Atriyal Fibrilasyonda Genel Tedavi Yaklaşımları
Hız Kontrolü ve Ritim Kontrolü

Dr. Fatma YİĞİT

Başkent Üniversitesi Adana Uygulama ve Araştırma Merkezi

Kardiyoloji Bölümü

25 Mayıs 2013, KKTC

Epidemiyoloji

- Genel toplumda sıklığı % 1-2
  - 40 yaş altında < % 0.5
  - 80 yaş üstü > % 5-15

- İnme riskininde 5 kat artış
- Ölüm riskinde 2 kat artış

Danelich IM et al. Pharmacotherapy 2013;33:422-446.

Tedavi Yaklaşımı

- AF tipinin belirlenmesi
- Altta yatan nedenlerin araştırılması
- Hız kontrolü
- Ritim kontrolü
- Antikoagülasyon

Singla S et al. J Card Phar Ther 2012;17:12-20

Tedavi Stratejileri

- Ritim kontrolü
  - Kardiyoversiyon
  - Antiaritmik ilaçlar
  - Ablasyon
  - Embolik olayların engellenmesi
- Hız kontrolü
  - Kalp hızının kontrol altına alınması
    - İlaçlar
    - AV nod ablasyonu + kalıcı kalp pili
  - Embolik olayların engellenmesi

Optimal Tedavi Stratejisi

Ritim Kontrolü

?

Hız Kontrolü

The New England Journal of Medicine

VOLUME 347 DECEMBER 5, 2002 NUMBER 23

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

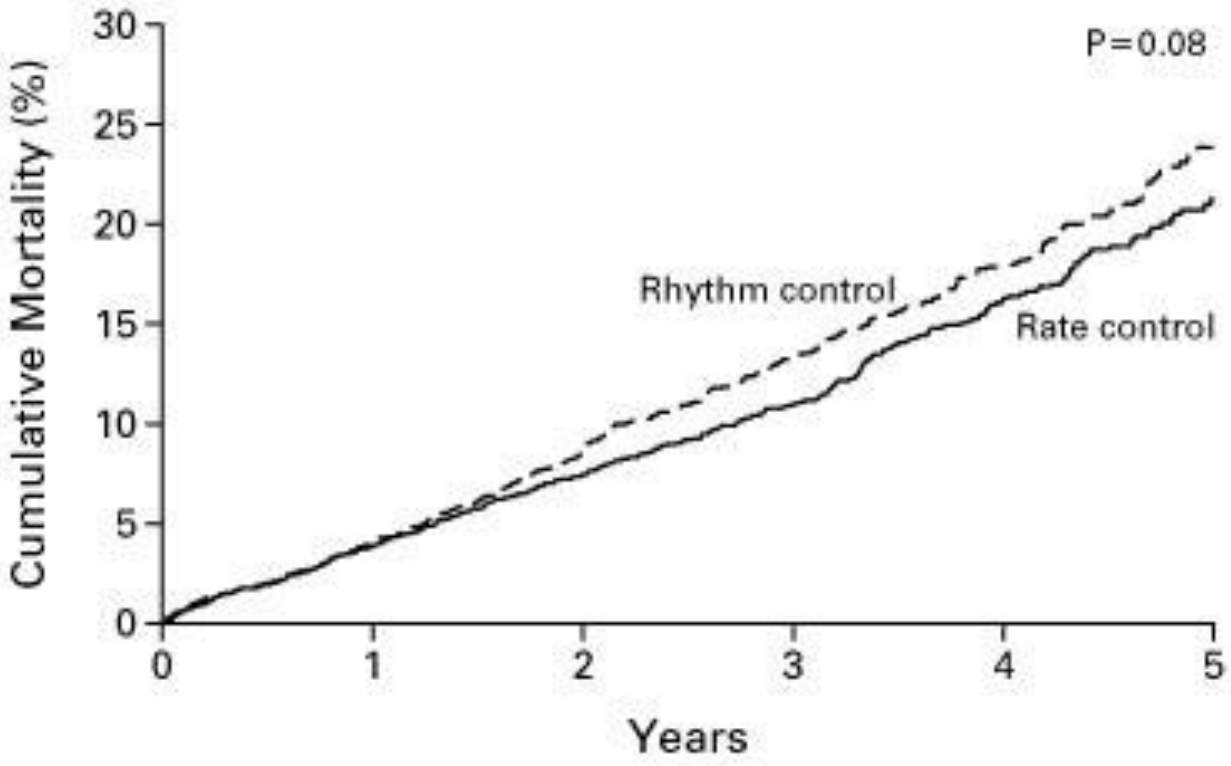
THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

ABSTRACT

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

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

AFFIRM - Mortalite



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)

AFFIRM : 5 Yıllık Sonuç

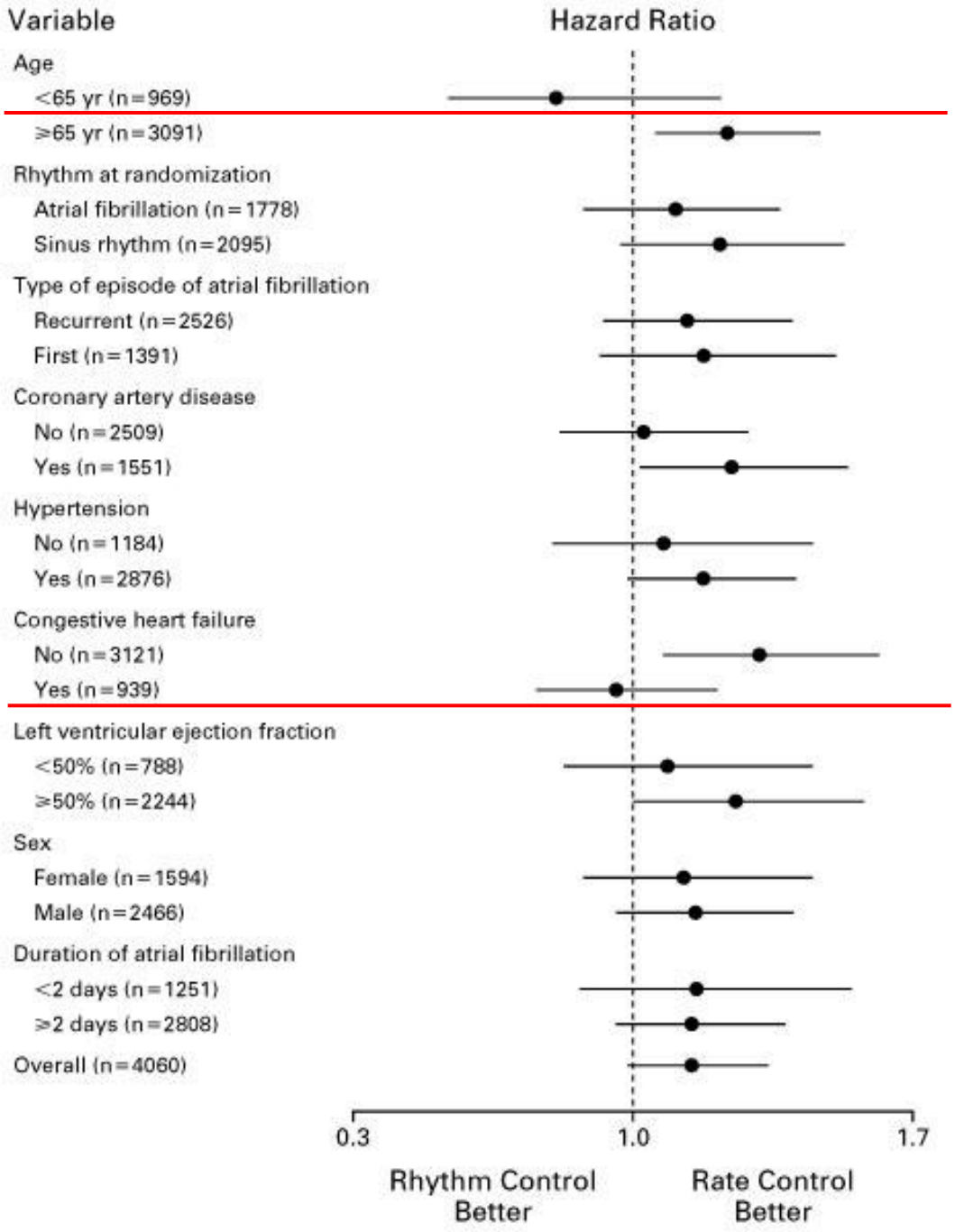
Sağkalım	Ritim Kontrolü	Hız Kontrolü
1 yıl	96%	96%
3 yıl	87%	89%
5 yıl	76%	79%

p = 0.058

Fark yok: Ölüm, strok, majör kanama veya kardiyak arrest

Sinüs ritmi ritim kontrol grubunda sadece % 63 oranında devam etti

NEJM 2002;347:1825


Variable
Hazard Ratio
Age
<65 yr (n=969)
≥65 yr (n=3091)
Rhythm at randomization
Atrial fibrillation (n=1778)
Sinus rhythm (n=2095)
Type of episode of atrial fibrillation
Recurrent (n=2526)
First (n=1391)
Coronary artery disease
No (n=2509)
Yes (n=1551)
Hypertension
No (n=1184)
Yes (n=2876)
Congestive heart failure
No (n=3121)
Yes (n=939)
Left ventricular ejection fraction
<50% (n=788)
≥50% (n=2244)
Sex
Female (n=1594)
Male (n=2466)
Duration of atrial fibrillation
<2 days (n=1251)
≥2 days (n=2808)
Overall (n=4060)
0.3
1.0
1.7
Rhythm Control Better
Rate Control Better

Archives of Cardiovascular Disease (2012) 105, 226—238

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www.sciencedirect.com

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EM|consulte
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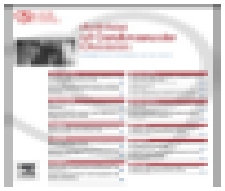

REVIEW

Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials

Contrôle de la fréquence ou du rythme cardiaque dans la fibrillation atriale : méta-analyse des études randomisées contrôlées

Daniel Caldeira[a], Cláudio David[a,*,b], Cristina Sampaio[a,c]

[a] Laboratory of Clinical Pharmacology and Therapeutics, School of Medicine, University of Lisbon, Lisbon, Portugal
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[c] Institute de Molecular Medicine, Lisbon, Portugal

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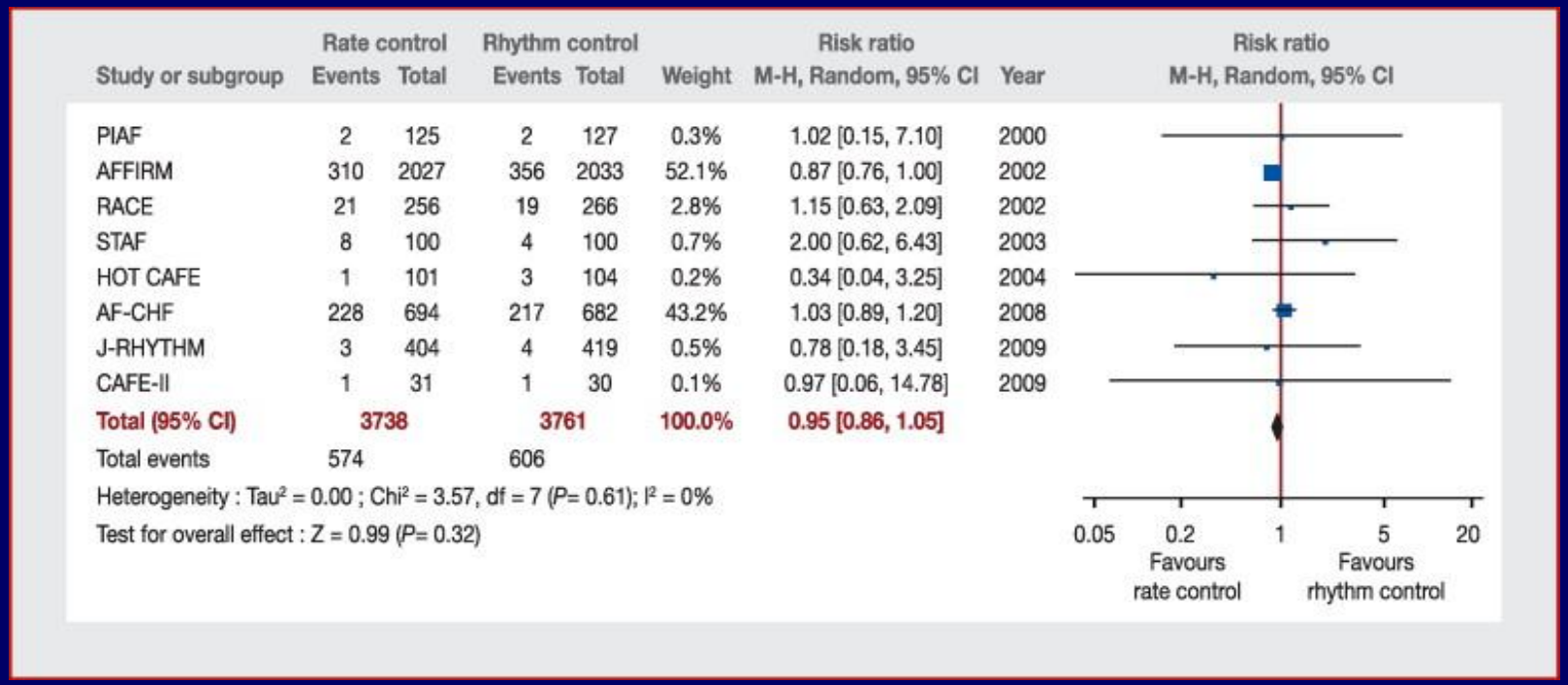
Available online 21 January 2012

