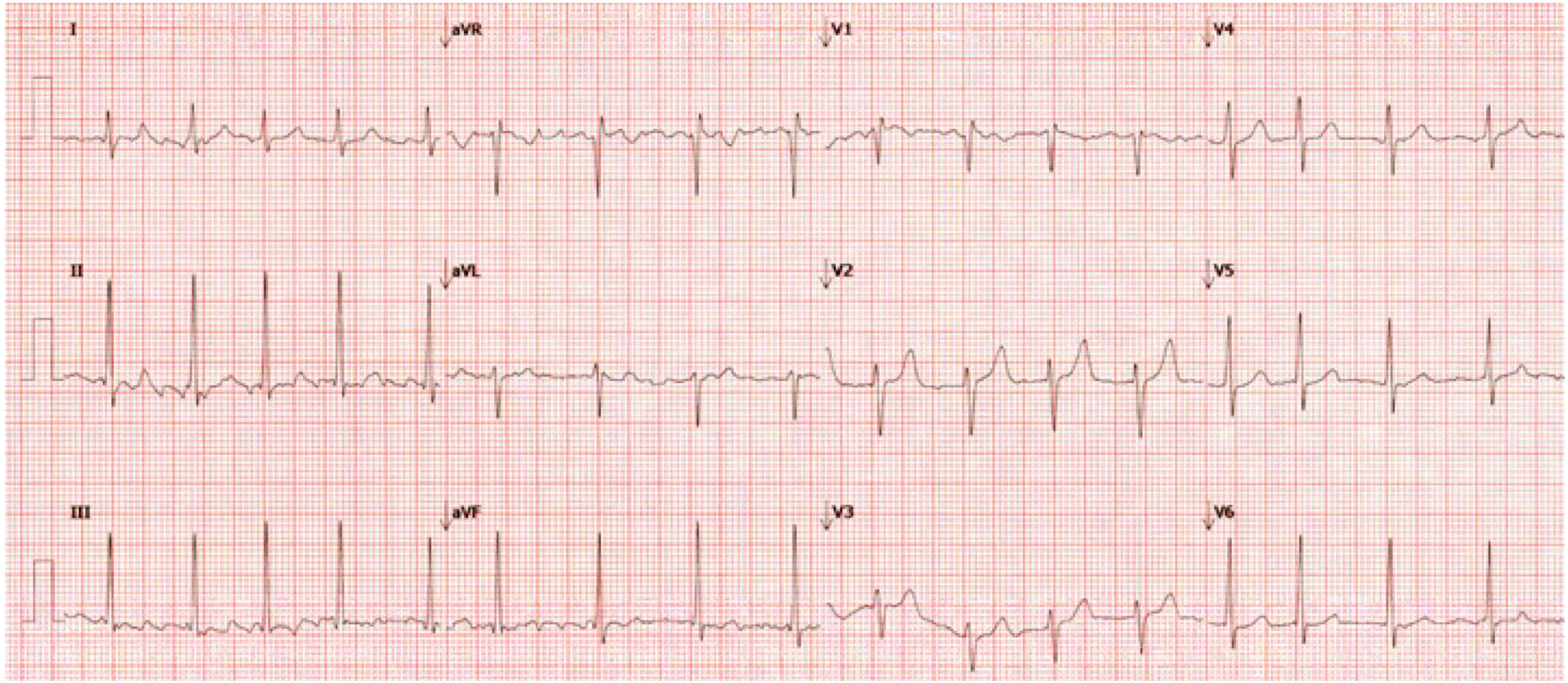
Arterial Fibrillation

Dr. Tung

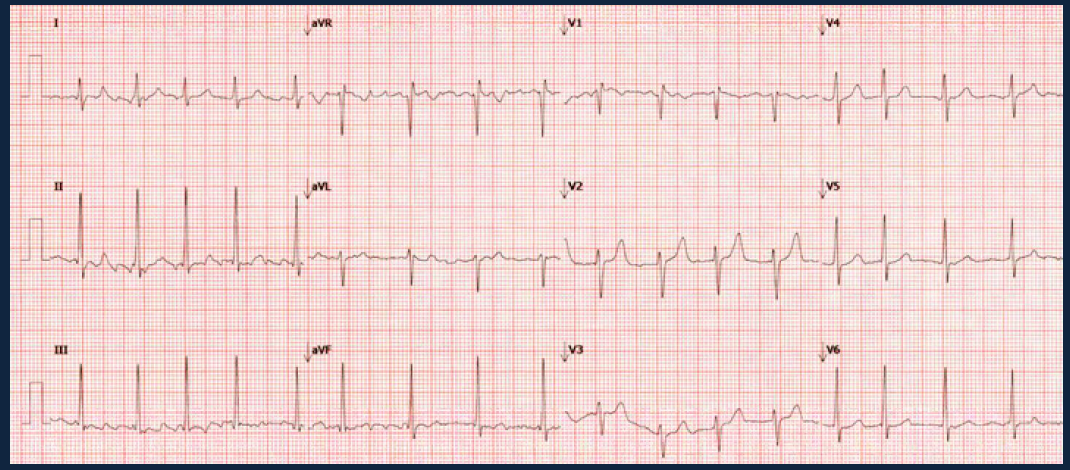
Case scenario

- 67 y/o man with DM2 presents to ED with 2 weeks of shortness of breath, LE edema, and PND. No known cardiac history.


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

EKG diagnosis

- 1. Atrial flutter with variable block
