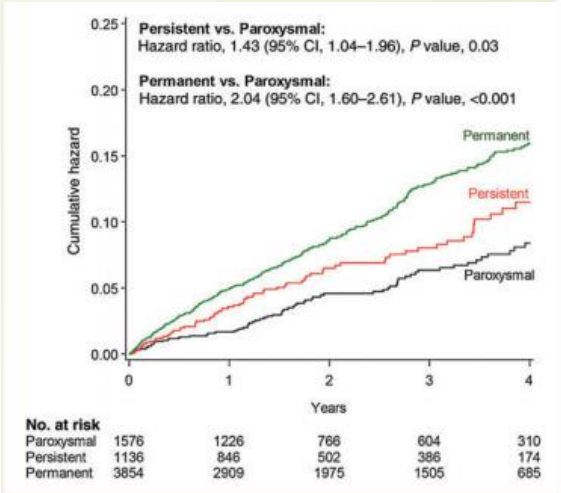
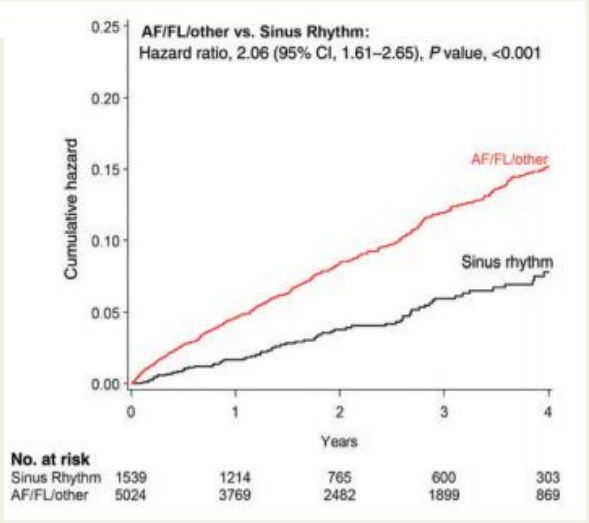




**Figure 1** Kaplan–Meier cumulative hazard rates of embolic events according to the pattern of atrial fibrillation occurrence.




**igure 2** Kaplan–Meier cumulative hazard rates of embolic ents according to the baseline ECG.

- HR 1,60 a 1,77
  - ENGAGE-TIMI38
  - AVERROES
  - AMADEUS

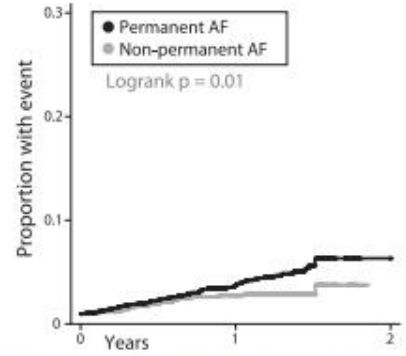



**Figure 1.** Kaplan–Meier event curves for cardiovascular death, stroke or systemic embolism by type of atrial fibrillation (AF).

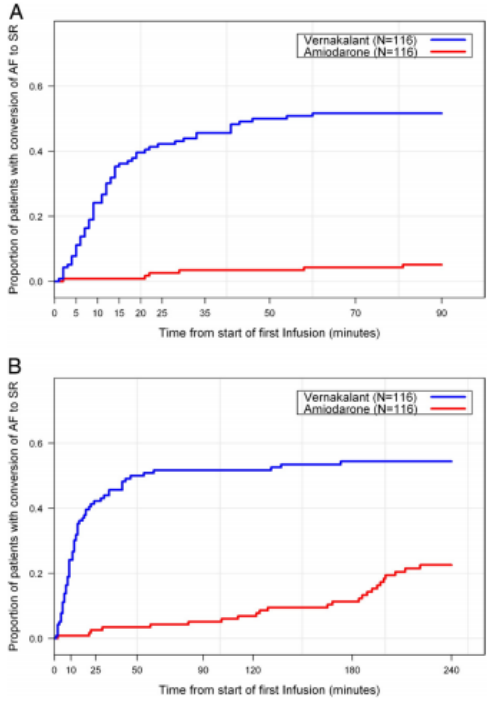
# CONTROL RITMO
# tratamiento farmacológico

# CVF

- 54% vs 22% reversión 4 horas post infusión 51% vs 5,6% en 90 min.
- 8,6% flutter en vernakalant
  - EAG en las 2-24h, tromboembólicos y TV en VKL y asistolia AMIO

**Table 6** Pooled efficacy rates for short-duration AF patients with cardioversion success at 2 h and 8–24 h by treatment

| Treatment | Cardioversion at 2 h | Cardioversion within 8–24 h |
|---|---|---|
| Vernakalant | 51.8% | — |
| Amiodarone-Oral | 9.3% | 87.1% |
| Amiodarone-IV | 16.2% | 61.2% |
| Flecainide-Oral | 67.5% | 80.6% |
| Flecainide-IV | 63.7% | 69.9% |
| Procainamide-IV | 62.5% | — |
| Propafenone-Oral | 21.2% | 78.7% |
| Propafenone-IV | 50.8% | 81.9% |
| Sotalol-IV | — | 61.2% |
| Placebo | 11.8% | 48.2% |




CME

## A Randomized Active-Controlled Study Comparing the Efficacy and Safety of Vernakalant to Amiodarone in Recent-Onset Atrial Fibrillation

A. John Camm, MD,* Alessandro Capucci, MD,† Stefan H. Hohnloser, MD,‡ Christian Torp-Pedersen, MD,§ Isabelle C. Van Gelder, MD,‖¶ Brian Mangal, MSc,# Gregory Beatch, PHD,# on behalf of the AVRO Investigators

*London, United Kingdom; Ancona, Italy; Frankfurt, Germany; Hellerup, Denmark; Groningen and Utrecht, the Netherlands; and Vancouver, British Columbia, Canada*

**Table 1** Demographic and Baseline Characteristics

| | Treatment Group | | |
|---|---|---|---|
| | Vernakalant (n = 116) | Amiodarone (n = 116) | Total (n = 232) |
| **Baseline characteristics** | | | |
| Male, n (%) | 75 (64.7) | 71 (61.2) | 146 (62.9) |
| White, n (%) | 111 (95.7) | 111 (95.7) | 222 (95.7) |
| Age (yrs), mean (SD) | 63.1 (10.81) | 62.2 (11.63) | 62.7 (11.21) |
| No previous episode of AF | 34 (29.3) | 33 (28.4) | 67 (28.9) |
| 1–3 previous episodes of AF | 44 (37.9) | 40 (34.5) | 84 (36.2) |
| >3 previous episodes of AF* | 38 (32.8) | 42 (36.2) | 80 (34.5) |
| Median duration of current AF, h (25%, 75% quartiles) | 17.7 (9.1, 28.7) | 17.9 (9.7, 31.4) | 17.7 (9.3, 30.4) |
| AF duration ≤24 h, n (%) | 73 (62.9) | 65 (56.0) | 138 (59.5) |
| **Medical history, n (%)** | | | |
| Hypertension | 86 (74.1) | 80 (69.0) | 166 (71.6) |
| Structural heart disease† | 36 (31.0) | 45 (38.8) | 81 (34.9) |
| Ischemic heart disease | 22 (19.0) | 30 (25.9) | 52 (22.4) |
| Myocardial infarction | 11 (9.5) | 8 (6.9) | 19 (8.2) |
| Valvular heart disease | 4 (3.4) | 12 (10.3) | 16 (6.9) |
| Heart failure | 20 (17.2) | 26 (22.4) | 46 (19.8) |
| NYHA functional class I‡ | 9 (45.0) | 12 (46.2) | 21 (45.7) |
| NYHA functional class II‡ | 11 (55.0) | 14 (53.8) | 25 (54.3) |
| LADD (mm), mean (SD) | 40.6 (6.77) | 41.0 (6.04) | 40.8 (6.40) |
| LADD >50 mm | 5 (4.3) | 7 (6.0) | 12 (5.2) |
| LVEF (%), mean (SD) | 57.6 (7.34) | 59.5 (6.97) | 58.5 (7.21) |
| LVEF <50% | 15 (12.9) | 4 (3.4) | 19 (8.2) |
| **Medications used within 7 days, n (%)** | | | |
| Any rate control§ | 71 (61.2) | 78 (67.2) | 149 (64.2) |
| Beta-blockers | 63 (54.3) | 76 (65.5) | 139 (59.9) |
| Calcium-channel blockers | 10 (8.6) | 4 (3.4) | 14 (6.0) |
| Digitalis glycosides | 6 (5.2) | 10 (8.6) | 16 (6.9) |