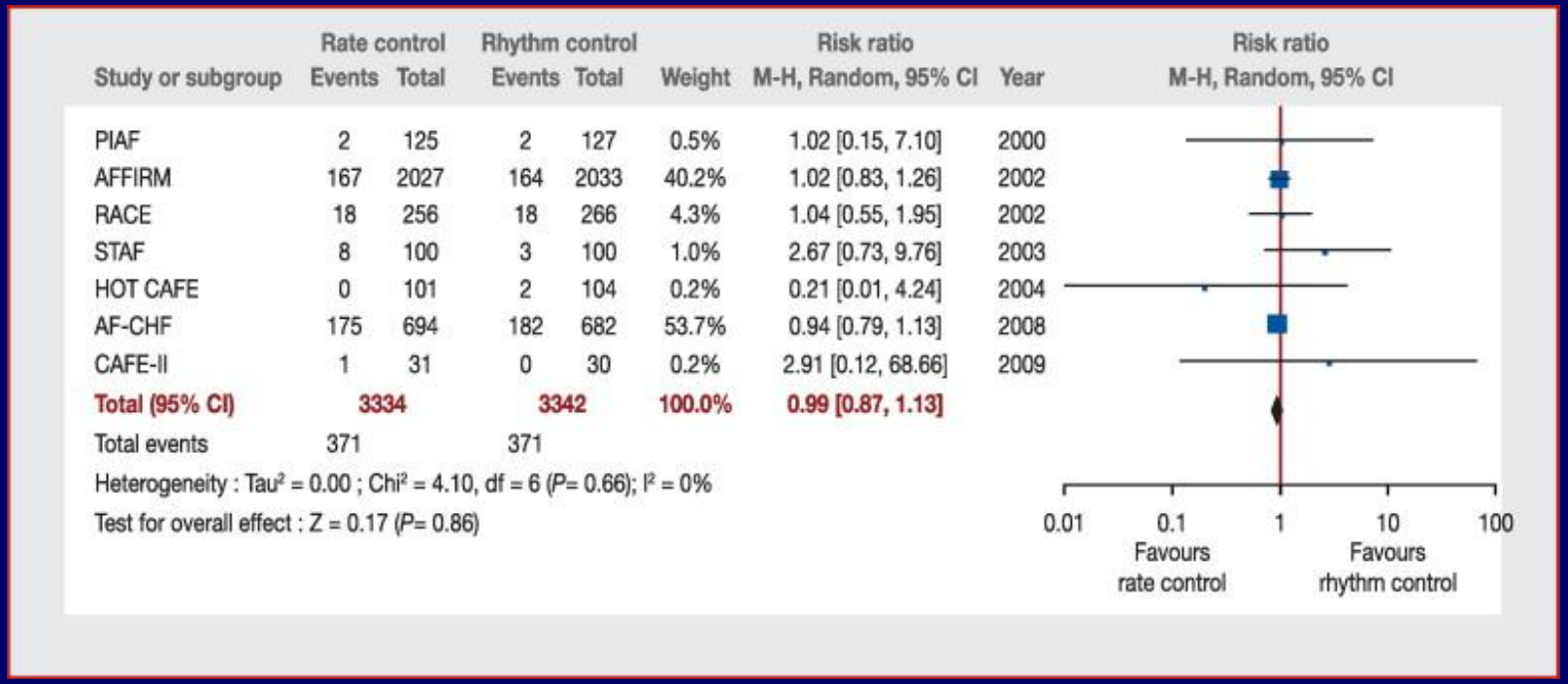
KEYWORDS
Adrenergic beta-antagonists;
Calcium-channel blockers;
Digitalis;
Antiarrhythmia agents;
Atrial fibrillation

Summary Atrial fibrillation is the most frequently occurring sustained cardiac arrhythmia and is associated with a significantly increased risk of thromboembolic events and death. We sought to compare the clinical efficacy of rate and rhythm control strategies in patients with non-postoperative atrial fibrillation. We searched the PubMed database and the Cochrane Central Register of Controlled Trials for randomised controlled trials comparing rate versus rhythm control in patients with atrial fibrillation. Studies were retrieved and we analysed major clinical outcomes. Risk ratios (RRs) and 95% confidence intervals were calculated assuming random effects due to the clinical heterogeneity of the study populations. Eight randomised controlled trials were identified, with a total of 7499 patients with atrial fibrillation. There were no significant differences in the effects of rate and rhythm control on any outcome:



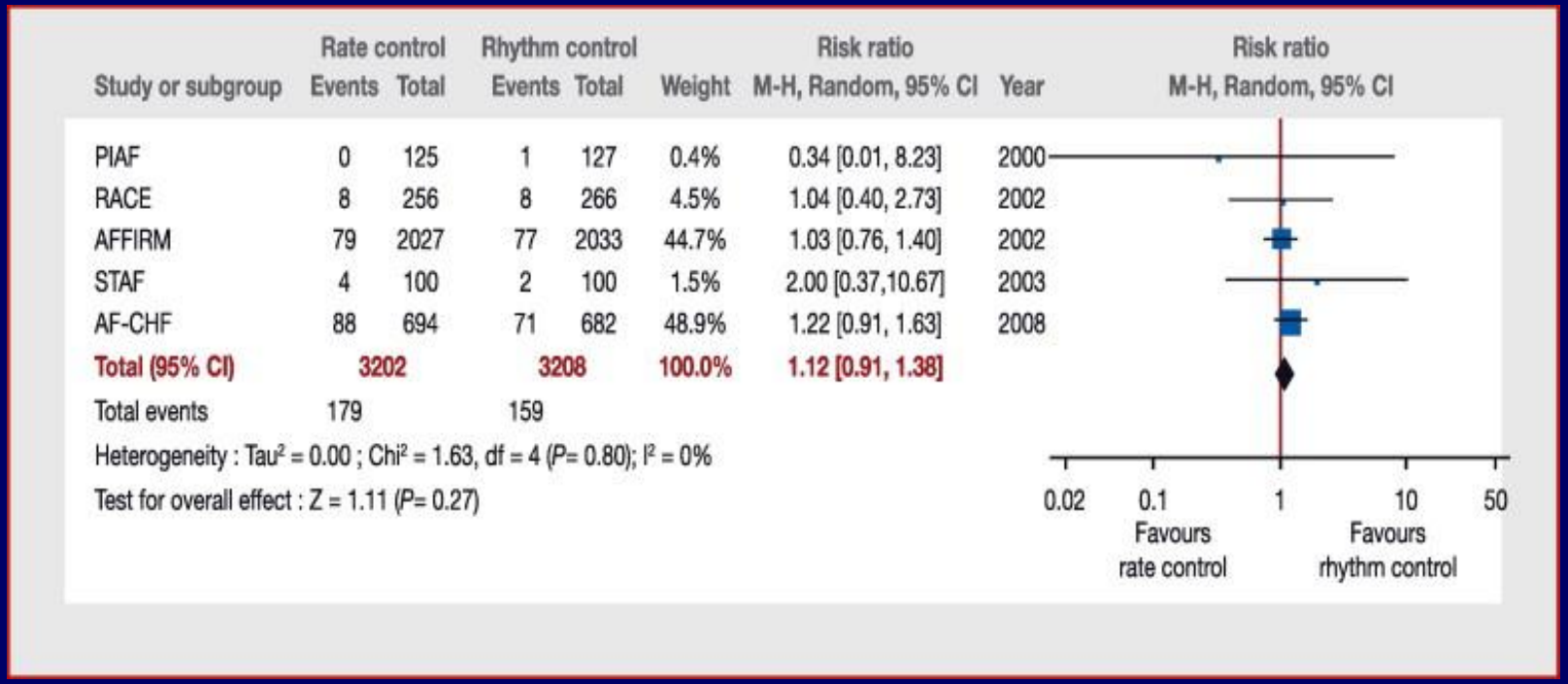
Forest plot for all-cause mortality.

Daniel Caldeira etal. **Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials.** Archives of Cardiovascular Diseases Volume 105, Issue 4 2012 226 - 238



Forest plot for cardiovascular mortality.

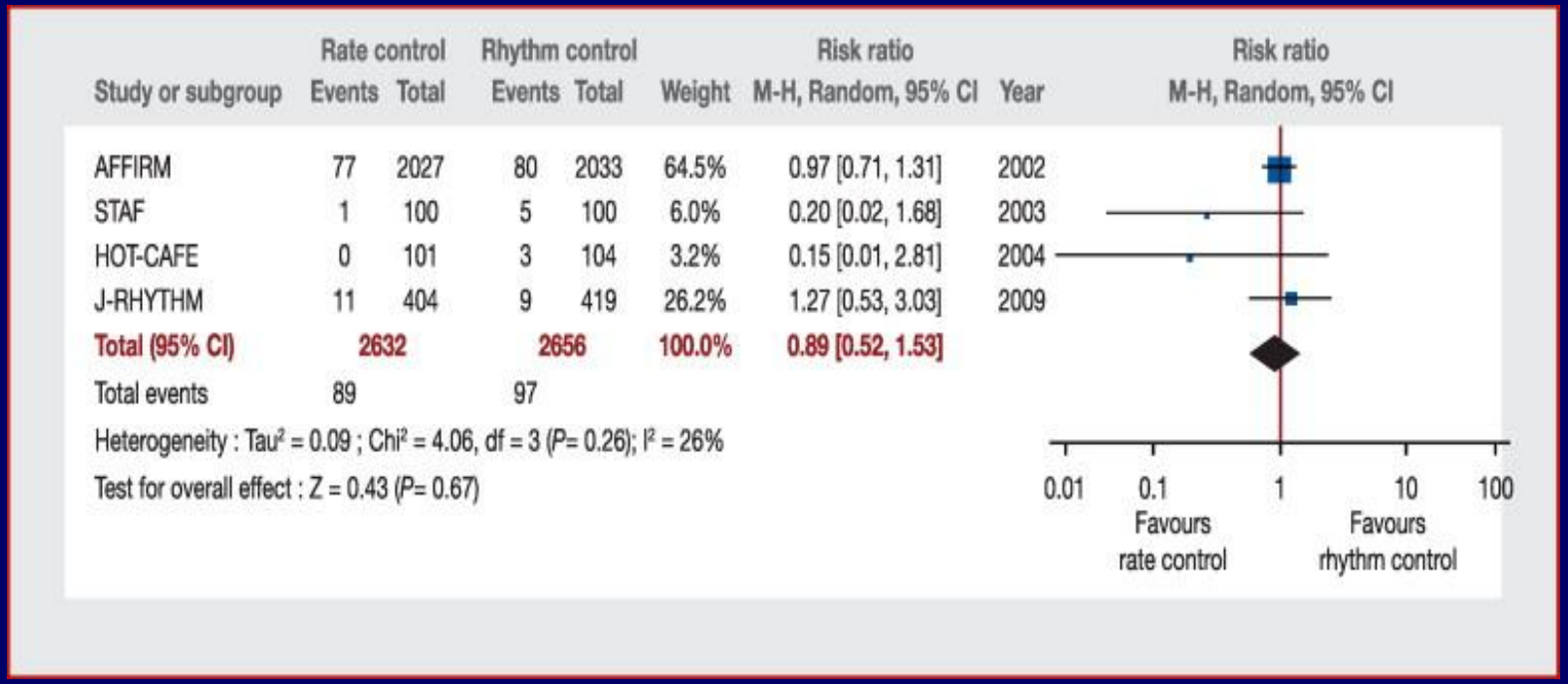
Daniel Caldeira etal. **Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials.** Archives of Cardiovascular Diseases Volume 105, Issue 4 2012 226 - 238



Forest plot for arrhythmic/sudden death mortality.

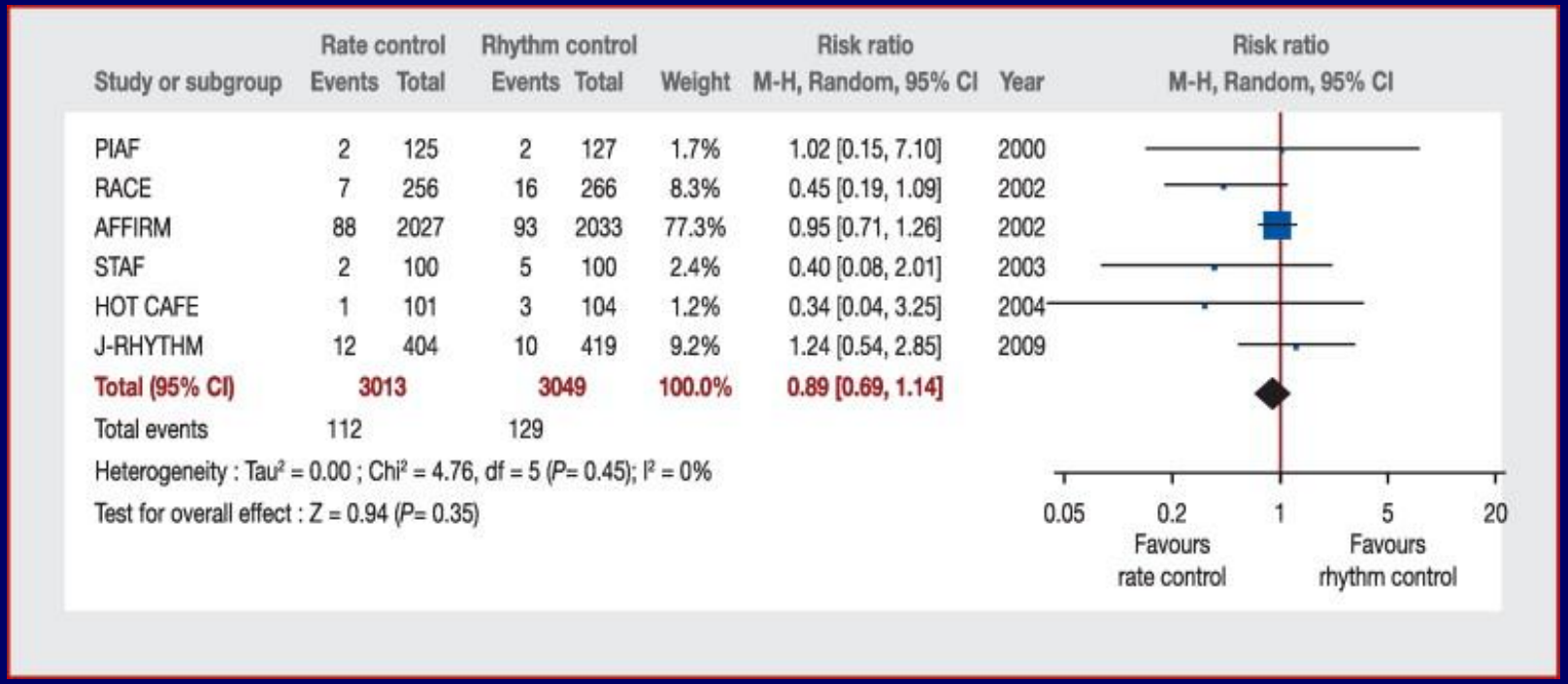
Daniel Caldeira etal. **Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials.** Archives of Cardiovascular Diseases Volume 105, Issue 4 2012 226 - 238

Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials



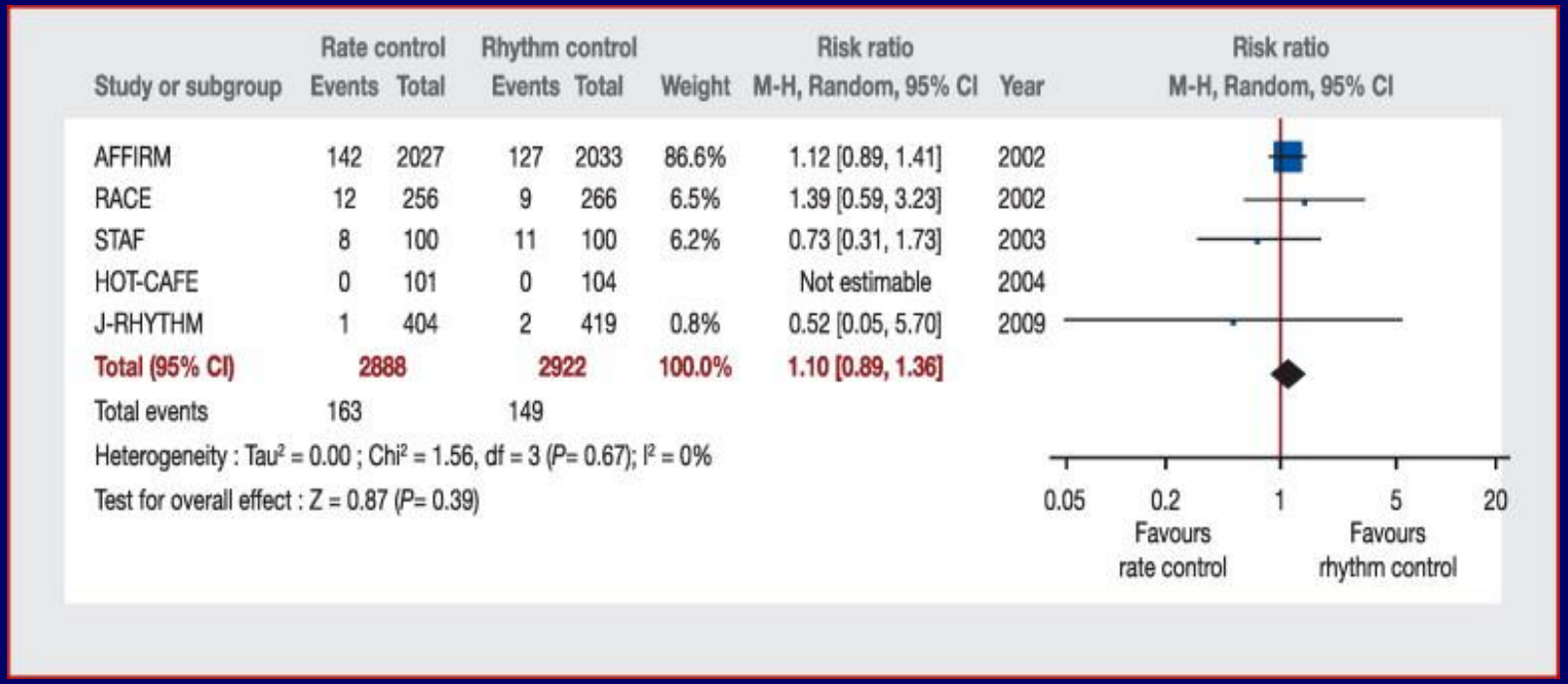
Forest plot for ischaemic stroke.

Daniel Caldeira etal. **Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials.** Archives of Cardiovascular Diseases Volume 105, Issue 4 2012 226 - 238



Forest plot for systemic embolism.

Daniel Caldeira etal. **Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials.** Archives of Cardiovascular Diseases Volume 105, Issue 4 2012 226 - 238



Forest plot for major bleeding.

Caldeira etal. **Rate versus rhythm control in atrial fibrillation and clinical outcomes: Updated systematic review and meta-analysis of randomized controlled trials.** Archives of Cardiovascular Diseases Volume 105, Issue 4 2012. 226-238.

KKY + AF

- Antiaritmik (amiodaron veya dofetilid) ile sinüs ritmine dönen kalp yetersizlikli hastalarda prognoz dönmeyenlere göre belirgin olarak daha iyi: CHF-STAT, DIAMOND-HF
- Kalp yetersizlikli AF'lu hastalarda ritim kontrolü kolunda mortalitede azalmaya eğilim: AFFIRM
- Ritim kontrol grubunda sol ventrikül fonksiyonlarında düzelme: HOT CAFE

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QUARTERLY FOCUS ISSUE: HEART FAILURE

Maintenance of Sinus Rhythm and Survival in Patients With Heart Failure and Atrial Fibrillation

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Montreal, Quebec, Hamilton and Toronto, Ontario, and Calgary, Alberta, Canada; Frankfurt, Germany; Durham, North Carolina; Copenhagen, Denmark; Boston, Massachusetts; and Cleveland, Ohio

Objectives The goal of this study was to evaluate the relationship between the presence of sinus rhythm and outcomes in patients with a history of congestive heart failure (CHF) and atrial fibrillation (AF).

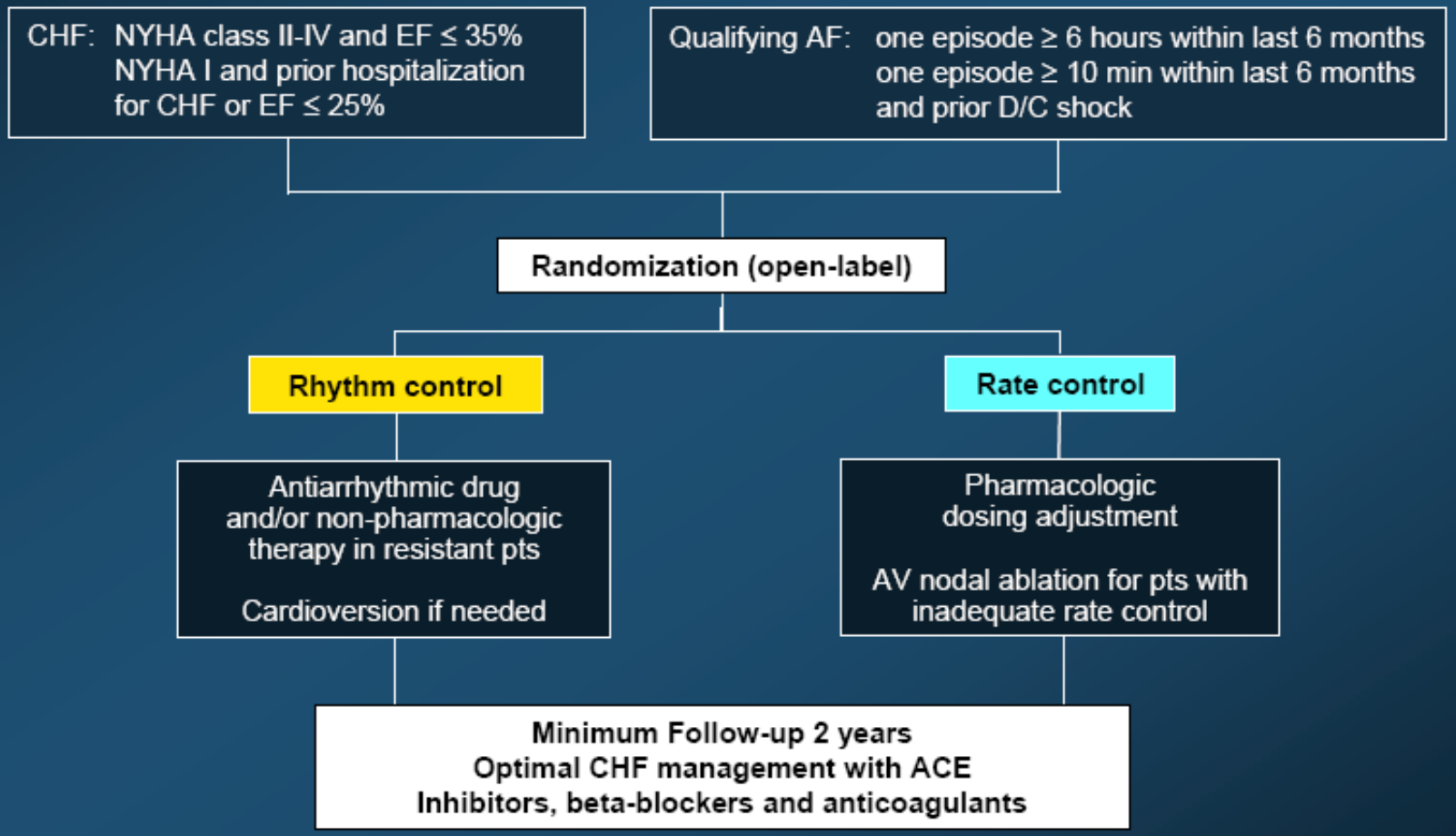
Background The value of sinus rhythm maintenance in patients with AF and heart failure (HF) is uncertain.

Methods A total of 1,376 patients with AF, ejection fraction ≤35%, and heart failure symptoms were randomized to a rhythm- or rate-control strategy. Detailed efficacy analyses were used to evaluate the independent effects of treatment strategy and the presence of sinus rhythm on cardiovascular outcomes.

Results Overall, 445 (32%) patients died and 402 (29%) experienced worsening HF. The rhythm-control strategy was not predictive of cardiovascular mortality (hazard ratio [HR]: 0.90, 95% confidence interval [CI]: 0.70 to 1.16; p = 0.41), all-cause death (HR: 0.86, 95% CI: 0.69 to 1.08; p = 0.19), or worsening HF (HR: 0.86, 95% CI: 0.68 to 1.10; p = 0.23). In analyses devised to isolate the effect of underlying rhythm, sinus rhythm was not associated with cardiovascular mortality [HR: 1.22, 95% CI: 0.80 to 1.87; p = 0.35), total mortality [HR: 1.11, 95% CI: 0.78 to 1.58; p = 0.57), or worsening HF [HR: 0.62, 95% CI: 0.37 to 1.02; p = 0.059).

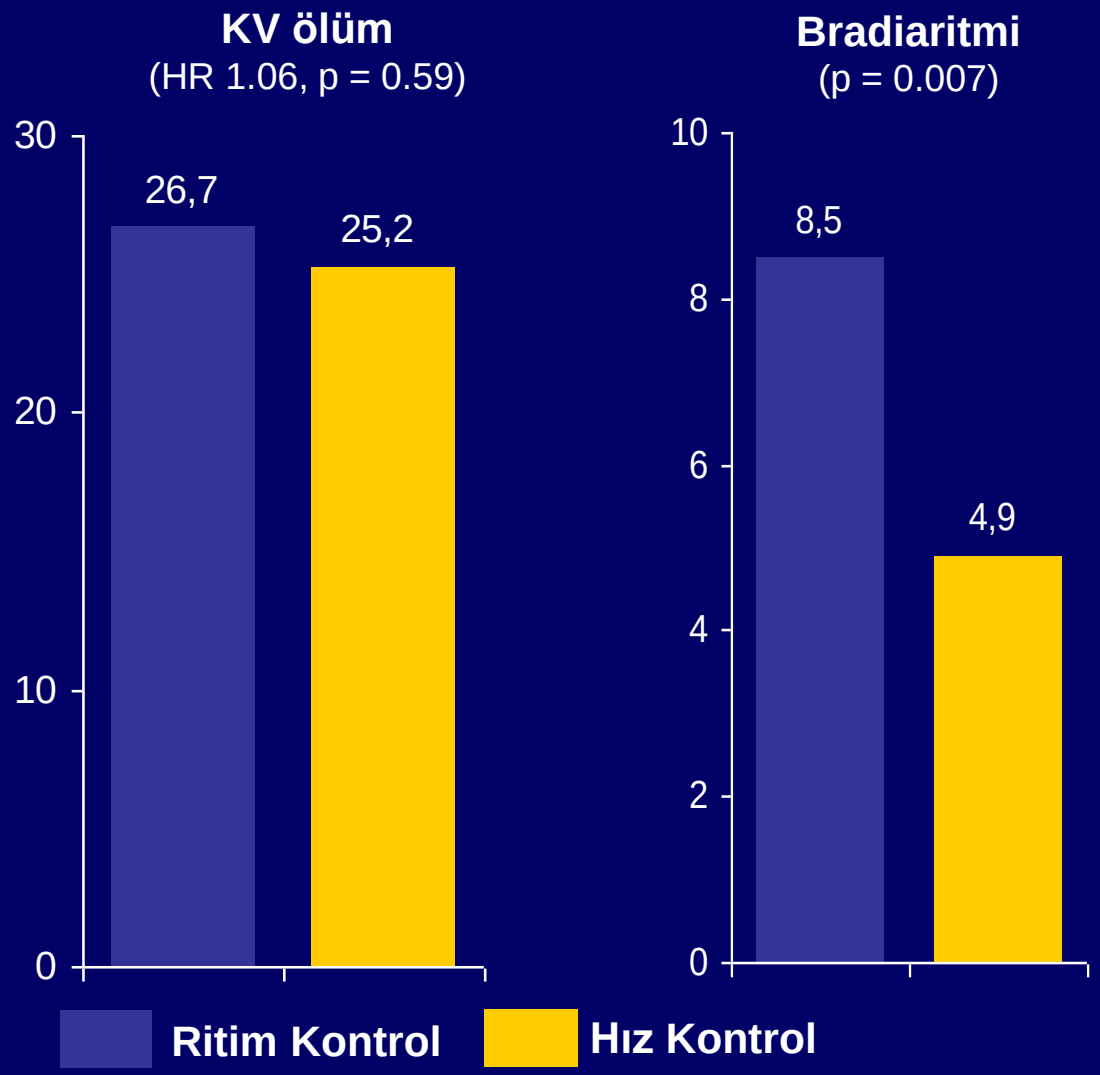
Conclusions A rhythm-control strategy or the presence of sinus rhythm are not associated with better outcomes in patients with AF and CHF. (J Am Coll Cardiol 2010;55:1796–802) © 2010 by the American College of Cardiology Foundation

Study Design



Am Heart J 2002;144:597

AF-CHF



Talajic et al. J Am Coll Cardiol 2010;55:1796–802

AF-CHF

- **Tüm ölümler**
  - Hız kontrol: %31.8
  - Ritim kontrol: %32.9
  - p = 0.73
- **İnme**
  - Hız kontrolü: %2.6
  - Ritim kontrolü: %3.6
  - p = 0.32
- **Kalp yetmezliğinde kötüleşme**
  - Hız kontrolü: %27.6
  - Ritim kontrolü: %30.8
  - p = 0.17
- **Hastaneye yatış**
  - Hız kontrolü: %39
  - Ritim kontrolü: %46
  - p = 0.006

Talajic et al. J Am Coll Cardiol 2010;55:1796–802

European Journal of Internal Medicine 22 (2011) 448–455

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Review article

Rate vs rhythm control in patients with atrial fibrillation and heart failure: A systematic review and meta-analysis of randomised controlled trials

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Keywords:
Rate
Rhythm
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Heart failure
Hospitalisation
Mortality

ABSTRACT

Background: Atrial fibrillation (AF) is a common arrhythmia that can promote or worsen heart failure (HF). Our purpose was to compare the effects of rate and rhythm control in patients with atrial fibrillation and heart failure.