- 2. Atrial flutter with 2:1 block
- 3. Multifocal atrial tachycardia (MAT)
- 4. Atrial fibrillation



Vital/PE/Labs

- HR 150 BP 110/65 92%RA
- JVP angle of jaw, IR S1S2, distant sounds, rales bilaterally, 2+ LE edema
- Na 140 K 3.5
- Cr 1.4

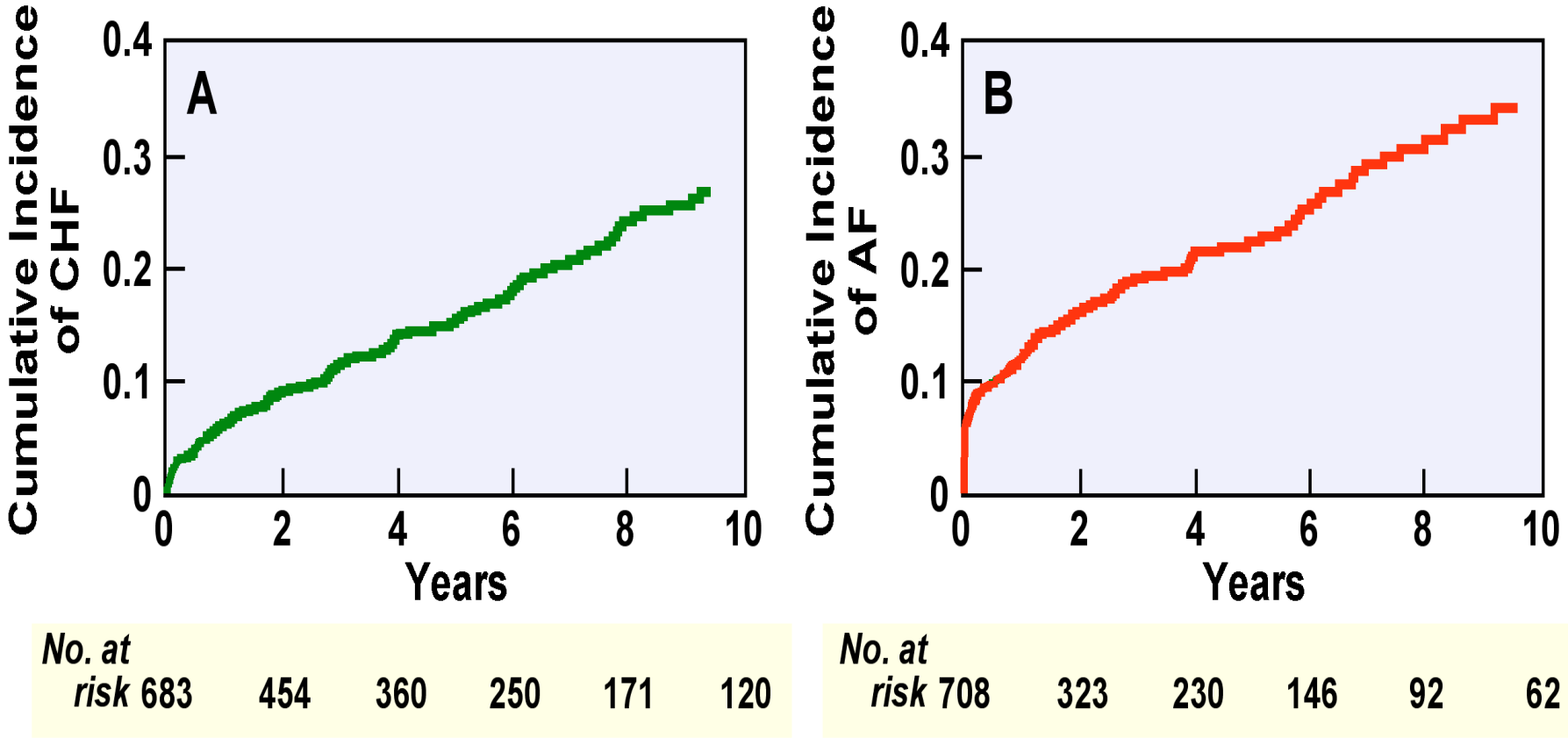
What is best next step in management?