*Data for 1 patient in the amiodarone group are missing. †Patients may have had >1 condition listed under the structural heart disease category. ‡Denominators are based on those who had a history of heart failure. §Beta-blockers included intravenous or oral nonselective and selective beta-blockers (excluding sotalol) and alpha- and beta-blocking agents (e.g., carvedilol); calcium-channel blockers included diltiazem and verapamil; and digitalis glycosides included digoxin, digitoxin, and digitalis.
AF = atrial fibrillation; LADD = left atrial diastolic dimension; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

J Am Coll Cardiol 2011;57:313–21)

| Recommendations | Class | Level |
|---|---|---|
| **Antiarrhythmic effects of non-antiarrhythmic drugs** | | |
| ACE-Is, ARBs and beta-blockers should be considered for prevention of new-onset AF in patients with heart failure and reduced ejection fraction. | **IIa** | **A** |
| ACE-Is and ARBs should be considered for prevention of new-onset AF in patients with hypertension, particularly with LV hypertrophy. | **IIa** | **B** |
| Pre-treatment with ACE-Is or ARBs may be considered in patients with recurrent AF undergoing electrical cardioversion and receiving antiarrhythmic drug therapy. | **IIb** | **B** |
| ACE-Is or ARBs are not recommended for the secondary prevention of paroxysmal AF in patients with little or no underlying heart disease. | **III (no benefit)** | **B** |

# Fármacos antiarrítmicos

**Short-term versus long-term antiarrhythmic drug treatment after cardioversion of atrial fibrillation (Flec-SL): a prospective, randomised, open-label, blinded endpoint assessment trial**

Lancet 2012; 380: 238–46

- Doblan eficacia en mantenimiento RS respecto a placeb
- NO efe cardiov
- Disminu
- Menor
- Indicac

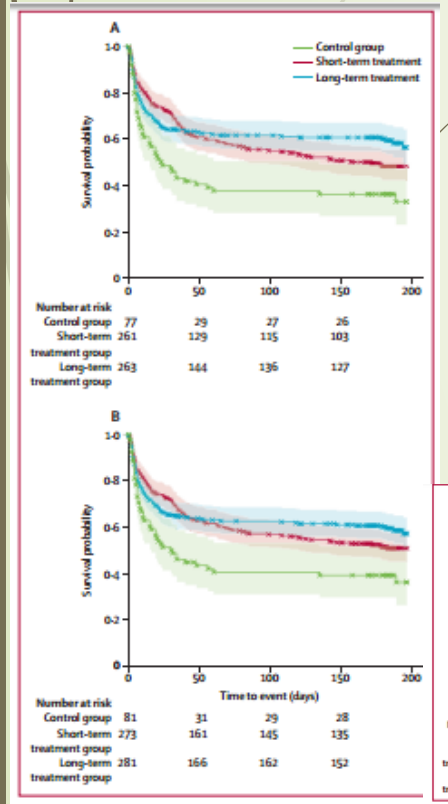



Figure 2: Survival free of persistent atrial fibrillation or death
Data for the per-protocol population (primary analysis; A) and for the intention-to-treat population (prespecified secondary analysis; B). Crosses indicate censoring. Shaded areas indicate 95% CIs.

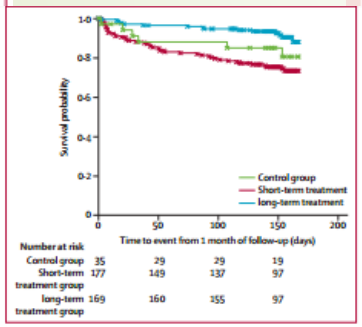



Figure 3: Survival free of persistent atrial fibrillation or death in patients who were event free at the 1 month follow-up visit
In the short-term treatment group, flecainide was withdrawn at 1 month. Crosses indicate censoring.

| | Control | Short-term treatment | Long-term treatment | Short-term treatment vs control | | Long-term treatment vs control | | Short-treatment vs long-term treatment | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Difference | p value | Difference | p value | Difference | p value |
| Documented atrial fibrillation episodes before reaching the primary endpoint | 9·0 (2 to 14); n=48 | 14 (5·5 to 23·5); n=120 | 13 (6 to 2[illegible]); n=106 | 4 (1 to 8)* | 0·0106† | 4 (0 to 8)* | 0·0319† | 1 (−3 to 4)* | 0·6979† |
| Days with documented atrial fibrillation before reaching the primary endpoint | 8·0 (2 to 12); n=48 | 12 (5 to 20); n=120 | 11 (5 to 2[illegible]); n=106 | 3 (1 to 7)* | 0·0147† | 3 (0 to 7)* | 0·0455† | 0 (−3 to 3)* | 0·7739† |
| Admissions to hospital because of atrial fibrillation | 0 (0 to 0); n=76 | 0 (0 to 0); n=260 | 0 (0 to 0); n=269 | 0 (0–0)* | 0·7101† | 0 (0–0)* | 0·9776† | 0 (0–0)* | 0·5484† |
| Visits without admission | 1 (0 to 3); n=76 | 1 (0 to 3); n=260 | 1 (0 to 3); n=269 | 0 (0 to 1)* | 0·1399† | 0 (0–0)* | 0·7667† | 0 (0–0)* | 0·0615† |
| Serious adverse events of special interest‡ | 1 (1·2%) | 9 (3·3%) | 10 (3·6%) | .. | 0·3252§ | .. | 0·2830§ | .. | 0·8655§ |
| Major adverse cardiovascular or cerebrovascular events | 1 | 5 | 4 | .. | .. | .. | .. | .. | .. |
| Resuscitation | 0 | 0 | 1 | .. | .. | .. | .. | .. | .. |
| Syncope | 0 | 2 | 4 | .. | .. | .. | .. | .. | .. |
| Sustained ventricular tachycardia | 0 | 2 | 0 | .. | .. | .. | .. | .. | .. |
| Transient cerebral ischemic event | 0 | 0 | 1 | .. | .. | .. | .. | .. | .. |
| Major adverse cardiovascular and cerebrovascular events during follow-up | 1 (1·2%) | 5 (1·8%) | 4 (1·4%) | .. | 0·7147§ | .. | 0·8979§ | .. | 0·7041§ |
| Stroke | 0 | 3 | 2 | .. | .. | .. | .. | .. | .. |
| Myocardial infarction | 0 | 0 | 0 | .. | .. | .. | .. | .. | .. |
| Death | 0 | 0 | 0 | .. | .. | .. | .. | .. | .. |
| Major bleed | 1 | 2 | 2 | .. | .. | .. | .. | .. | .. |
| Left ventricular ejection fraction at 6 months¶ | 62·1% (59·6 to 64·5); n=45‖ | 62·3% (61·0 to 63·5); n=172‖ | 63·0% (61·9 to 64·2); n=190‖ | 0·2 (−2·6 to 3·0) | 0·8206** | 0·9 (−1·8 to 3·6) | 0·5381** | −0·7 (−2·4 to 1·0) | 0·4588** |

# EVIDENCIA FARMACOLÓGICA

| TRIAL | FAA | PAROX | AÑOS | RESULTADO (ausencia recurrencia) |
|---|---|---|---|---|
| **CTAF** | Amio vs Sot/Propa | 50% | 1,3 | 65% Amio<br>36% sotalol propa |
| **PIAF** | Amio | 0 | 1 | 56% vs 10% placebo (RS al año) |
| **RACE** | IC, III | 0 | 2,3 | 39% RS al año vs 10% placebo |
| **AFFIRM** | eleccion | 1/3 tras primer episodio | 1<br>3<br>5 | 82% RS<br>73% RS<br>62% RS vs 34,6% grupo control |
| **DIAMOND** | Dofetilide | No datos | 1 | 79% RS vs 42% placebo |
| **AF-CHF** | Amio/sot/dofe | 67% | 3 | 73% RS vs < 30% (58% recurrencias) |
| **Singh** | Dronedarona | No datos | 1 | 36% vs 25% |

J Am Coll Cardiol. May 21 2003;41(10):1690–1696.
N Engl J Med.Dec 5 2002;347(23):1825 –1833
Circulation. Mar 30 2004;109(12):1509–1513.