Methods: We developed a systematic search in August 2010 through CENTRAL and MEDLINE databases to identify randomised controlled trials (RCTs) comparing rate control with rhythm control in patients with both AF and HF.

We analysed mortality, hospitalisations, stroke/thromboembolic events, quality of life, and drugs adverse events. Relative risks (RR) and 95% confidence intervals (95% CI) were calculated for mortality and hospitalisations. The remaining outcomes were analysed qualitatively.

Results: Four RCTs with a total of 2486 patients with atrial fibrillation and heart failure were identified. Mortality and stroke/thromboembolic events were not significantly different in rate and rhythm control arms [RR 1.03; 95% CI: 0.90–1.17] and [RR 1.09; 95% CI: 0.61–1.96], respectively. Hospitalisations were less frequent with rate control than with rhythm control [RR 0.92; 95% CI: 0.86–0.98; p = 0.008], in 3 studies involving 2425 patients. Number needed to treat to prevent one hospitalisation was 19 patients.

Conclusions: In patients with AF and HF, rate control compared with rhythm control showed inferior risk of hospitalisation.

Table 1
Trials' main characteristics.

Trials	RACE [20,23]	AFFIRM [21,24]	AF–CHF [18]	CAFE-II [22]
AF population	Recurrent persistent AF or flutter for less than 1 year	Likely to be recurrent AF in pts older than 65 years old with risk factors for stroke or death	Paroxysmal or persistent AF less than 1 year	Persistent AF
Heart failure	NYHA II–III	LVEF less than 50%	LVEF equal or less than 35% and NYHA II–IV	NYHA II–III
No. pts	261	788	1376	61
Age	69 (mean)	71% >65 years	67 (mean)	72 ± 7
Male	65%	75%	82%	84%
Anticoagulation	Acenocoumarol or fenprocoumon 4 weeks before and after electrical cardioversion. Rate arm anticoagulated if more than 65 year-old or cardiac disease.	Both arms anticoagulated, if after 4–12 weeks with antiarrhythmic agents sinus rhythm is restored, anticoagulation could be stopped	Recommended for all pts: ACC/AHA/ESC 2006 AF guidelines	Recommended[a] for all pts: warfarin (INR 2–3)
Rate intervention	Digitalis, non-dihydropyridine calcium-channel blocker and beta-blocker	Beta-blocker, non-dihydropiridine calcium-channel blocker and digoxin.	Beta-blocker and digoxin. AV nodal ablation and pacemaker (if refractory)	Digoxin and beta-blocker
Rhythm intervention	Electrical cardioversion and sotalol, flecainide, propafenone or amiodarone	Many antiarrhythmic agents and/or electrical cardioversion	Electrical cardioversion and amiodarone (or sotalol or dofetilide)	Amiodarone and electrical cardioversion
Years follow-up	2.3 ± 0.6	3.5 (mean)	3.1 ± 1.6	1.2 (median)
Primary outcome	Composite of cardiovascular death, heart failure, embolism, bleeding, pacemaker implantation, severe adverse effects of drugs	All-cause mortality	Cardiovascular death	QoL SF-36vII at 1 year
Conclusions in HF subset	In patients with mild to moderate CHF, rate control is not inferior to rhythm control. However, if sinus rhythm can be maintained, outcome may be improved.	There was no significant improvement in mortality, hospitalisation, and NYHA class with the strategy of rhythm control in mild, moderate or severe ejection left ventricular dysfunction.	Primary outcome was not different in both interventions. Hospitalizations were more frequent in rhythm control.	Rhythm control improved the primary outcome, LV function and NT-proBNP. NYHA and 6MWT were similar in both interventions.
PEDro score	7	6	6	7

Caldeira et al. European Journal of Internal Medicine 2011;22:448–455

Study or Subgroup	Rate control Events	Total	Rhythm control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
AF-CHF	228	694	217	682	69.6%	1.03 [0.89, 1.20]
AFFIRM	93	380	104	408	27.7%	0.96 [0.75, 1.22]
CAFE-II	1	31	1	30	0.2%	0.97 [0.06, 14.78]
RACE	15	130	8	131	2.4%	1.89 [0.83, 4.30]
Total (95% CI)		**1235**		**1251**	**100.0%**	**1.03 [0.90, 1.17]**
Total events	337		330			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.42$, df = 3 (P = 0.49); $I^2 = 0\%$
Test for overall effect: Z = 0.40 (P = 0.69)

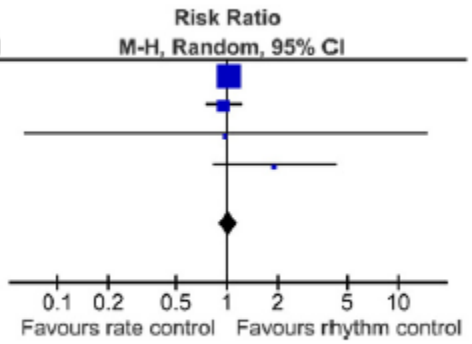


Fig. 2. Forest plot comparing rate and rhythm control for total mortality in patients with AF and HF.

Caldeira et al. Rate versus rhythm control in patients with atrial fibrillation and heart failure: A systematic review and meta-analysis of randomized controlled trials. Eur J Int Med 2011;22:448-455.

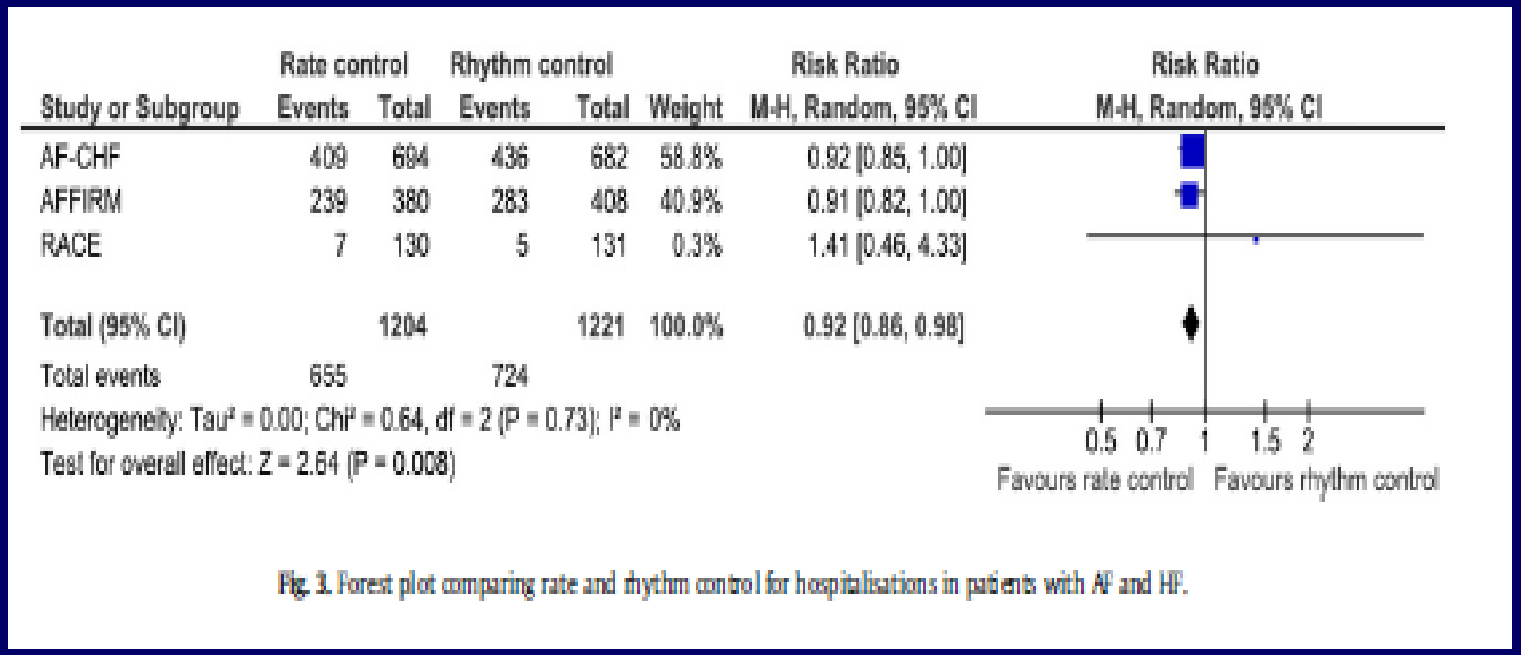


Fig. 3. Forest plot comparing rate and rhythm control for hospitalisations in patients with AF and HF.

Caldeira et al. Rate versus rhythm control in patients with atrial fibrillation and heart failure: A systematic review and meta-analysis of randomized controlled trials. Eur J Int Med 2011;22:448-455.

Hız ve Ritim Kontrolünü Etkileyen Faktörler

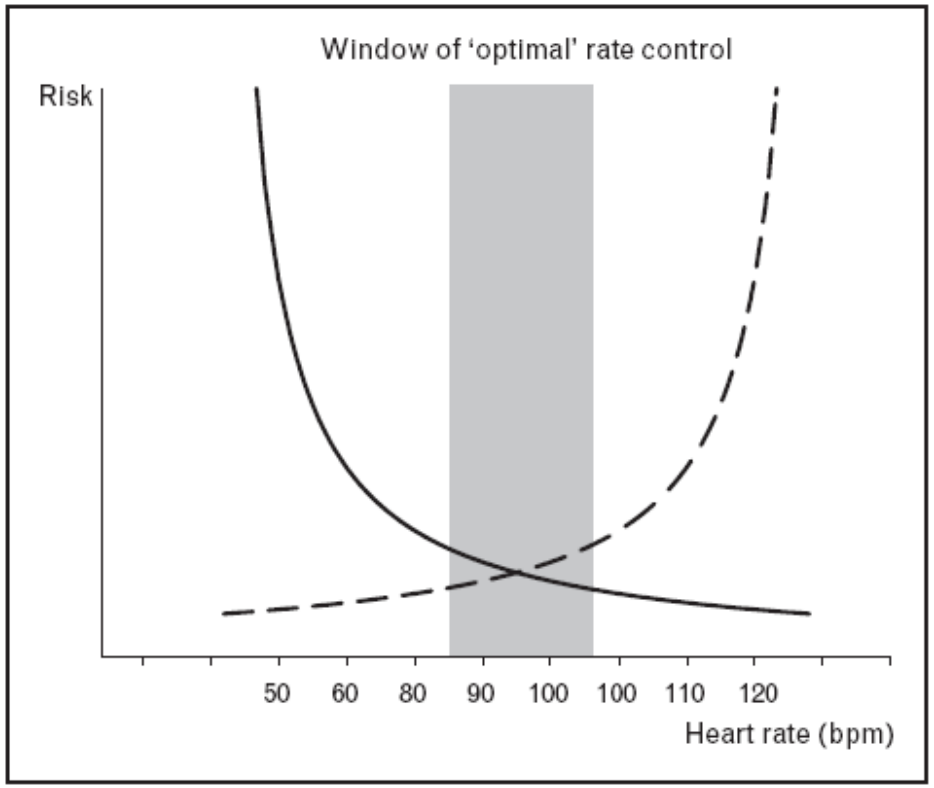
Hız Kontrolü Lehine	Ritim Kontrolü Lehine
Persistan AF	Paroksismal AF veya yeni tanı AF
Asemptomatik hasta	Semptomatik hasta
≥ 65 yaş	< 65 yaş
Kardiyoversiyona uygun olmayan hasta (AF > 1 yıl, dilate LA > 5,5 cm, multipl kardiyoversiyona rağmen AF)	Lone AF ve tetikleyici faktörlere bağlı AF (hipertiroidi, alkol, kafein, cerrahi sonrası)
Komorbid durumların varlığı	AF'ye bağlı taşikardiyomiyopati
Antiaritmik tedavi başarısızlığı veya yan etkisi	Hız kontrolüne rağmen semptomatik olan hasta
Hasta tercihi	Hasta tercihi

Bajpai A et al. British Medical Bulletin 2008;88:75-94.

Hız Kontrolü

- Optimal kalp hızı
  - İstirahatte 60-80 atım/dk
  - Egzersizle 90-115 atım/dk
  - RACE II çalışması (< 110 atım/dk)
- Optimal kalp hızını hangi yöntemle değerlendirelim?
  - Holter?
  - EKG?
  - Loop recorder?
  - 6 dk yürüme testi?

Figure 1 Hypothetical curve of 'optimal' heart rate control during atrial fibrillation



——— Adverse effects of rate control on pacemaker implantations; costs; – – – symptoms of atrial fibrillation, impaired quality of life, incidence of coronary heart failure; risk of stroke; applicability.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

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

Ilımlı hız kontrolü
KH < 110 atım/dk

Katı hız kontrolü
İst. KH < 80 atım/dk
Orta egzersizde KH < 110

Ilımlı gruptaki çoğu hasta
KH < 100 atım/dk

ABSTRACT

BACKGROUND

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

METHODS

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

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

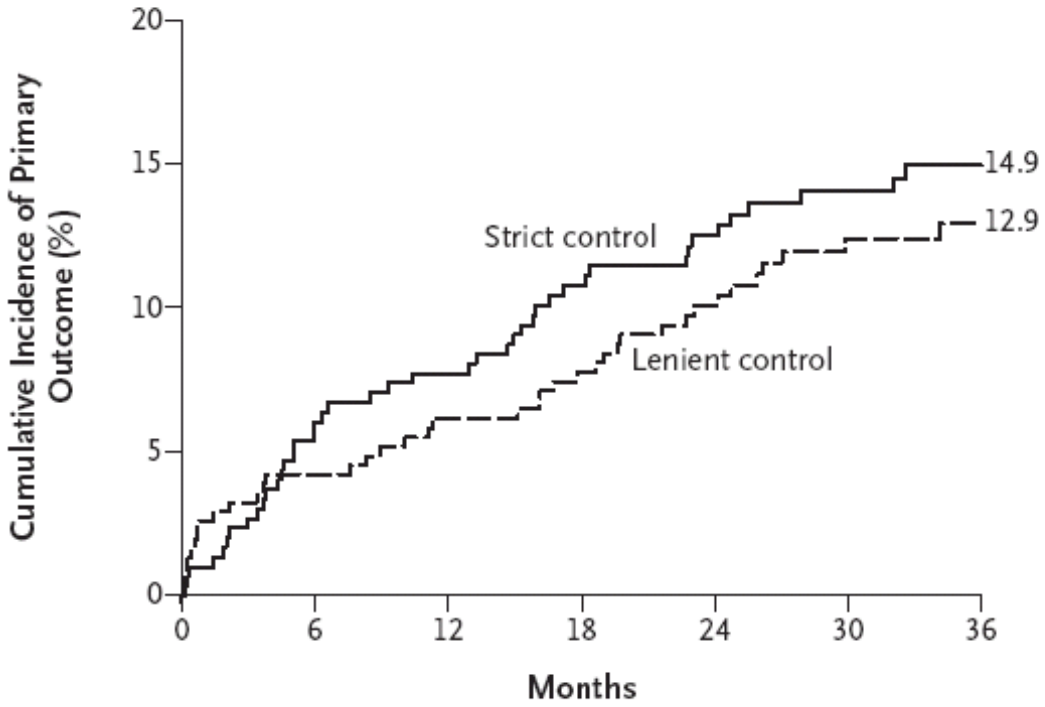


Figure 2. Kaplan–Meier Estimates of the Cumulative Incidence of the Primary Outcome, According to Treatment Group.

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

Primer Son Nokta

Kardiyak ölüm
Kalp yetersizliği
Strok
Sistemik emboli
Major kanama
Senkop
Sustained VT
Kardiyak arrest
Antiaritmiklerin hayatı tehdit eden komplikasyonları
Pacemaker

Sekonder Son Nokta

Semptom

RACE 2 Kısıtlılıkları

- Hastaların çoğu düşük riskli
  - 2/3'ünden azı semptomatik
  - CHADS2 = 1.4
  - Hastaların çoğu NYHA I-II
- İki grup arasında sadece median 9 atım/dk fark var
  - Ilımlı hız kontrolünde 85 ± 14 atım/dk
  - Sıkı hız kontrolünde 76 ± 14 atım/dk
  - Her ikisi de ılımlı hız kontrol hedefinin altında

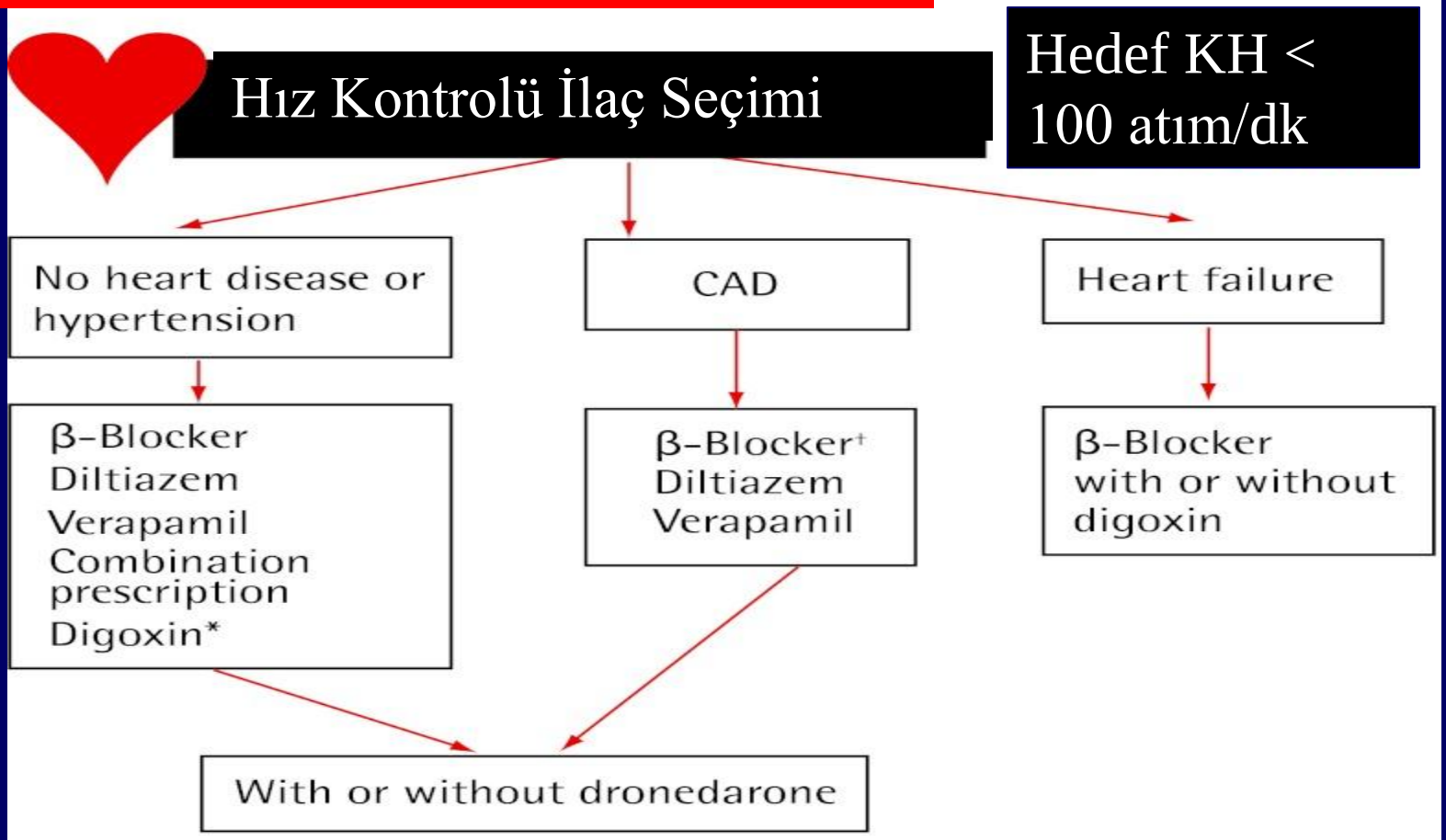
Van Gelder et al. NEJM 2010;362:1363-73

RACE 2 Öneri

- Ilımlı hız kontrolü (istirahat kalp hızı < 110/dk)
  - Persistan
  - Asemptomatik
  - EF > % 40
- Semptomatik hasta istirahat kalp hızı 80-100/dk

Van Gelder et al. NEJM 2010;362:1363-73

Hız Kontrol Algoritması



BPM—beats per minute, CAD—coronary artery disease, HR—heart rate.
*Digoxin can be considered as monotherapy in sedentary individuals.
†β-Blockers are preferred in CAD.
Data from Jin and Kosar.[4]

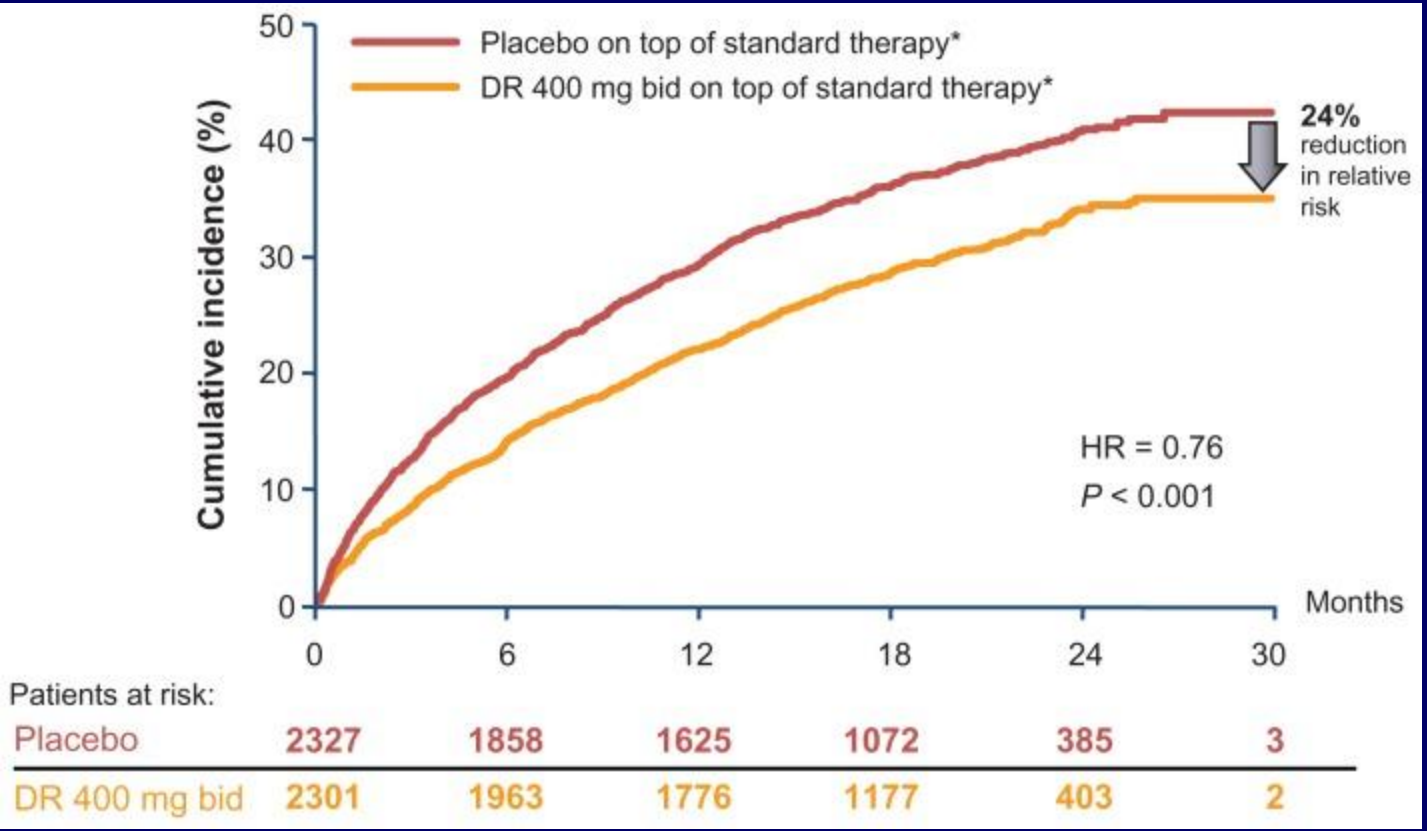
Frankel G et al. Can Fam Phys 2013;59:161-168

Ritm kontrolü: Uzun dönem antiaritmik tedavi

- Sınıf III antiaritmikler
  - Amiodarone — 800-1600 mg/gün (yükleme) (1-3 hafta)
600-800 mg/gün (1 ay)
100-400 mg/gün (idame)
  - Dronedarone — 400 mg (günde 2 kez)
  - Sotalol — 80 mg (günde 2 kez)
- Sınıf Ic antiaritmikler
  - Flekainid — 50-150 mg (günde 2 kez)
200-300 mg (tek seferde; cep hapı)
  - Propafenen — 150 mg (günde 1-3 kez)
450-600 mg (tek seferde; cep hapı)

Frankel G et al. Can Fam Phys 2013;59:161-168

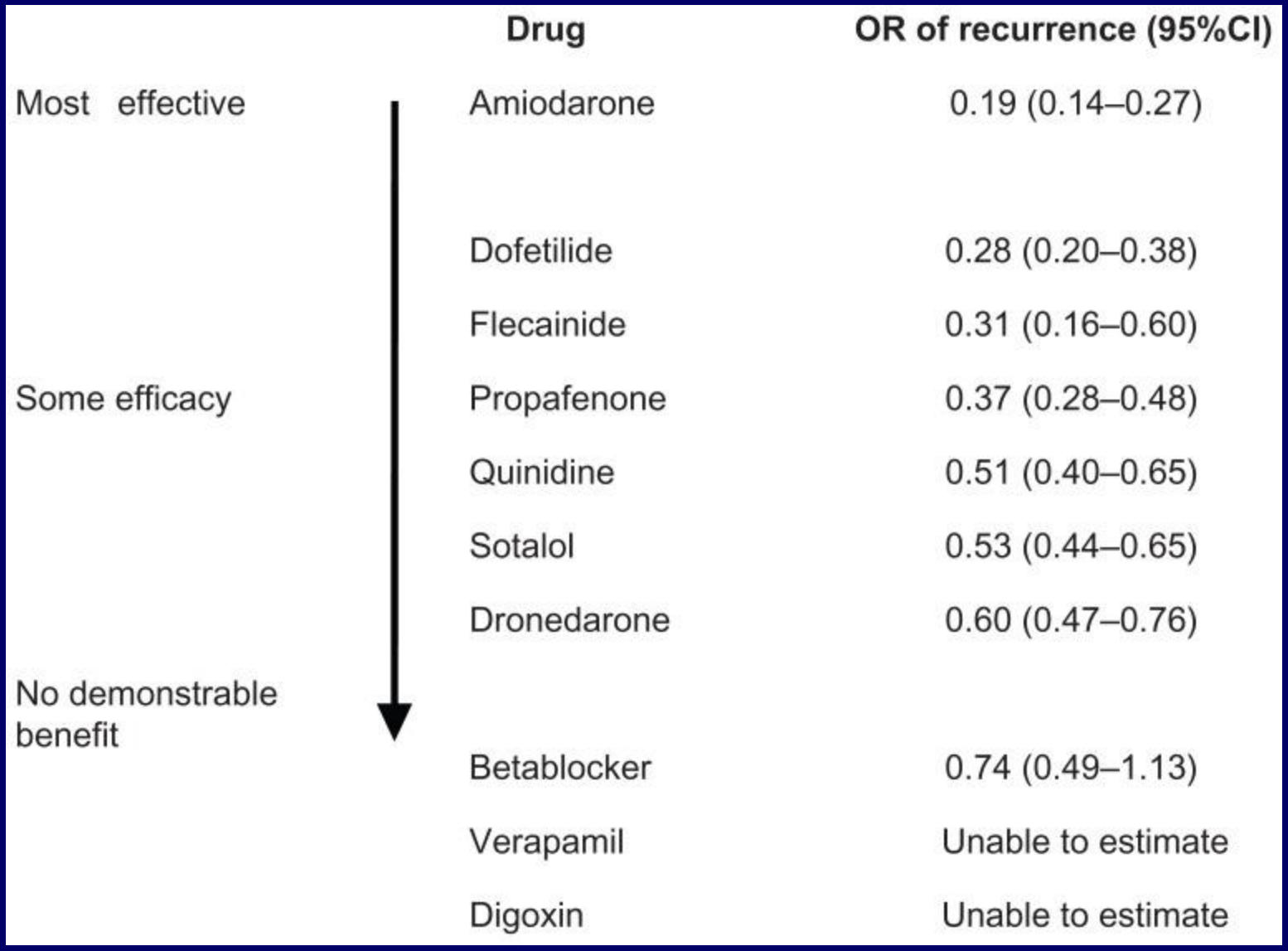
ATHENA: Ölüm veya KV nedenlerden hastaneye yatış birleşik son noktası üzerine dronedarone'un etkisi



ATHENA Investigators. N Engl J Med. 2009 Feb 12; 360(7):668-78.