N Engl JMed.Dec 5 2002;347(23):1834 – 1840.
Lancet.Nov 25 2000;356(9244):1789 –1794.
Circulation.Jul 17 2001;104(3):292–296
European Heart Journal (2010)31, 1046–1054

**Table 2. Study Outcomes.***

| Outcome | Dronedarone | | Placebo | | Hazard Ratio (95% CI)† | P Value |
|---|---|---|---|---|---|---|
| | No. of Events | Rate/100 Patient-Yr | No. of Events | Rate/100 Patient-Yr | | |
| First coprimary outcome | 43 | 8.2 | 19 | 3.6 | 2.29 (1.34–3.94) | 0.002 |
| Second coprimary outcome | 127 | 25.3 | 67 | 12.9 | 1.95 (1.45–2.62) | <0.001 |
| Death | | | | | | |
| From any cause | 25 | 4.7 | 13 | 2.4 | 1.94 (0.99–3.79) | 0.049 |
| From cardiovascular causes | 21 | 4.0 | 10 | 1.9 | 2.11 (1.00–4.49) | 0.046 |
| From arrhythmia | 13 | 2.5 | 4 | 0.8 | 3.26 (1.06–10.0) | 0.03 |
| Stroke | | | | | | |
| Any‡ | 23 | 4.4 | 10 | 1.9 | 2.32 (1.11–4.88) | 0.02 |
| Ischemic | 18 | 3.4 | 9 | 1.7 | 2.01 (0.90–4.48) | 0.08 |
| Systemic embolism | 1 | 0.2 | 0 | 0.0 | NA | NA |
| Myocardial infarction or unstable angina | 15 | 2.9 | 8 | 1.5 | 1.89 (0.80–4.45) | 0.14 |
| Myocardial infarction | 3 | 0.6 | 2 | 0.4 | 1.54 (0.26–9.21) | 0.63 |
| Unplanned hospitalization for cardiovascular causes | 113 | 22.5 | 59 | 11.4 | 1.97 (1.44–2.70) | <0.001 |
| Hospitalization for heart failure | 43 | 8.3 | 24 | 4.6 | 1.81 (1.10–2.99) | 0.02 |
| Heart-failure episode or hospitalization§ | 115 | 23.2 | 55 | 10.7 | 2.16 (1.57–2.98) | <0.001 |

* The first coprimary outcome was a composite of stroke, myocardial infarction, systemic embolism, or death from cardiovascular causes. The second coprimary outcome was a composite of unplanned hospitalization for cardiovascular causes or death. NA denotes not applicable.
† Hazard ratios are for the comparison between the dronedarone group and the placebo group.
‡ The types of five strokes (four in the dronedarone group and one in the placebo group) were not specified, and one stroke in the dronedarone group was hemorrhagic.
§ This category includes two patients who died from reported heart failure.

Figure 2. Kaplan–Meier Cumulative Incidences of the Primary and Secondary Outcomes.

N Engl J Med 2007;357:987-99.



**Table 3. Adverse Events and Abnormalities on Laboratory Testing.***

| Event | Dronedarone (N=1614) | Placebo (N=1609) | P Value |
|---|---|---|---|
| | *number (percent)* | | |
| Any adverse event | 797 (49.4) | 600 (37.3) | <0.001 |
| Any serious adverse event | 113 (7.0) | 77 (4.8) | 0.008 |
| Any adverse event leading to treatment discontinuation | 212 (13.1) | 80 (5.0) | <0.001 |
| Any reported liver-function abnormality | 61 (3.8) | 28 (1.7) | <0.001 |
| Asthenic conditions (asthenia, fatigue) | 89 (5.5) | 46 (2.9) | <0.001 |
| Breathing abnormalities (dyspnea) | 75 (4.6) | 36 (2.2) | <0.001 |
| Diarrhea | 101 (6.3) | 38 (2.4) | <0.001 |
| Electrocardiographic investigations (QT prolonged) | 33 (2.0) | 16 (1.0) | 0.02 |
| Edema (peripheral edema) | 60 (3.7) | 29 (1.8) | <0.001 |
| Gastrointestinal or abdominal pain | 33 (2.0) | 15 (0.9) | 0.009 |
| Increased creatinine level | 49 (3.0) | 11 (0.7) | <0.001 |
| Lower respiratory tract or lung infection | 40 (2.5) | 42 (2.6) | 0.81 |
| Nausea or vomiting | 76 (4.7) | 28 (1.7) | <0.001 |
| Neurologic signs or symptoms (dizziness) | 76 (4.7) | 39 (2.4) | <0.001 |
| Rate and rhythm disorders (bradycardia) | 67 (4.2) | 19 (1.2) | <0.001 |
| Renal failure or impairment | 35 (2.2) | 12 (0.7) | <0.001 |
| Upper respiratory tract infection | 34 (2.1) | 35 (2.2) | 0.89 |
| Alanine aminotransferase and bilirubin† | | | |
| Alanine aminotransferase >3× ULN | 23 (1.5) | 9 (0.6) | 0.013 |
| Alanine aminotransferase >3× ULN and bilirubin >2× ULN | 1 (<0.1)‡ | 0 | NA |

* Listed are adverse events and serious adverse events that occurred in patients receiving at least one dose of a study drug with a reported frequency of 2% or more in each study group. The preferred term is provided for explanatory purposes in parentheses when one preferred term predominated. NA denotes not applicable, and ULN upper limit of the normal range.
† Alanine aminotransferase was measured in 1574 patients in the dronedarone group and in 1589 in the placebo group; the combination of alanine aminotransferase and bilirubin was measured in 1571 patients in the dronedarone group and in 1589 in the placebo group.
‡ One patient received the diagnosis of biliary stasis that was not considered to be related to dronedarone.

Figure 1. Risk of the First Coprimary Outcome (Stroke, Myocardial Infarction, Systemic Embolism, or Death from Cardiovascular Causes).

Figure 2. Risk of the Second Coprimary Outcome (Unplanned Hospitalization for Cardiovascular Causes or Death).

N Engl J Med 2011;365:2268-76.

Europace (2011) 13, 329–345
doi:10.1093/europace/euq450



# Mixed treatment comparison of dronedarone, amiodarone, sotalol, flecainide, and propafenone, for the management of atrial fibrillation

**Nick Freemantle[1], Carmelo Lafuente-Lafuente[2], Stephen Mitchell[3], Laurent Eckert[4]*, and Matthew Reynolds[5]**

[1]School of Health and Population Sciences, 90 Vincent Drive, University of Birmingham Edgbaston, Birmingham B15 2SP, UK; [2]Service de Médecine Interne A. Hôpital Lariboisière, 2, rue Ambroise Paré, Paris 75010, France; [3]Abacus International, 4 Market Square, Bicester, Oxfordshire OX26 6AA, UK; [4]sanofi-aventis R&D, 182 avenue de France, 75013 Paris, France; and [5]Division of Cardiology, Beth Israel Deaconess Medical Center, Harvard Clinical Research Institute, Boston, MA, USA

*Received 16 July 2010; accepted after revision 17 November 2010; online publish-ahead-of-print 11 January 2011*