Dronedarone Çalışmaları

Trial name	No of patients (D/C)	Dose	Inclusion criteria	Relevant exclusion criteria	Mean follow-up
DAFNE[20,8]	102 (54/48)	400 mg bid vs placebo	Persistent AF	NYHA III–IV; QT > 500 ms; LVEF < 35%; use of other antiarrhythmic drugs; ICD	6 months
EURIDIS/ ADONIS[21]	1237 (828/409)	400 mg bid vs placebo	At least one episode of AF in the last 3 months; in sinus rhythm for at least 1 hour before randomization	Permanent AF; HR < 50 beats/min; NYHA III–IV; creatinine > 1.7; use of class I–III antiarrhythmic drugs	12 months
ATHENA[22]	4628 (2301/2327)	400 mg bid vs placebo	Paroxysmal or persistent AF or atrial flutter and at least one cardiovascular risk factor (age > 70 years, hypertension needing at least two drugs, diabetes, previous stroke, transient ischemic attack or systemic embolism, left atrial diameter > 50 mm, LVEF < 40%)	Permanent AF; HR < 50 beats/min; NYHA IV; GFR < 10 mL/min	21 months
DIONYSOS[23]	504 (249/255)	400 mg bid vs amiodarone 600 mg/day for 28 days and then 200 mg/day for 6 months	Persistent or permanent AF (>72 hours)	Paroxysmal AF; QT > 500 ms; NYHA III–IV; use of class I–III antiarrhythmic drugs; previous chronic treatment with amiodarone	6 months*
ERATO[24]	174 (85/89)	400 mg bid vs placebo	Permanent AF (>6 months)	NYHA III–IV; use of other antiarrhythmic drugs	6 months
PALLAS[25]	3236 (1619/1617)	400 mg bid vs placebo	Permanent AF or atrial flutter (>6 months); age > 65 years with additional cardiovascular risk factors (coronary artery disease, symptomatic heart failure, LVEF < 40%, or a combination of age > 70, hypertension, and diabetes)	Non-permanent AF; HR < 50 beats/min; QT > 500 ms; ICD	3.5 months
ANDROMEDA[26]	627 (310/317)	400 mg bid vs placebo	Patients hospitalized with worsening CHF (NYHA class III or IV)	HR < 50 beats/min; QT > 500 ms; use of class I–III antiarrhythmic drugs	2 months†



C Anwar A Chahal et al. *Patient Relat Outcome Meas. 2012; 3: 95–103.*

ACCF/AHA/HRS Focused Update

2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline)

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

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European Heart Journal (2010) **31**, 2369–2429
doi:10.1093/eurheartj/ehq278

ESC GUIDELINES

Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA)†

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: A. John Camm (Chairperson) (UK)*, Paulus Kirchhof (Germany), Gregory Y.H. Lip (UK), Ulrich Schotten (The Netherlands), Irene Savelieva (UK), Sabine Ernst (UK), Isabelle C. Van Gelder (The Netherlands), Nawwar Al-Attar (France), Gerhard Hindricks (Germany), Bernard Prendergast (UK), Hein Heidbuchel (Belgium), Ottavio Alfieri (Italy), Annalisa Angelini (Italy), Dan Atar (Norway), Paolo Colonna (Italy), Raffaele De Caterina (Italy), Johan De Sutter (Belgium), Andreas Goette (Germany), Bulent Gorenek (Turkey), Magnus Heldal (Norway), Stefan H. Hohloser (Germany), Philippe Kolh (Belgium), Jean-Yves Le Heuzey (France), Piotr Ponikowski (Poland), Frans H. Rutten

Altta Yatan Patolojiye Göre Antiaritmik İlaç Seçimi: ACCF/AHA ve ESC Önerisi

Table I Choice of antiarrhythmic drug according to underlying pathology: comparison of ACCF/AHA[2,3] and ESC[4] guidelines

Underlying pathology	ACCF/AHA	ESC
Minimal or no heart disease	Dronedarone flecainide propafenone sotalol	Dronedarone flecainide propafenone sotalol
Hypertension		
With LVH	Amiodarone	Dronedarone
Without LVH	Dronedarone flecainide propafenone sotalol	Dronedarone flecainide propafenone sotalol
CAD	Dronedarone sotalol dofetilide	Dronedarone sotalol
Heart failure		
Stable NYHA I/II	Amiodarone dofetilide	Dronedarone
NYHA III/IV or unstable NYHA II	Amiodarone dofetilide	Amiodarone

Notes: In the congestive heart failure category, ACCF/AHA has two different subcategories: stable NYHA I/II and NYHA III/IV or unstable NYHA II. Unstable is defined as cardiac decompensation within the prior 4 weeks.

Abbreviations: ACCF/AHA, American College of Cardiology Foundation/American Heart Association; ESC, European Society of Cardiology; LVH, left ventricular hypertrophy; CAD, coronary artery disease; NYHA, New York Heart Association.

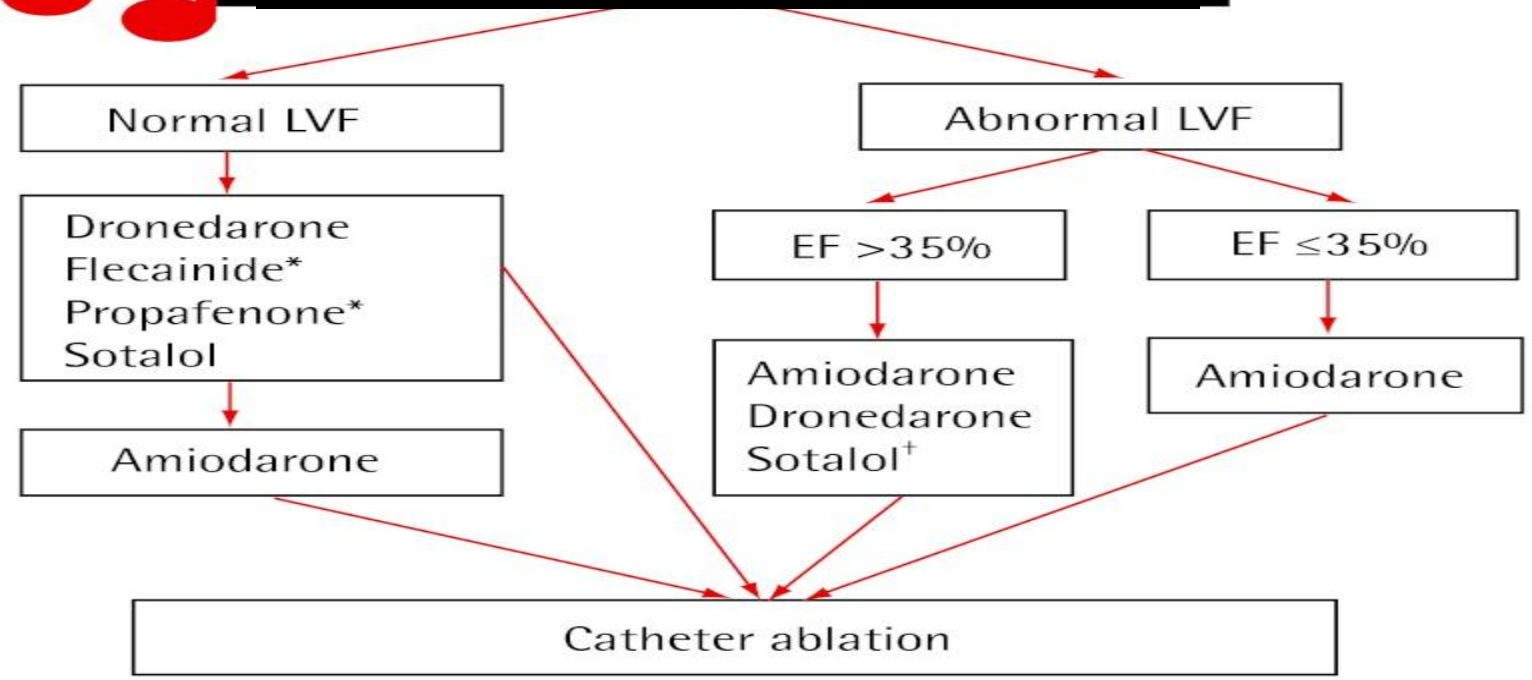
Podda GM et al. J General Medicine 2012;5:465-478.

HARMONY (the Study to Evaluate the Effect of Ranolazine and Dronedarone When Given Alone and in Combination in Patients with Paroxysmal Atrial Fibrillation)

- Dronedarone ve ranolazine'in atriyal dokuda sinerjistik antiaritmik etki gösterdiği deneysel çalışmalarda gösterilmiş
- PAF
- Dronedarone / Ranolazine / fiks doz dronedarone + ranolazine kombinasyonu

Ritim Kontrol Algoritması

Ritim Kontrolü İlaç Seçimi



AV—atrioventricular, CAD—coronary artery disease, EF—ejection fraction, LVF—left ventricular function.
*Class I agents should be AVOIDED in CAD; they should be combined with AV-nodal blocking agents (eg, β-blocker, digoxin, diltiazem, or verapamil).
†Sotalol should be used with caution with EF 35% to 40%; contraindicated in women >65 y who are taking diuretics.
Data from Jin and Kosar.[4]

Frankel G et al. Can Fam Phys 2013;59:161-168

Gerçek Hayat

Rhythm Versus Rate Control in the Contemporary Management of Atrial Fibrillation In-Hospital†

Nancy M. Allen LaPointe, PharmD[a,*], Jie-Lena Sun, MS[a], Sigal Kaplan, PhD, BPharm[b], Phil d'Almada, MS[a], and Sana M. Al-Khatib, MD, MHS[a]

Little is presently known regarding whether a rhythm-control or a rate-control strategy is more frequently used in patients hospitalized for atrial fibrillation (AF). This study was conducted to assess patient and physician characteristics associated with each treatment strategy and with the use of anticoagulants. Hospitalizations for primary diagnoses of AF were examined using hospital claims from January 2000 to December 2004. Patients who received antiarrhythmic drugs, ablation, or cardioversion for AF were categorized as receiving rhythm control. Patients managed only with β blockers, calcium channel blockers, or digoxin were categorized as receiving rate control. Characteristics associated with rhythm compared with rate control and anticoagulant use with $CHADS_2$ score were determined. The study cohort included 155,731 hospitalizations from 464 hospitals. Of these, 75,397 (48%) were categorized as involving rhythm control and 80,334 (52%) as involving rate control. Care by a noncardiologist (adjusted odds ratio [OR] 0.33, 95% confidence interval [CI] 0.31 to 0.36) and increasing age >65 years (adjusted OR 0.87, 95% CI 0.86 to 0.88) were associated with lower odds of rhythm versus rate control; hypertrophic cardiomyopathy was associated with greater odds (adjusted OR 2.3, 95% CI 1.81 to 2.84) of rhythm control. Warfarin use was greater in the rhythm-control group compared with the rate-control group (adjusted OR 1.56, 95% CI 1.52 to 1.60), and warfarin use was greater with a $CHADS_2$ score ≥2 (unadjusted OR 1.21, 95% CI 1.19 to 1.24). In conclusion, rhythm- and rate-control strategies were used equally in patients hospitalized for AF. Some observations, such as greater use of the rate-control strategy with increasing age, were consistent with recommendations, but others, such as lower use of warfarin in the rate-control group, were not. (Am J Cardiol 2008;101: 1134–1141)

Gerçek hayat

2000 – 2004 arası, 464 hastane, 155.731 hasta, AF nedeniyle hastaneye yatış

- Ritm kontrolü: %48
- Hız kontrolü: %52

- Ritim kontrol stratejisi seçimini belirleyen faktörler
  - Hipertrofik KMP (OR 2.3, 95% CI 1.81 to 2.84)
  - Warfarin kullanımı (OR 1.56, 95% CI 1.52 to 1.60)
  - Kardiyolog dışı doktor (OR 0.33, 95% CI 0.31 to 0.36)
  - 65 yaş üzeri (OR 0.87, 95% CI 0.86 to 0.88)