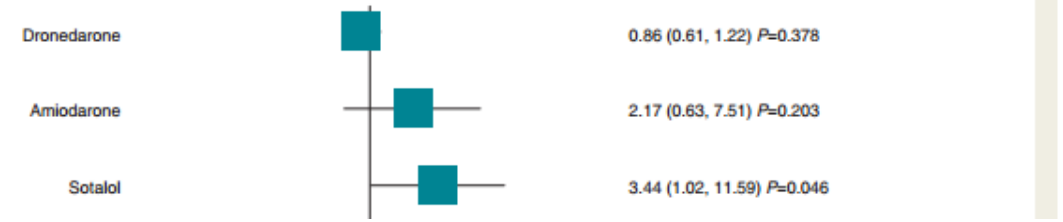



**Figure 2** Mixed treat
vals. Note—odds ratio

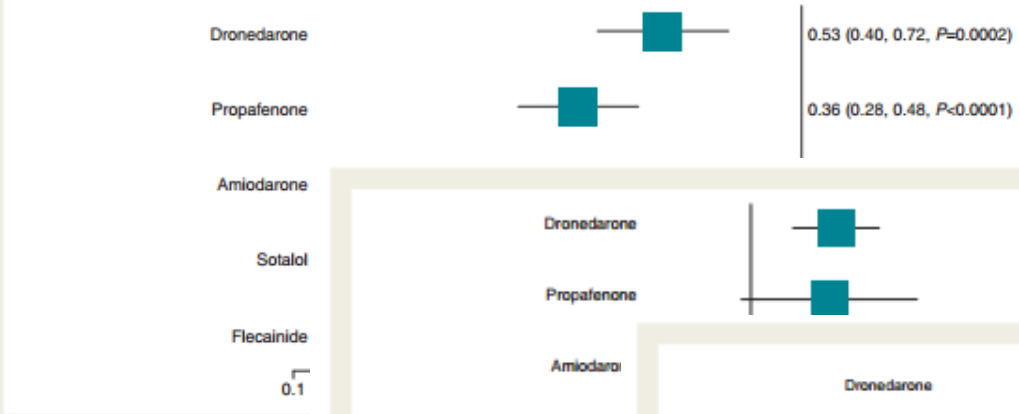



**Figure 5** Mixed treatment compa
dence intervals. Note—odds ratio l




**Figure 7** Mixed treatment con
confidence intervals.

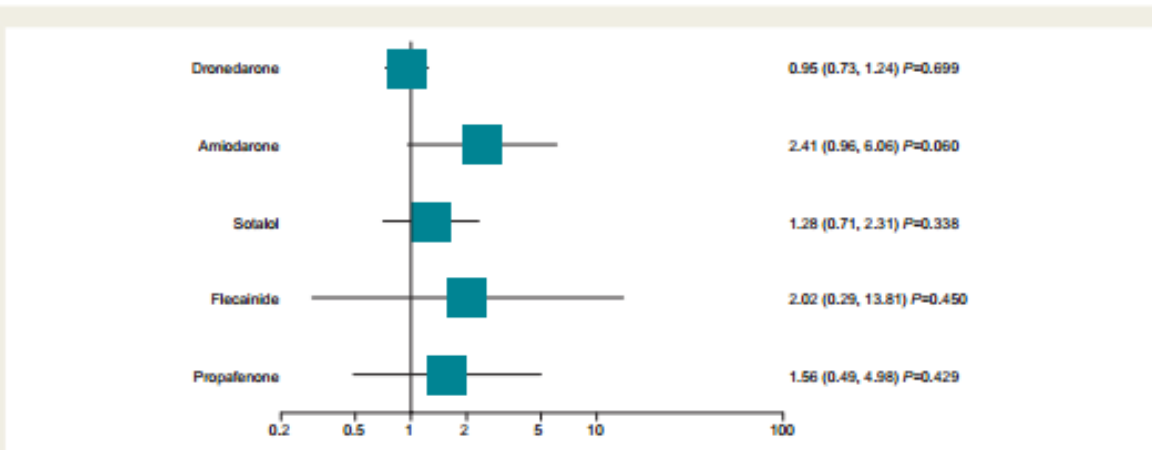



**Figure 8** Mixed treatment comparison analysis: effect of anti-arrhythmic drugs on incidence of serious adverse events. Odds ratios and 95% confidence intervals. Note—odds ratio lower than 1 describes a lower rate of serious adverse events for the active treatment.

**Table 1 Baseline characteristics summary of the included studies**

| Patient characteristics | Range of values | Mean (SD) |
|---|---|---|
| Number of patients randomized | 16–4628 | 245 (580) |
| Age (years) | 49–78 | 61.6 (5.2) |
| Gender (% male) | 35–99 | 59.2 (12.6) |
| AF Type (paroxysmal)[a] | 33 | — |
| AF type (persistent)[a] | 23 | — |
| AF type (permanent)[a] | 7 | — |
| Structural heart disease (%) | 0–100 | 60.1 (23.4) |
| Left ventricular ejection fraction (LVEF) (%) | 30–68 | 55.1 (9.1) |
| Left atrium diameter (LAD) (mm) | 34–50 | 42.9 (3.8) |

[a]Number of studies reported across the included studies.

# CONTROL RITMO
# tratamiento no farmacológico

Europace
doi:10.1093/europace/euu376



# Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis

**Table 5** Outcome of patients who underwent radiofrequency ablation or antiarrhythmic drug treatment for atrial fibrillation in three randomized studies

| Outcome endpoints | No. of studies | Participants | RFA 238 patients | AAD 242 patients | *P* value | Effect estimate RR (95% CI) | $I^2$ |
|---|---|---|---|---|---|---|---|
| Symptomatic AF recurrence | 3 | 480 | 66 | 102 | | | |
| Freedom from recurrent AF | 3 | 480 | – | – | | | |
| Cross-over | 3 | 480 | 19 | 80 | | | |
| Additional ablations | 3 | 480 | 78 | 80 | | | |
| Tamponade | 2 | 413 | 7 | 0 | | | |
| Pulmonary vein stenosis >70% | 3 | 480 | 1 | 0 | | | |
| Symptomatic bradycardia | 2 | 353 | 0 | 8 | | | |
| Stroke | 3 | 480 | 1 | 0 | | | |
| Atrial flutter with 1:1 AV conduction | 2 | 413 | 0 | 3 | | | |
| Syncope | 2 | 413 | 0 | 3 | | | |
| Hospitalization | 2 | 353 | 89 | 99 | | | |

AF, atrial fibrillation; RFA, radiofrequency catheter ablation; AAD, antiarrhythmic drug therapy; RR, risk ratio; CI, confidence i

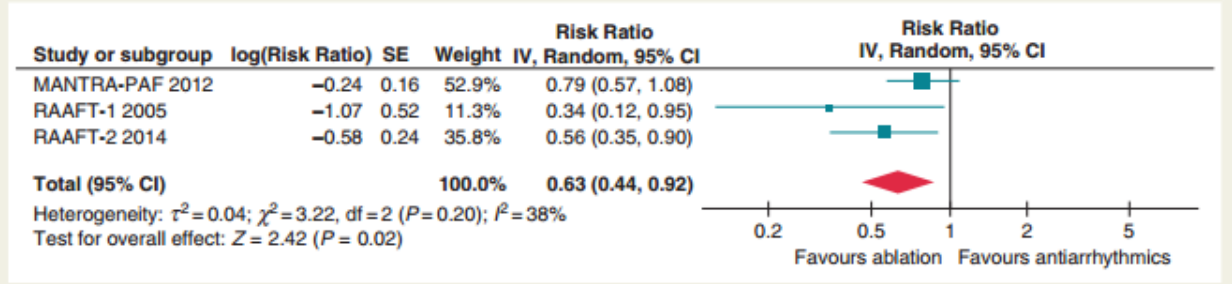



**Figure 2** Forest plot showing the risk of recurrence of atrial fibrillation after radiofrequency ablation or antiarrhythmic drug treatment in three randomized studies. RAAFT-2 study included also the occurrence of atrial tachycardia and flutter.

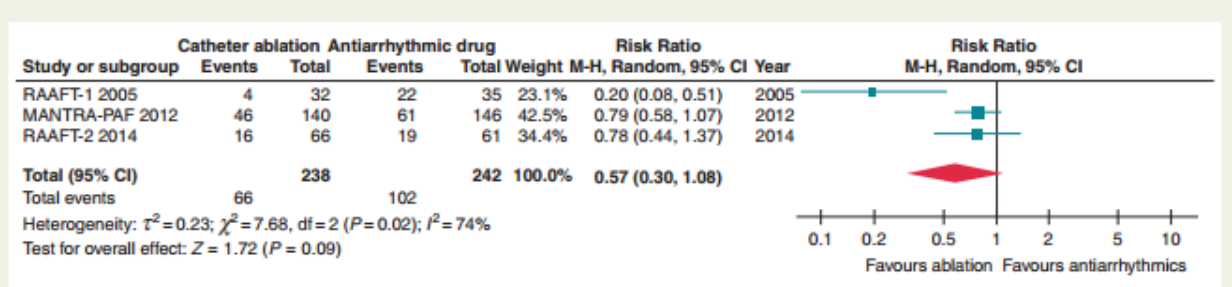



**Figure 3** Forest plot showing the risk of symptomatic atrial fibrillation after radiofrequency ablation or antiarrhythmic drug treatment in three randomized studies.

Europace. 2015;17(3):370-8

# FA persistente

- 146p 2:1 (CA vs ADT) 1 año seguimiiento
- Endpoint >24h FA post 3 meses
  - 70% vs 44% p0,002
  - OR 3,28 (1,5-6,9)
- Endpoint >30s FA
  - 60,2 vs 29,2% p0,001
- CVE
  - 34,7% vs 50%  p 0,018
- 60% bajo tto con amiodarona ADT
- Blanking 13% de recurrencias tempranas únicas
  - 29,6% recurrencias en CA
  - OR de recurrencia si recurren en blanking 5,30 (2,05-13,69)
- Crossover 34% en grupo CA por FA parox.
  - 33% en ADT tras alcanzar enpoint. Ninguno previo.
- QoL e Ingresos sin diferencias entre grupos.

European Heart Journal (2014) 35, 501–507

European Heart Journal (2014) 35, 501–507
doi:10.1093/eurheartj/eht457

FASTTRACK CLINICAL RESEARCH

## Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study)

Lluís Mont[1]*, Felipe Bisbal[1], Antonio Hernández-Madrid[2], Nicasio Pérez-Castellano[3], Xavier Viñolas[4], Angel Arenal[5], Fernando Arribas[6], Ignacio Fernández-Lozano[7], Andrés Bodegas[8], Albert Cobos[9], Roberto Matía[2], Julián Pérez-Villacastín[3], José M. Guerra[4], Pablo Ávila[5], María López-Gil[6], Victor Castro[7], José Ignacio Arana[8], and Josep Brugada[1], on behalf of SARA investigators

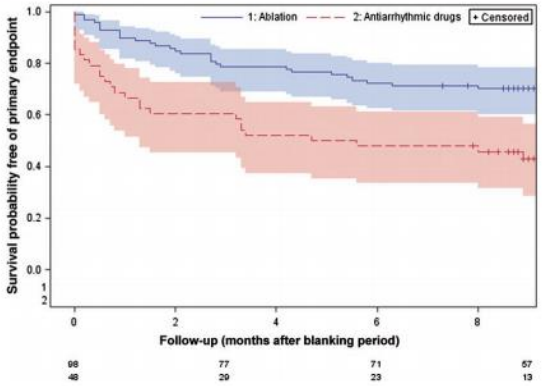



**Figure 2** Survival curves for the primary endpoint.

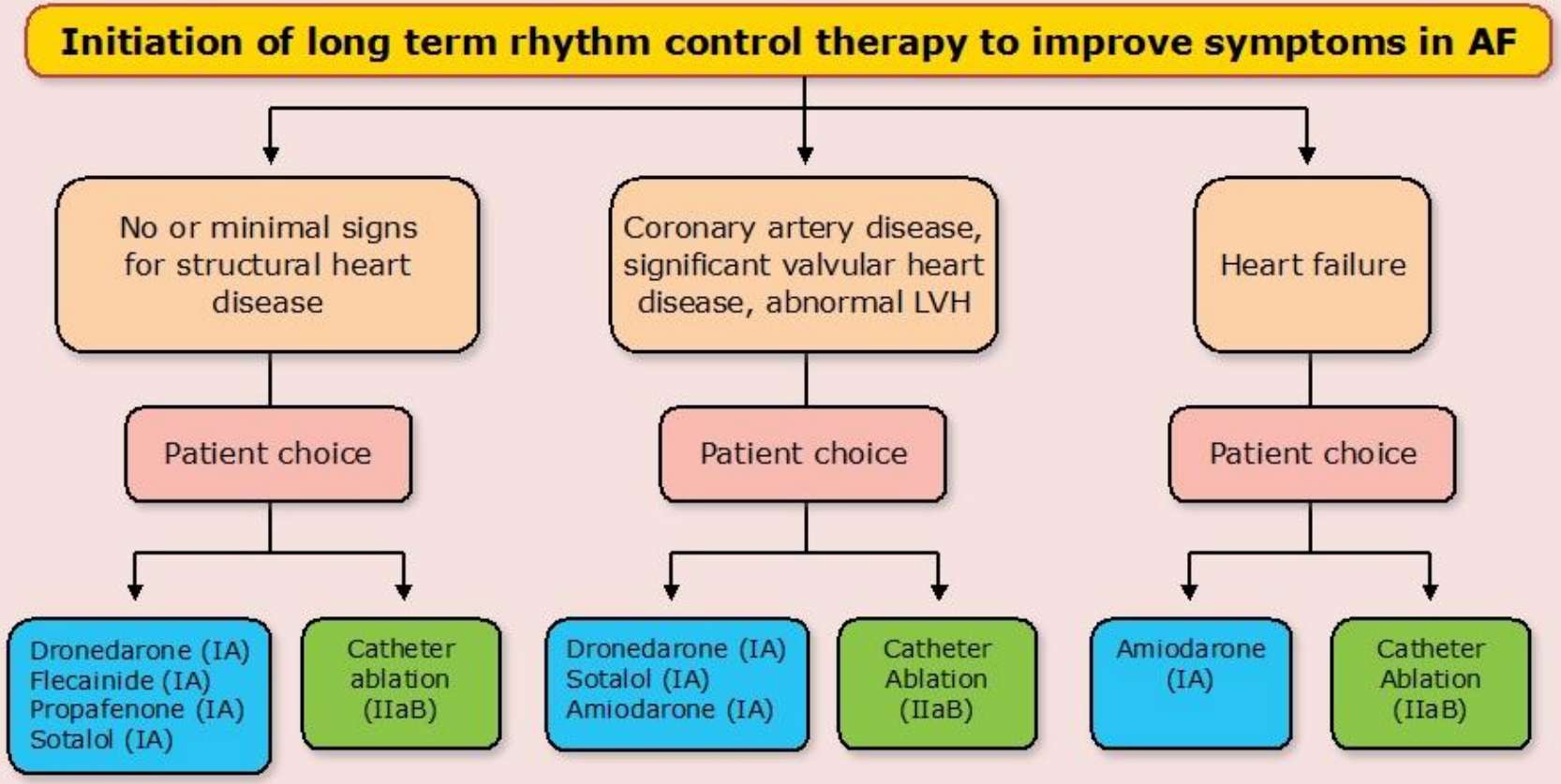
| Outcome | Ablation ($n$ = 98) | Drug therapy ($n$ = 48) |
|---|---|---|
| Free of any recurrence of AF or flutter (confirmed during >30 s) | 59 (60.2) | 14 (29.2)[a,***] |
| Crossovers | 35 (35.7) | 0 (0)[a,***] |
| Cardioversions | | |
| None | 64 (65.3) | 24 (50.0)[b,*] |
| 1 | 22 (22.4) | 10 (20.8) |
| 2 or more | 12 (12.2) | 14 (29.2) |
| Hospitalizations related to arrhythmia | 2 (2.0) | 3 (6.25)[c] |

AF, atrial flutter.
[a]$\chi^2$ test.
[b]Cochrane–Armitage test.
[c]Fisher's exact test.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

## Freedom from recurrence of atrial fibrillation or atrial arrhythmias, comparing catheter ablation with antiarrhythmic drug therapy in patients with persistent or long-standing persistent atrial fibrillation

| Study | Ablation Events | Ablation N | AAD Events | AAD N | Primary outome: Freedom from atrial arrhythmia / recurrence | RR | 95% CI | W(fixed) | W(random) |
|---|---|---|---|---|---|---|---|---|---|
| Forleo | 28 | 35 | 15 | 35 | | 1.87 | [1.23; 2.83] | 17.5% | 27.7% |
| Mont 2009 | 69 | 98 | 21 | 48 | | 1.61 | [1.14; 2.27] | 32.8% | 32.0% |
| Oral 2006 | 57 | 77 | 40 | 69 | | 1.28 | [1.00; 1.62] | 49.1% | 38.9% |
| Stabile 2006 | 13 | 26 | 0 | 19 | | 20.00 | [1.26; 319.89] | 0.7% | 1.4% |
| Fixed effects model | | 236 | | 171 | | | | | |
| Random effects model | | | | | | | | | |

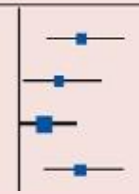
*Heterogeneity: I-squared = 58,9%, p= 0.063*