Nancy M. Allen LaPointe. Am J Cardiol 2008;101:1134 –1141

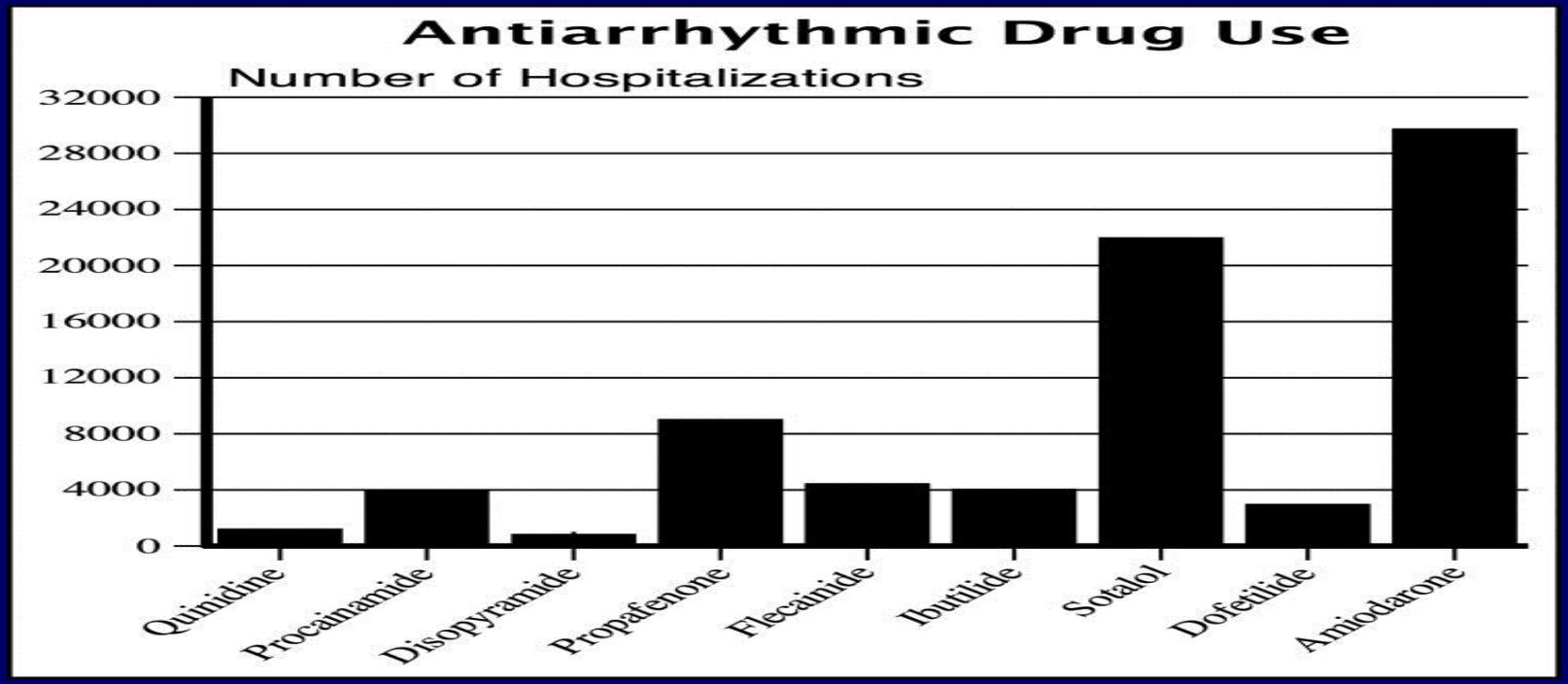


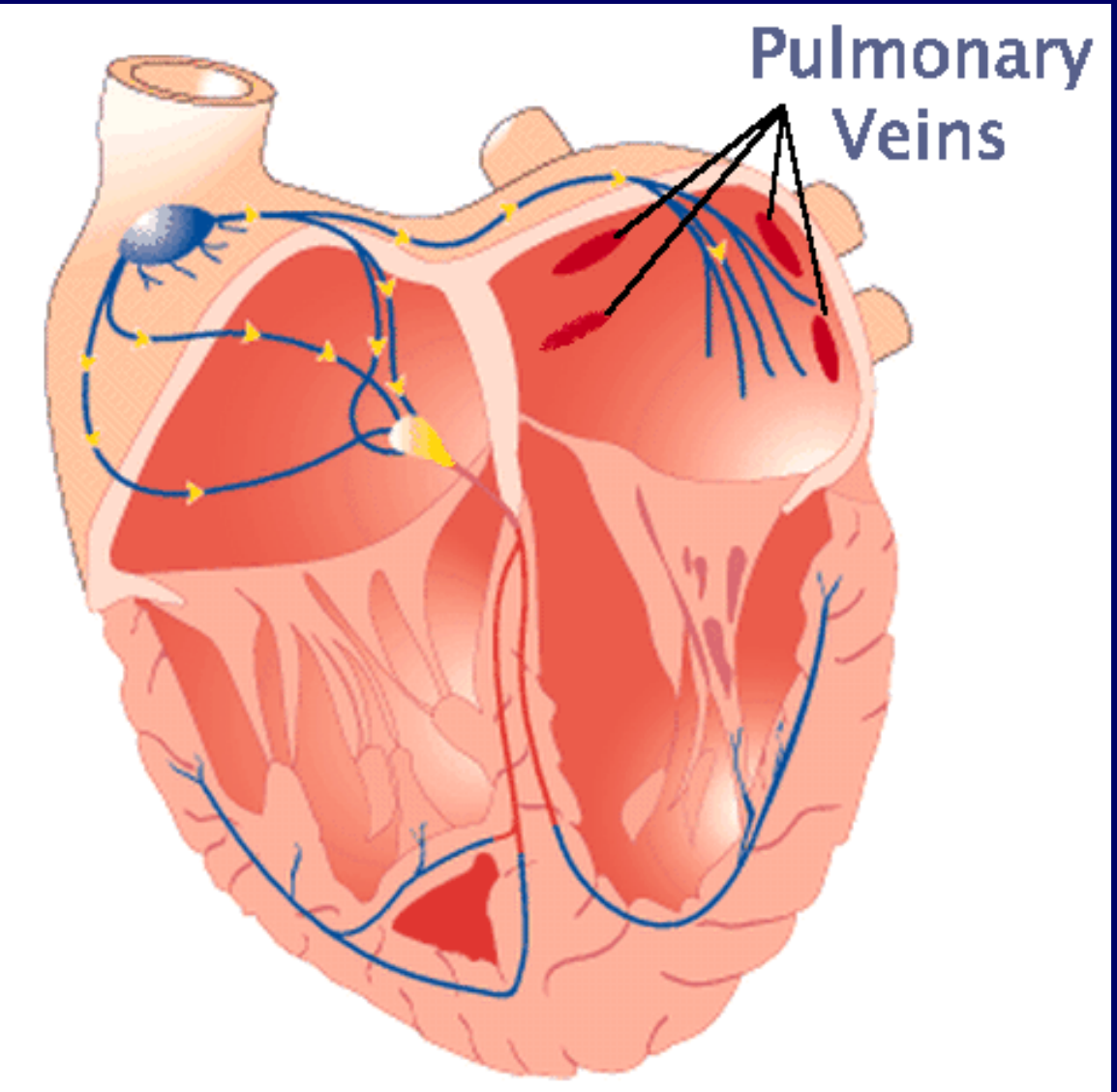
Figure 1 Number of hospitalizations in which antiarrhythmic drugs were used.

Nancy M. Allen LaPointe , Jie-Lena Sun , Sigal Kaplan , Phil d?Almada , Sana M. Al-Khatib

Rhythm Versus Rate Control in the Contemporary Management of Atrial Fibrillation In-Hospital

The American Journal of Cardiology Volume 101, Issue 8 2008 1134 - 1141

Ritim Kontrolünde AF Ablasyonu



Atriyal fibrilasyon

a. Tetikleyici

p. venler

b. Devam ettiren

sol atriyum

dilate

fibrotik

Study	Reference	Patients (n)	Age, years	Type of AF	Previous use of AAD	Ablation technique	Repeat ablation in the ablation group	Crossed to ablation in the AAD group	AF free at 1 year	
									Ablation	AAD
Krittayaphong *et al.* 2003	Online	30	55 ± 10 (ablation) 47 ± 15 (AAD)	Paroxysmal, persistent	≥1[a]	PVI + LA lines + CTI ablation + RA lines	Not stated	Not stated	79%	40%
Wazni *et al.* 2005 (RAAFT)	134	70	53 ± 8 (ablation) 54 ± 8 (AAD)	Mainly paroxysmal	No	PVI	12%[b]	49%[c]	87%	37%
Stabile *et al.* 2005 (CACAF)[d]	Online	245	62 ± 9 (ablation) 62 ± 10 (AAD)	Paroxysmal, persistent	≥2	PVI + LA lines ± CTI ablation	No exact data	57%	56%	9%
Oral *et al.* 2006[e]	Online	245	57 ± 9	Persistent	≥1 (mean 2.1 ± 1.2)	CPVA	26% for AF; 6% for LA flutter	77%	74%	4%
Pappone *et al.* 2006 (APAF)	135	198	55 ± 10 (ablation) 57 ± 10 (AAD)	Paroxysmal	≥2 (mean 2 ± 1)	CPVA + CTI ablation	6% for AF; 3% for atrial tachycardia	42%	86%	22%
Jais *et al.* 2008 (A4 study)	133	112	51 ± 11	Paroxysmal	≥1	PVI ± LA lines ± CTI ablation	Mean 1.8 ± 0.8, median 2 per patient	63%	89%	23%
Forleo *et al.* 2008[f]	Online	70	63 ± 9 (ablation) 65 ± 6 (AAD)	Paroxysmal, persistent	≥1	PVI ± LA lines ± CTI ablation	Not stated	Not stated	80%	43%
Wilber *et al.* 2010 (Thermocool)[g]	96	167	55.5 (ablation) 56.1 (AAD)	Paroxysmal	≥1 (mean 1.3)[h]	PVI ± LA lines ± CFAEs ± CTI ablation ± RA lines	12.6% within 80 days after 1st procedure[i]	59%[c]	66%	16%
Packer *et al.* 2010 (STOP-AF)[j]	Online	245	56.7 (ablation) 56.4 (AAD)	Paroxysmal	≥1[b]	Cryo-PVI ± LA lines	19% within 90 days after 1st procedure	79%	69.9%	7.3%

Six Year Follow-Up After Catheter Ablation of Atrial Fibrillation: A Palliation More Than a True Cure

Antonio Sorgente, MD[a,b,*], Patricia Tung, MD[a], Jack Wylie, MD[a], and Mark E. Josephson, MD[a]

Long-term outcomes after pulmonary vein isolation for atrial fibrillation (AF) remain uncertain. In particular, the influence of rigorous arrhythmia monitoring on outcomes is not yet clear. In this study, 103 patients with symptomatic AF who underwent catheter ablation at a single academic medical center from 2002 to 2006 were evaluated, with a median follow-up time of 6 years. The primary end point was the success rate of catheter ablation, defined as the absence of any atrial arrhythmia recurrence lasting >10 seconds at the clinical visit and electrocardiographic or long-term cardiac rhythm recording after a single procedure and after the last procedure. In all, 153 procedures were performed, with a median of 1 (interquartile range 1 to 2) per patient as follows: 61 had 1, 35 had 2, 6 had 3, and 1 had 4 catheter ablations. Freedom from all atrial arrhythmias was present in 23% of patients at 6 years after a single procedure and in 39% of patients after the last procedure. No clinical predictors of AF recurrence were recognized after a single procedure, whereas after the last procedure, in univariate and multivariate Cox regression analysis, only nonparoxysmal AF (hazard ratio 1.92, 95% confidence interval 1.07 to 3.47, $p = 0.02$) was a predictor of recurrence. In conclusion, AF recurrence at 6-year follow-up after catheter ablation in a selected group of patients with symptomatic drug-refractory AF was relatively high, with 2/3 of AF relapses occurring in the first year of follow-up. Strict clinical surveillance after catheter ablation should be considered to help guide clinical decisions. (Am J Cardiol 2012;109:1179–1186)

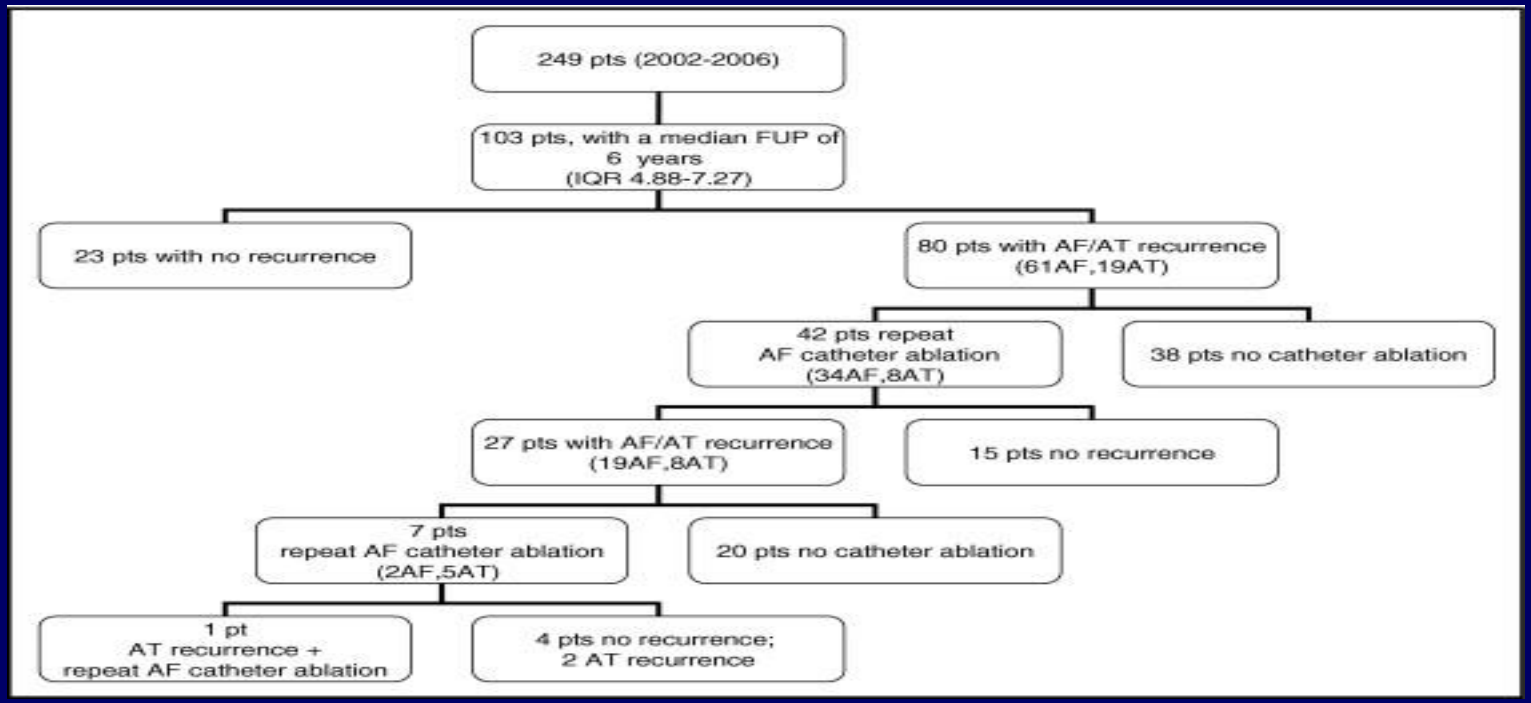


Figure 1 Study flow chart. FUP = follow-up; IQR = interquartile range; pts = patients.

Antonio Sorgente , Patricia Tung , Jack Wylie , Mark E. Josephson

Six Year Follow-Up After Catheter Ablation of Atrial Fibrillation: A Palliation More Than a True Cure

The American Journal of Cardiology Volume 109, Issue 8 2012 1179 - 1186

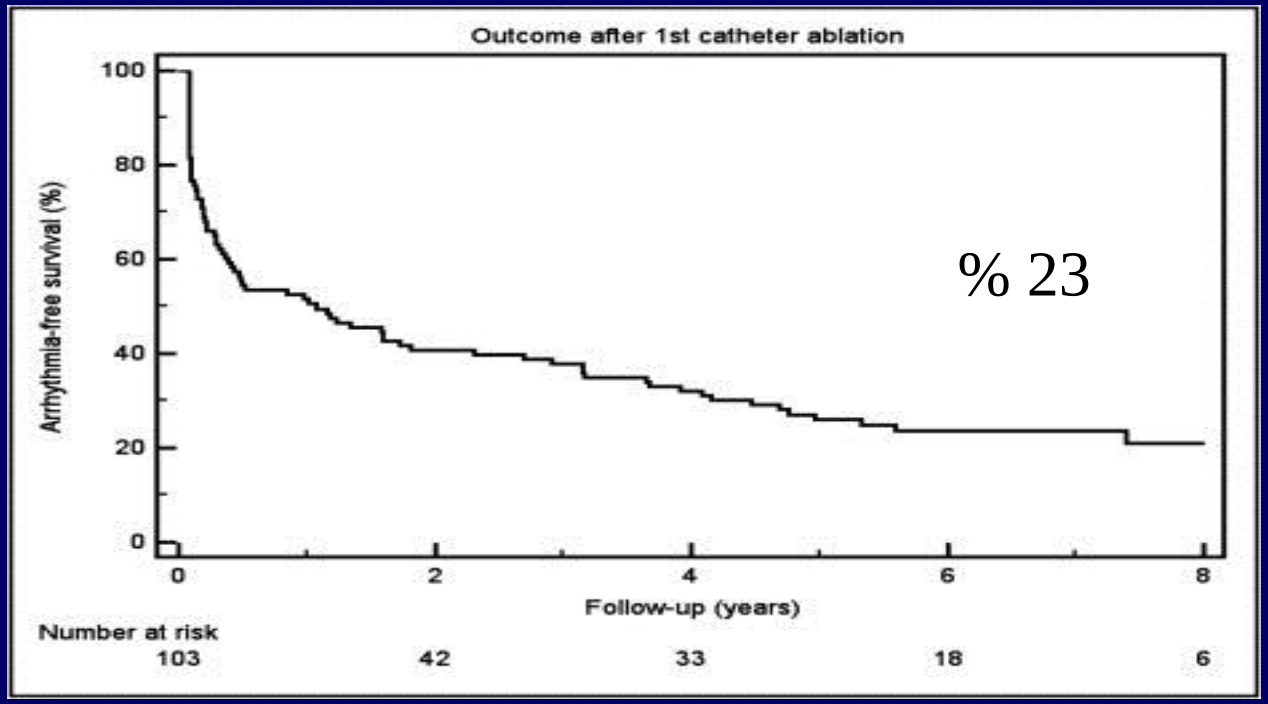


Figure 2 Kaplan-Meier arrhythmia-free survival curve after single catheter ablation of AF.