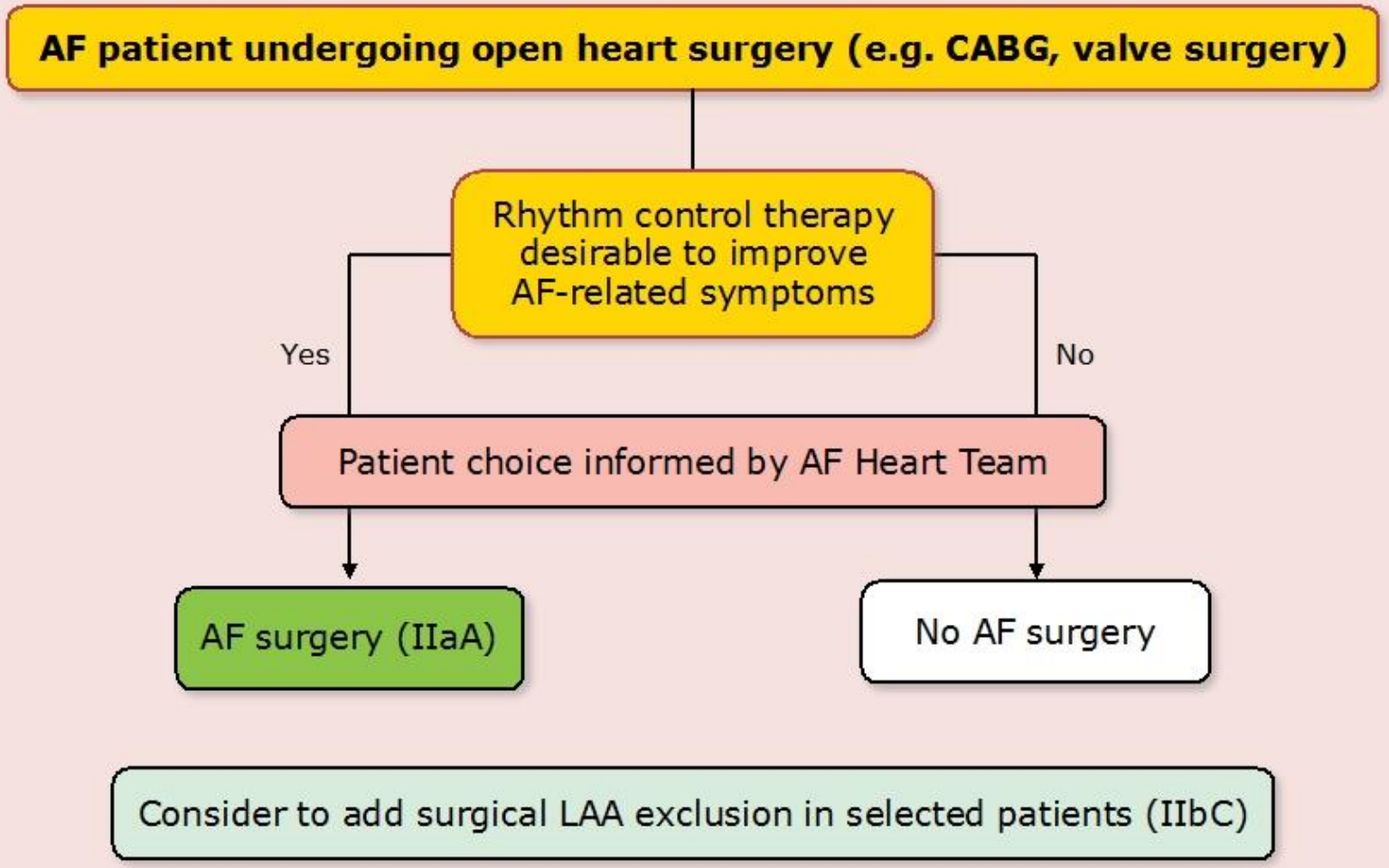



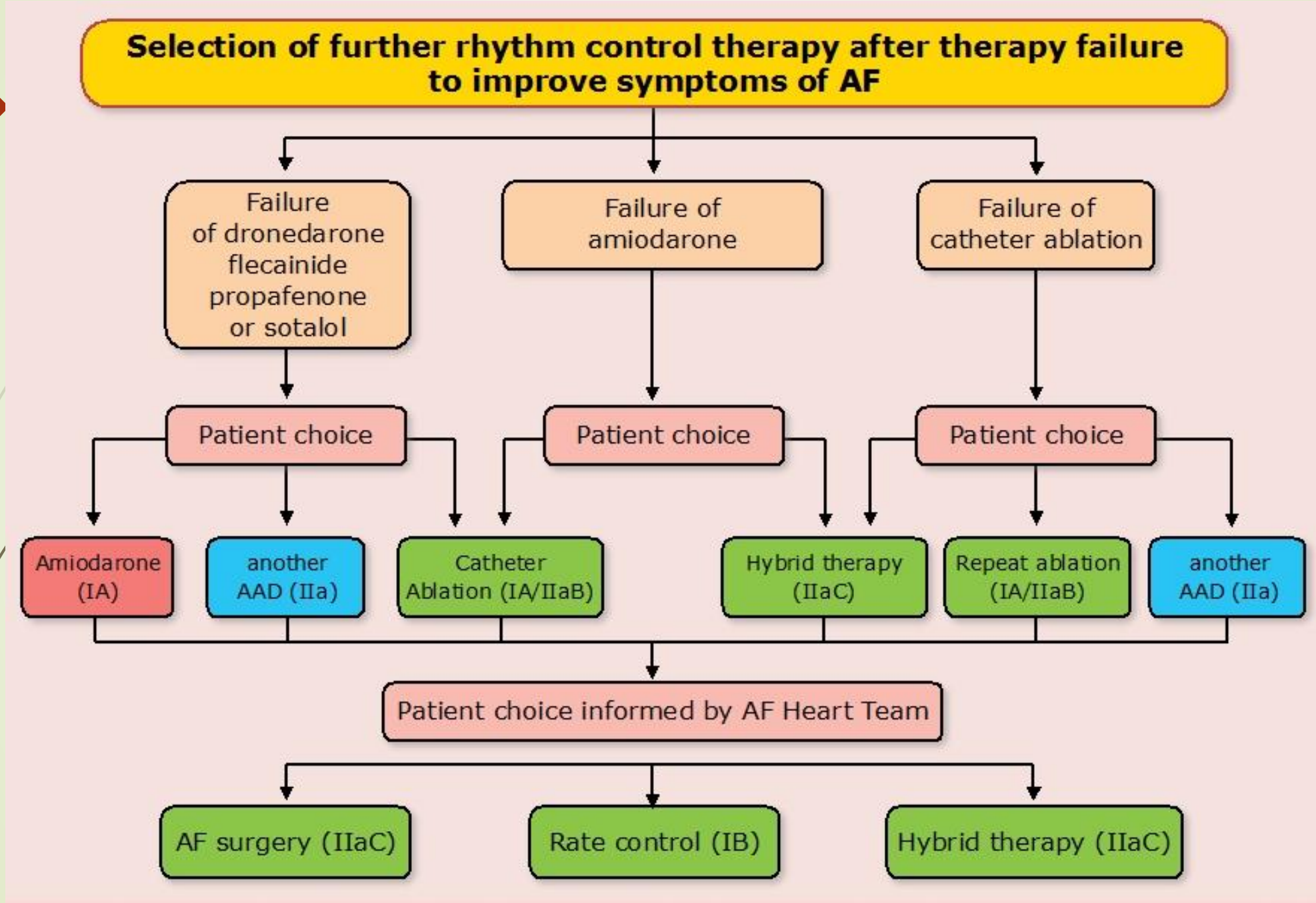
**Freedom from atrial fibrillation, atrial flutter and atrial tachycardia after surgical atrial fibrillation ablation**

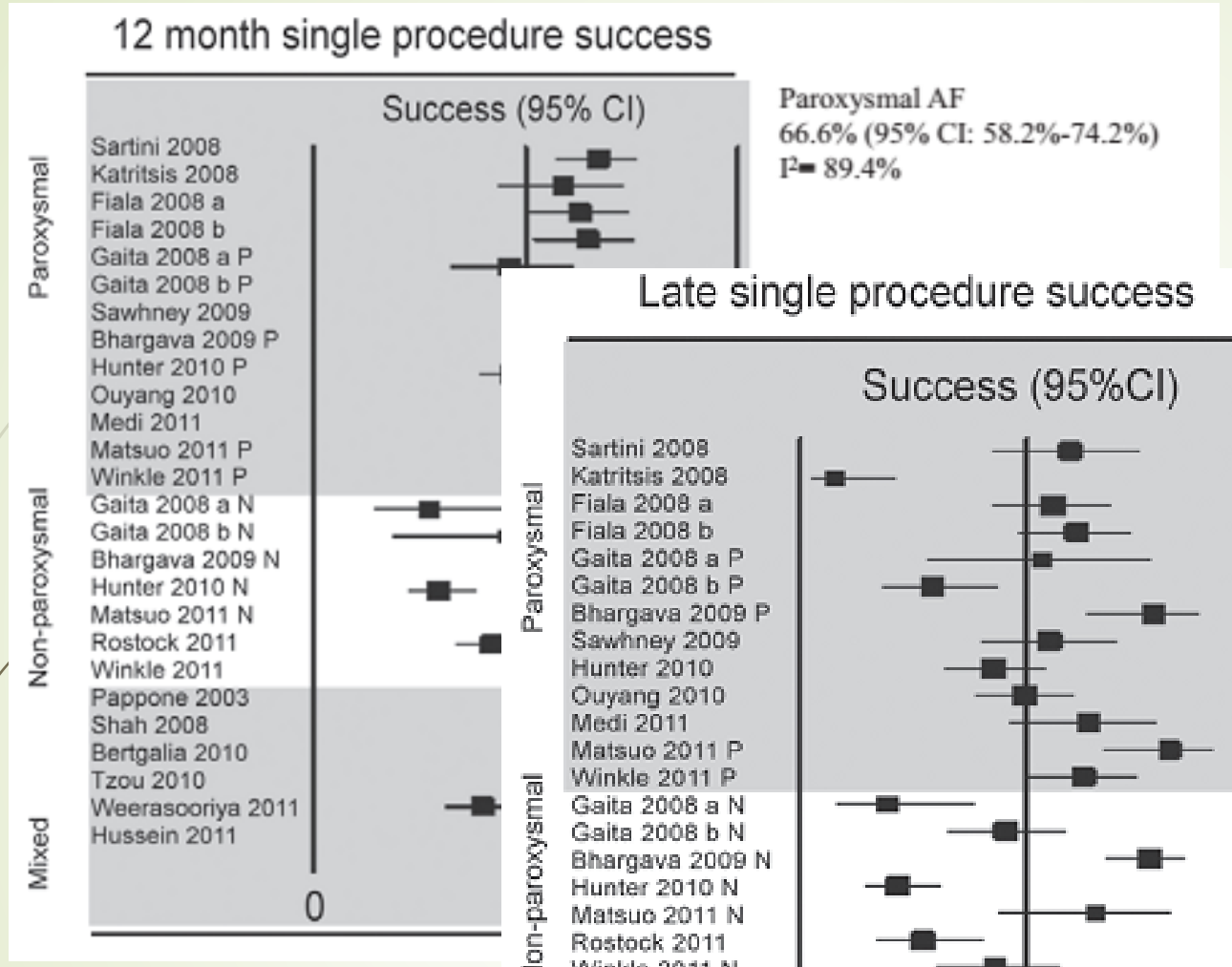
| Study or Subgroup | Surgical ablation Events | Total | No ablation Events | Total | Weight | Risk Ratio Fixed effects, 95% CI |
|---|---|---|---|---|---|---|
| Abreu Filho 2005 | 31 | 42 | 7 | 28 | 10.9% | 2.95 [1.52, 5.75] |
| Blomstrom-Lundqvist 2007 | 16 | 34 | 8 | 35 | 10.2% | 2.06 [1.02, 4.17] |
| Budera 2012 | 36 | 117 | 20 | 105 | 27.3% | 1.62 [1.00, 2.61] |
| Cherniavsky 2014 | 49 | 61 | 11 | 34 | 18.3% | 2.48 [1.50, 4.10] |
| Jonsson 2012 | 19 | 35 | 9 | 35 | | |
| Knaut 2010 | 11 | 24 | 7 | 21 | | |
| Pokushalov 2012 | 16 | 18 | 8 | 17 | | |
| Schuetz 2003 | 3 | 24 | 1 | 19 | | |
| **Total (95% CI)** | | **355** | | **294** | | |
| Total events | 181 | | 71 | | | |

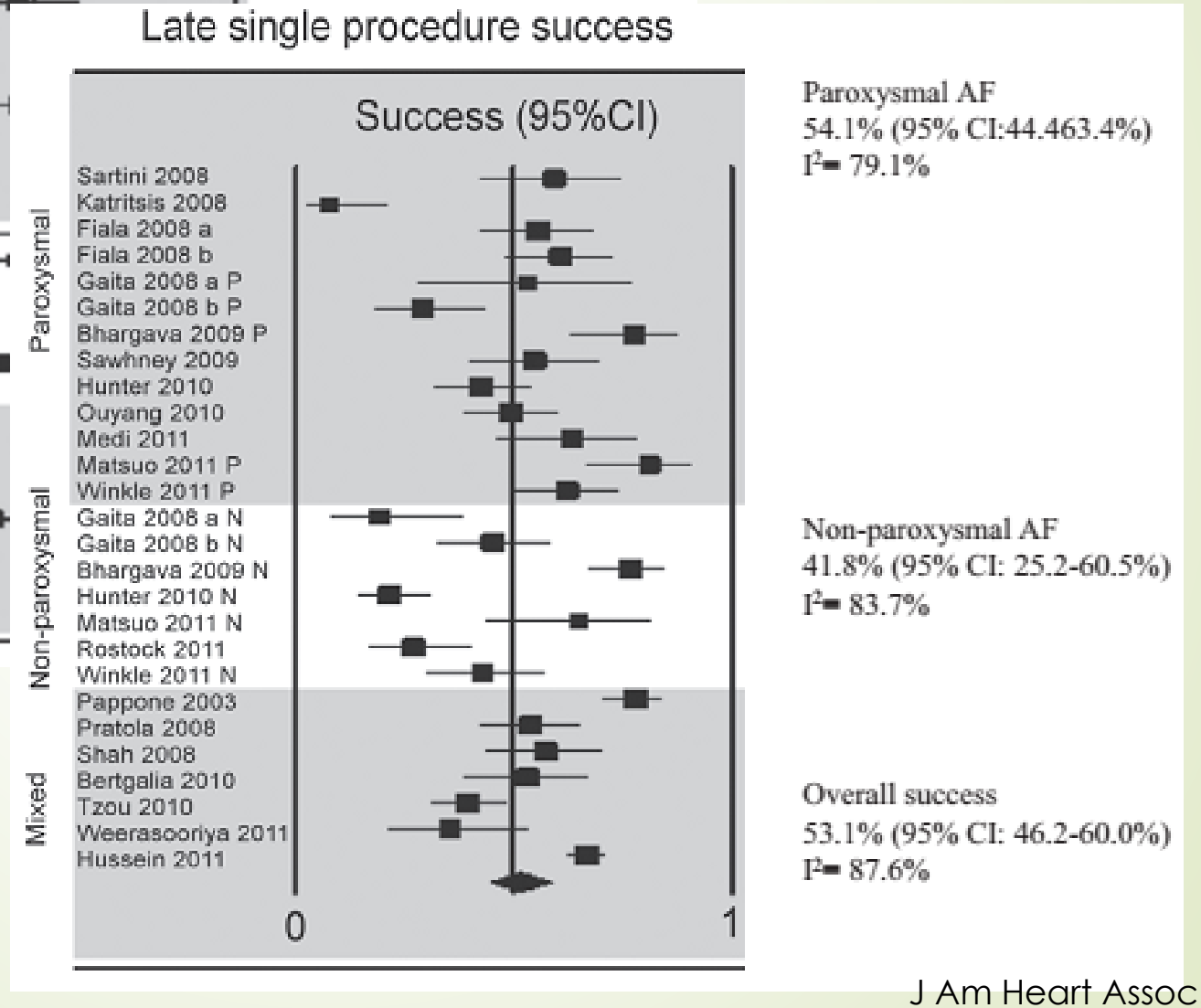
*Heterogeneity Chi² = 3.87, df = 7 (P = 0.79); I² = 0%*
*Test for overall effect: Z = 6.25 (P <0.00001)*



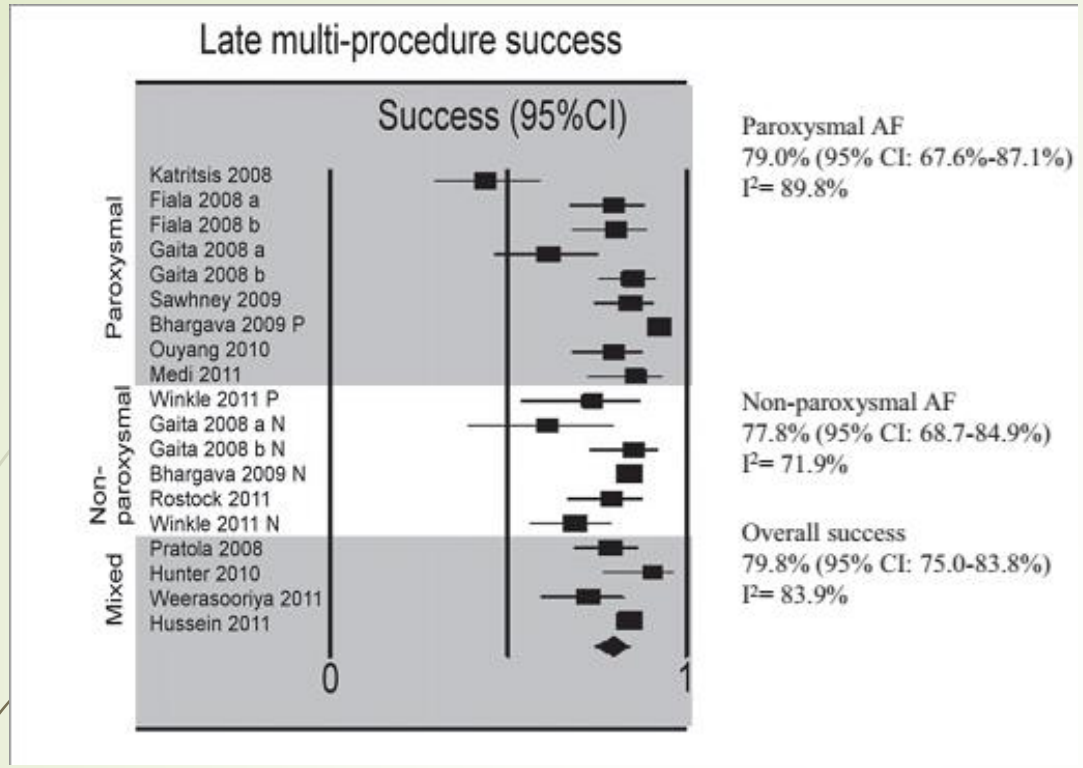




Selection of further rhythm control therapy after therapy failure to improve symptoms of AF
Failure of dronedarone flecainide propafenone or sotalol
Failure of amiodarone
Failure of catheter ablation
Patient choice
Patient choice
Patient choice
Amiodarone (IA)
another AAD (IIa)
Catheter Ablation (IA/IIaB)
Hybrid therapy (IIaC)
Repeat ablation (IA/IIaB)
another AAD (IIa)
Patient choice informed by AF Heart Team
AF surgery (IIaC)
Rate control (IB)
Hybrid therapy (IIaC)