Antonio Sorgente , Patricia Tung , Jack Wylie , Mark E. Josephson

Six Year Follow-Up After Catheter Ablation of Atrial Fibrillation: A Palliation More Than a True Cure

The American Journal of Cardiology Volume 109, Issue 8 2012 1179 - 1186

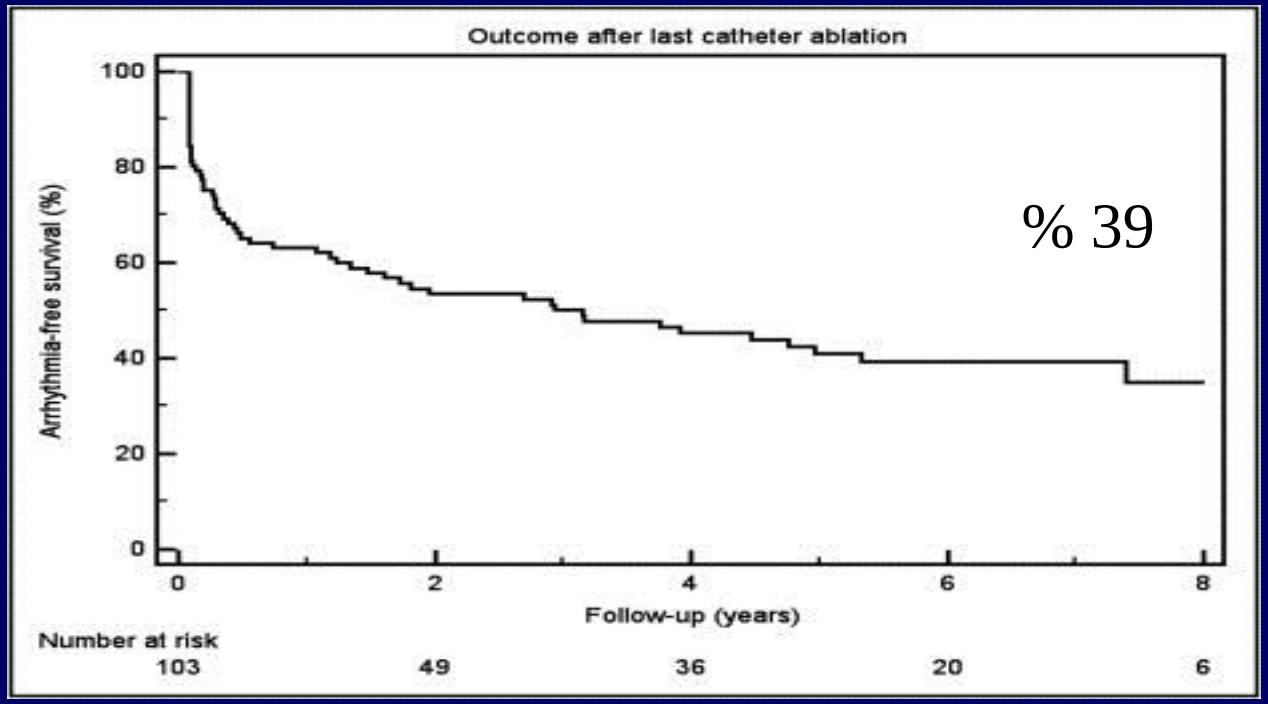


Figure 3 Kaplan-Meier arrhythmia-free survival curve after the last catheter ablation of AF.

Antonio Sorgente , Patricia Tung , Jack Wylie , Mark E. Josephson

Six Year Follow-Up After Catheter Ablation of Atrial Fibrillation: A Palliation More Than a True Cure

The American Journal of Cardiology Volume 109, Issue 8 2012 1179 - 1186

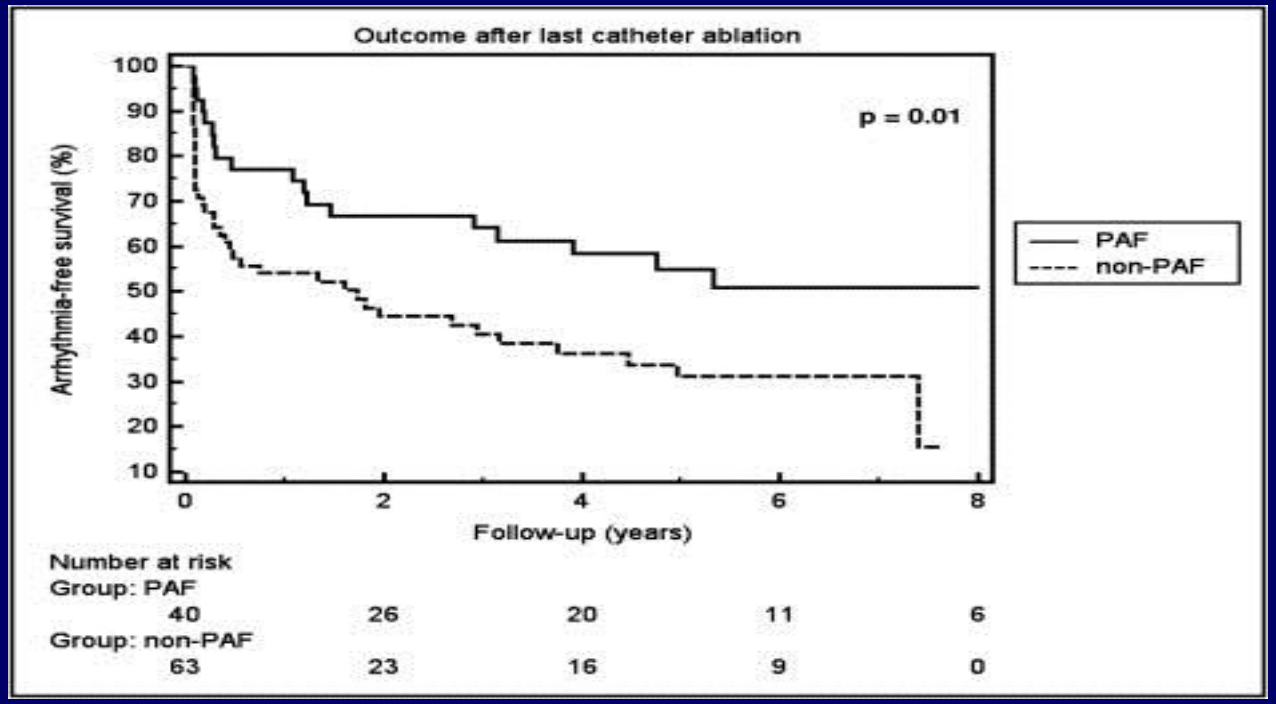


Figure 5 Kaplan-Meier arrhythmia-free survival curve after the last catheter ablation of AF according to the nature of AF. PAF = paroxysmal AF.

Antonio Sorgente , Patricia Tung , Jack Wylie , Mark E. Josephson

Six Year Follow-Up After Catheter Ablation of Atrial Fibrillation: A Palliation More Than a True Cure

The American Journal of Cardiology Volume 109, Issue 8 2012 1179 - 1186

AF Ablasyon Sonuçları

- Yorumlamak zor
  - Başarı oranı
    - Optimal hasta:
      - Tek işlem: % 60 - 80
      - Çoklu işlem: % 80 - 90
  - En iyi sonuç: Paroksismal AF ve sağlıklı kalp
  - En kötü sonuç: Kronik AF ve dilate LA
  - Başlangıçtaki başarıya rağmen rekürrens olabilir
  - Asemptomatik rekürrens olabilir
  - ??? Warfarin
- Esas amaç: Toksik antiaritmik ilaç olmaksızın ritim kontrolü

En Uygun Hasta

- ✓ Paroksismal AF
- ✓ Genç hasta (<70 yaş)
- ✓ Yapısal kalp hastalığı yok veya minimal
- ✓ İşlemi tolere edebilecek ve takip edilebilecek hasta

Kateter Ablasyonuna Refere Edilecek Hastayı Bilgilendirme

- Başarı oranı % 60-70
- 2. işlem ihtiyacı % 10-40
- Antiaritmik ilaç gereksinimi % 10-15
- Komplikasyon oranı % 2-3

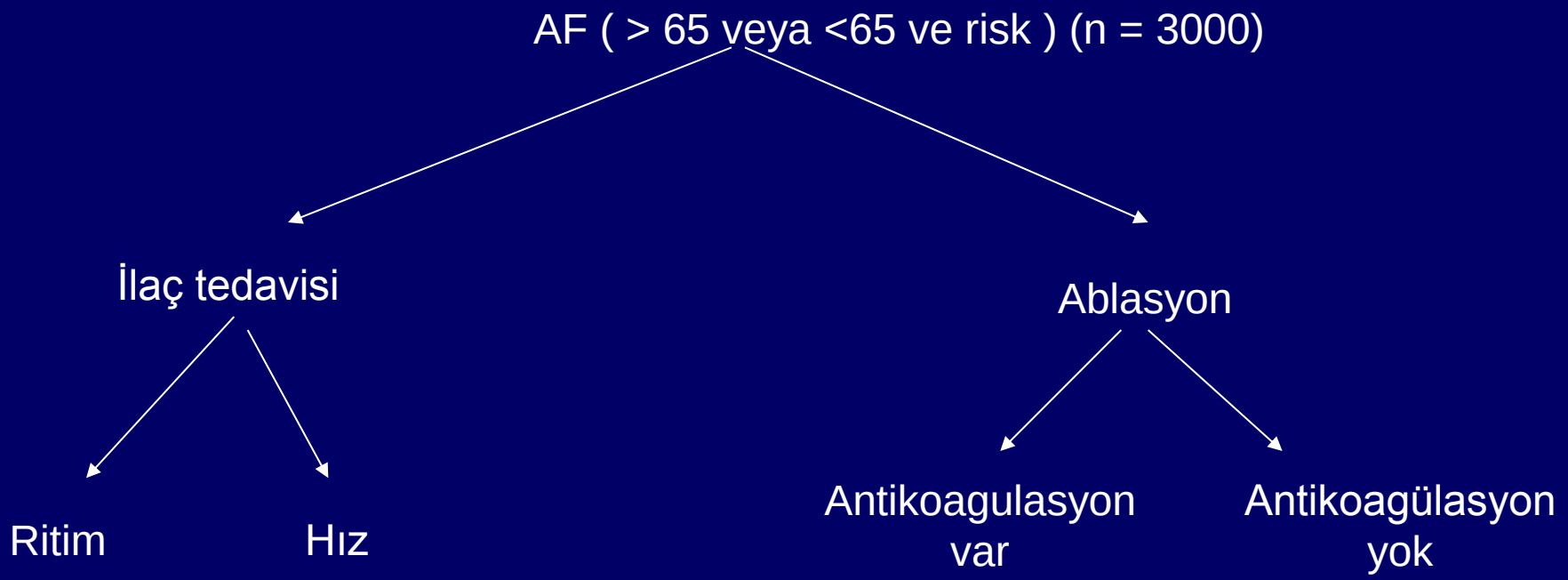
Crandall et al. Mayo Clin Proc 2009;84:643-62.

AF'de Erken Ritim Kontrolünün Etkisini Araştıran Çalışmalar

- RAAFT 2 (The Radiofrequency Ablation versus Antiarrhythmic drugs as first-line treatment of sypmtomatic atrial fibrillation Treatment)
  - 130 semptomatik AF hastası
  - antiaritmik ilaç / ablasyon (ilk tedavi seçeneği)
  - Birincil son nokta: > 30 sn süren semptomatik AF rekürrensi
  - İlk tedavi seçeneği olarak kullanıldığında kateter ablasyonu AF rekürrensini azaltmada antiaritmik ilaçlardan daha fazla etkilidir.

Heart Rhythm Society 2012 Scientific Sessions, 2012;Boston,MA. Abstract.

CABANA (Catheter Ablation vs. Antiarrhytmic Drug Therapy for Atrial Fibrillation trial)



Hipotez: AF'yi elimine etmek total mortaliteyi azaltacaktır.

RACE 3 (The Routine versus Aggressive upstream rhythm Control for the prevention of Early atrial fibrillation in heart failure study)

- Kısa süreli AF (total AF öyküsü < 2 yıl, total persistan AF süresi < 6 ay ve ≤ 1 elektriksel kardiyoversiyon)
- Hafif-orta erken kalp yetersizliği (total kalp yetersizliği öyküsü < 1 yıl)
- Fizik aktiviteyle birlikte agresif "upstream" tedavi veya rutin ritim kontrolü
- Birincil son nokta: 1 yıl sonunda sinüs ritmi

“Upstream” tedaviler

- Renin anjiyotensin-aldosteron inhibitörleri
  - Altta yatan ciddi kalp hastalığı olanlarda (sol ventrikül disfonksiyonu ve hipertrofi) ACEI/ARB ile tedavi yeni başlangıçlı AF’yi azaltır
- Statin
  - Kardiyak cerrahi geçiren hastalarda postop AF riskini azaltır
- PUFA
  - Primer korumadaki etkisi gösterilmemiştir

Savelieva I et al. Europace 2011;13:308-28

	Daha az semptom	Aynı semptom	Daha çok semptom
Daha uzun yaşam		Antikoagülan	
Aynı yaşam	Ablasyon	Hız Kontrolü	
Daha kısa yaşam	Antiaritmik ilaçlar		