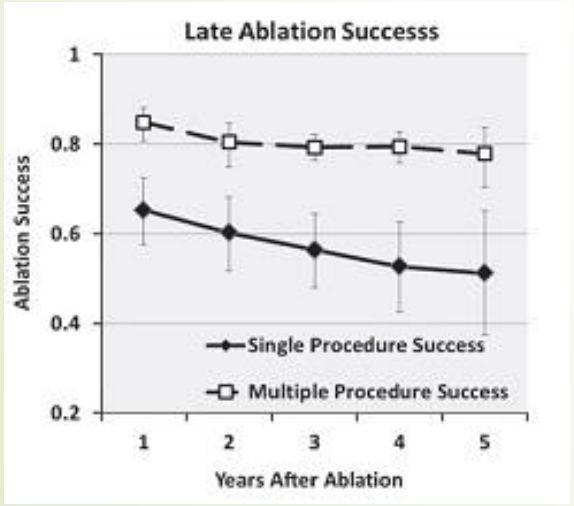



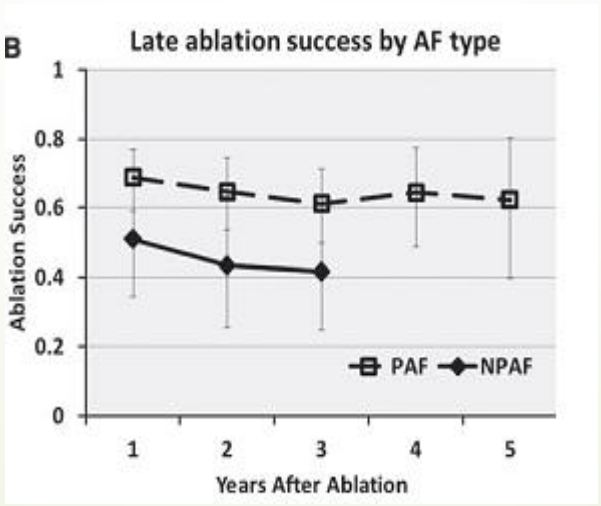

J Am Heart Assoc. 2013;2:e004549




- AL AÑO.
  - GLOBAL 64,2%
  - PAROX 66,6%
  - PERSISTENTE 51,9%

- LARGO PLAZO. 30% varios procedimientos
  - GLOBAL 79,8%
  - PAROX 79%
  - PERSISTENTE 77,8%




J Am Heart Assoc. 2013

# Driver Domains in Persistent Atrial Fibrillation

Michel Haissaguerre, MD; Meleze Hocini, MD; Arnaud Denis, MD; Ashok J. Shah, MD; Yuki Komatsu, MD; Seigo Yamashita, MD; Matthew Daly, MD; Sana Amraoui, MD; Stephan Zellerhoff, MD; Marie-Quitterie Picat, MD; Adam Quotb, PhD; Laurence Jesel, MD; Han Lim, MD; Sylvain Ploux, MD; Pierre Bordachar, MD; Guillaume Attuel, PhD; Valentin Meillet, MSc; Philippe Ritter, MD; Nicolas Derval, MD; Frederic Sacher, MD; Olivier Bernus, PhD; Hubert Cochet, MD; Pierre Jais, MD; Remi Dubois, PhD

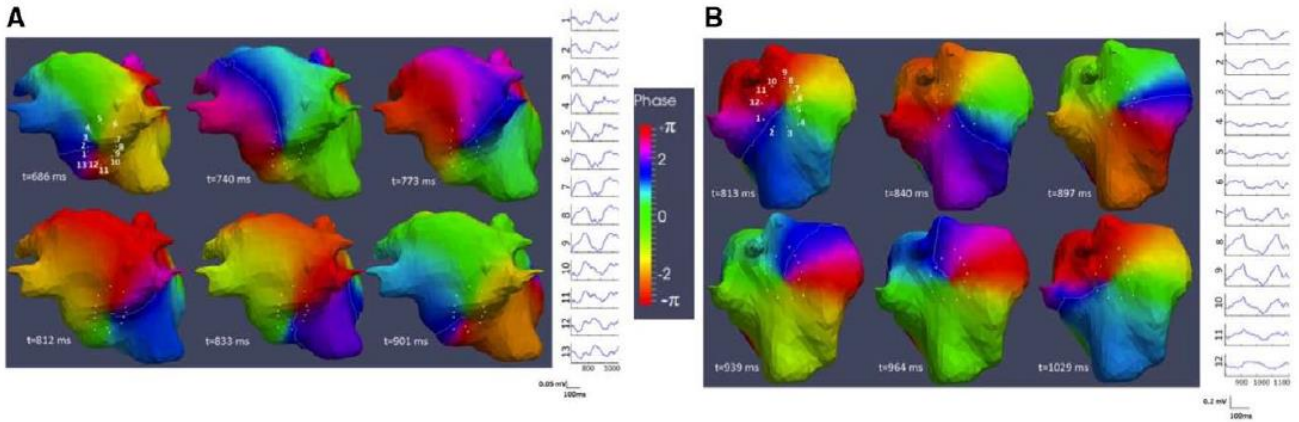
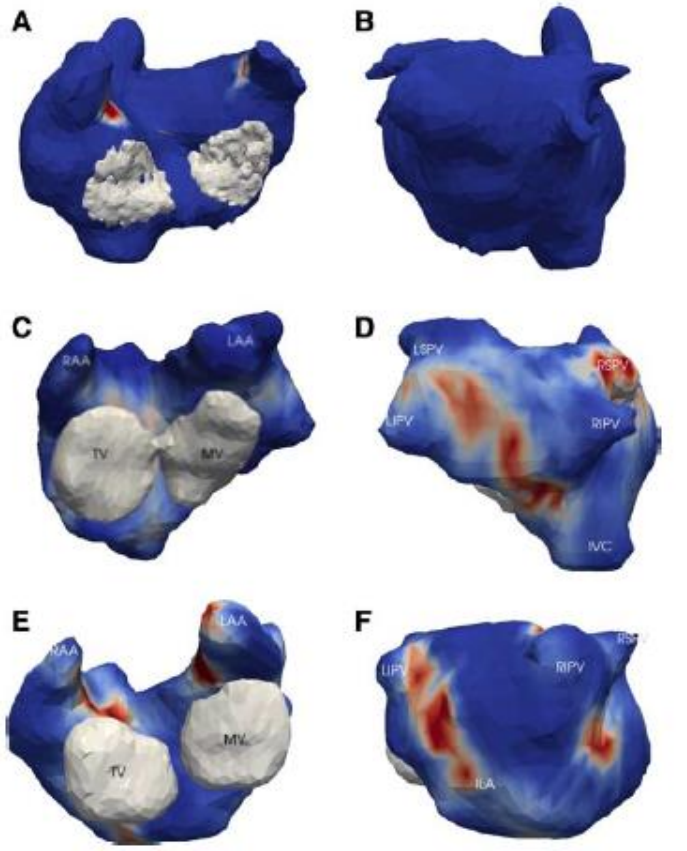



**Figure 4.** The phase maps of ≥1000-ms-long AF window show reentry events visualized intermittently in the right and left atria with their prephase electrograms on the right. The time (milliseconds) below each map is the instantaneous time of the snapshot in that AF window **A,** One of the 2 consecutive rotations involving the inferior left atrium and the prephase electrograms around its core (sites 1–12). **B,** One of the 2 consecutive rotations involving the posterior upper right atrium and the prephase electrograms around its core (sites 1–12). The color code is explained in the legend to Figure 3.

Haissaguerre et al



# Highlights

- Anticoagulación. NACOS primera opción.
  - Oclusión de orejuela izquierda
- Control de factores de riesgo
- Control de frecuencia. Calcioantagonistas.
- Control de ritmo
  - Control de ritmo con ablación como primera posibilidad
- Investigación en
  - persistente, nuevos fármacos antiarrítmicos más seguros

# Is time to think in sinus rythm?