- 1) Immediate cardioversion
- 2) Amiodarone
- 3) Bring to EP lab for ablation
- 4) Class Ic (flecainide, propafenone)
- 5) POCUS

Unadjusted Cumulative Incidence of First CHF in Individuals with AF

Unadjusted Cumulative Incidence of First AF in Individuals with CHF

1 in 5 will develop the other at 5 years



Wang et al. Circulation 2003; 107: 2929-2925

Atrial Fibrillation Associated with Poor Prognosis in Chronic Systolic HF

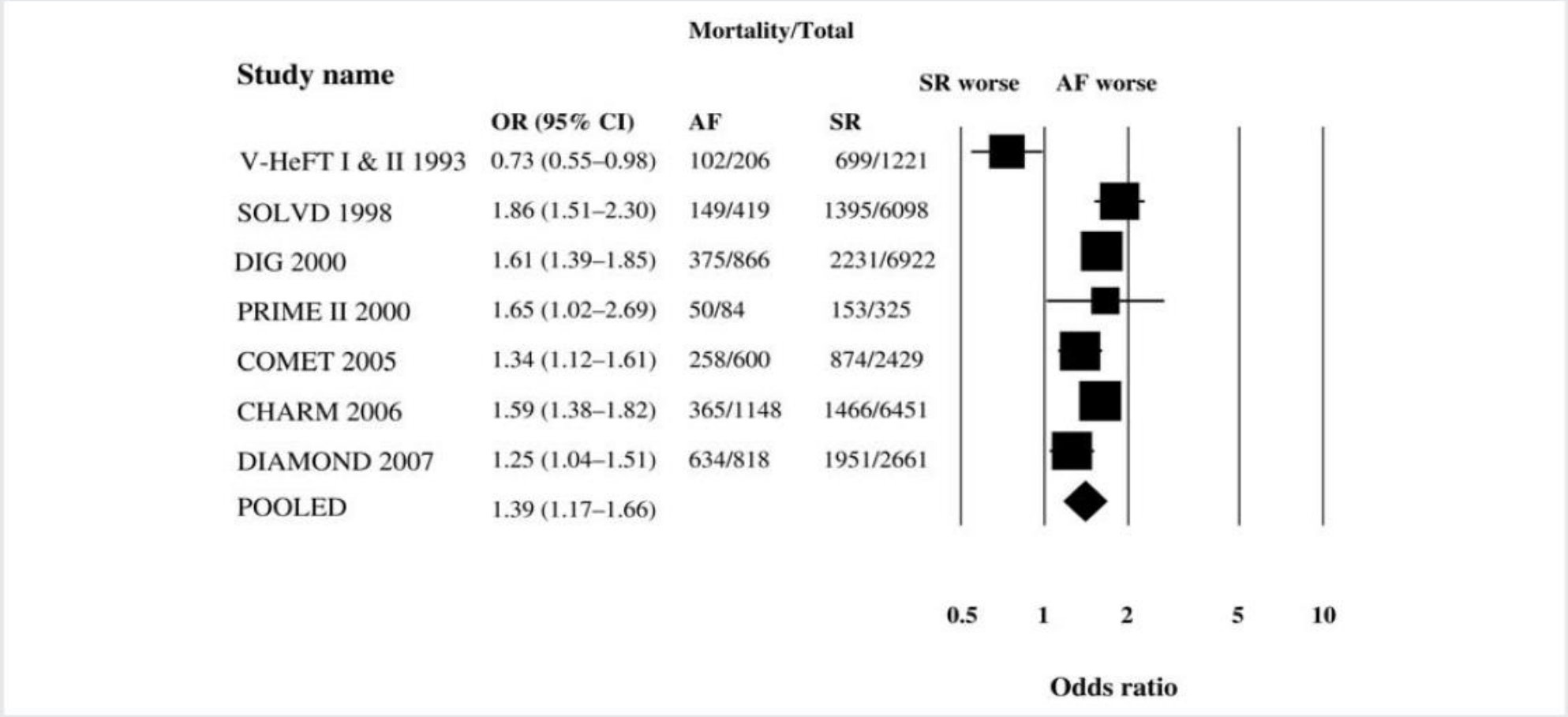
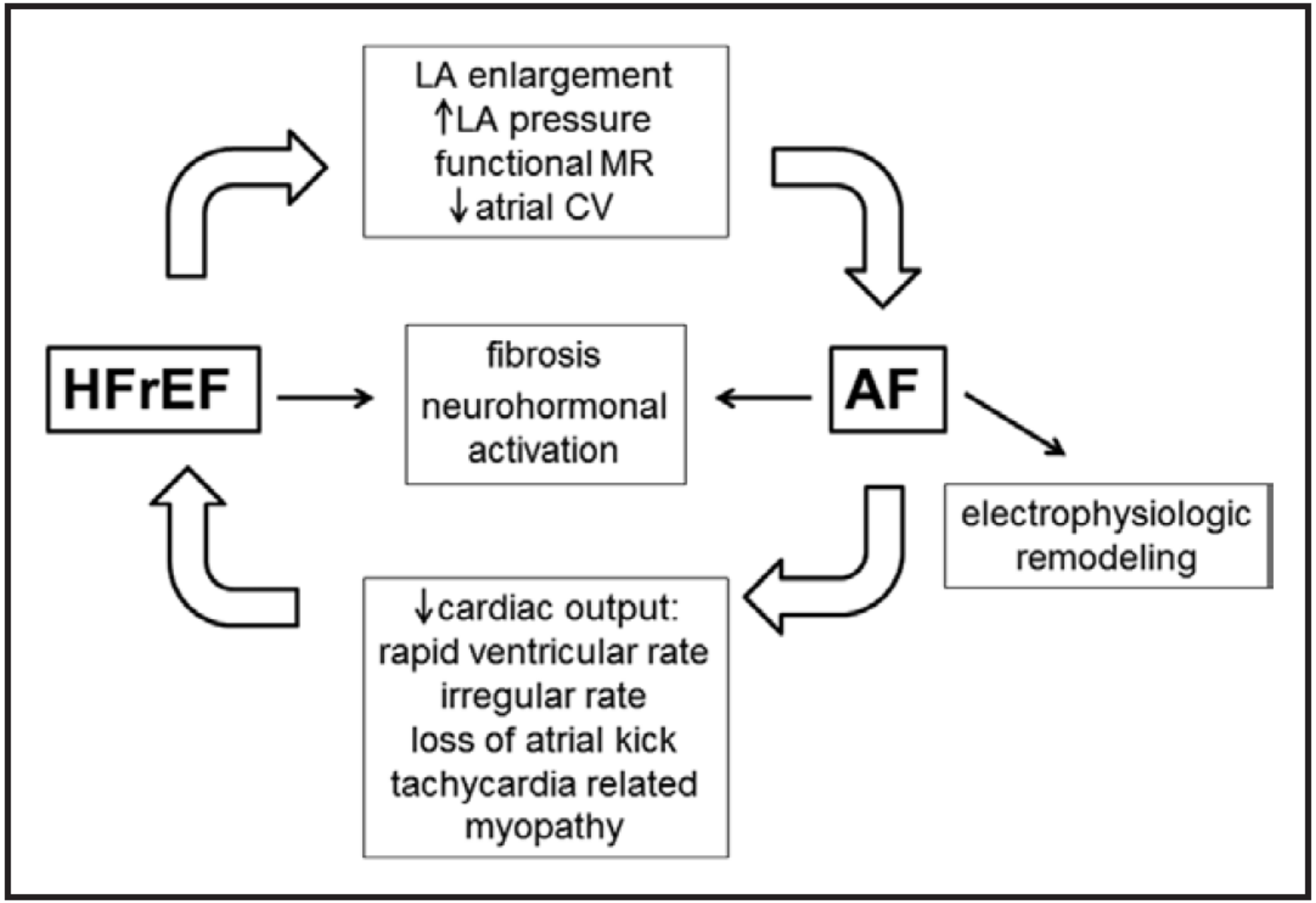


Figure 1 Forest plot comparing mortality outcomes in randomized trials in chronic heart failure patients in sinus rhythm and atrial fibrillation. Odds ratios and 95% confidence intervals are presented for individual studies and pooled data.

Mamas MA., et al. *European Heart Journal of HF* 2009;11:676

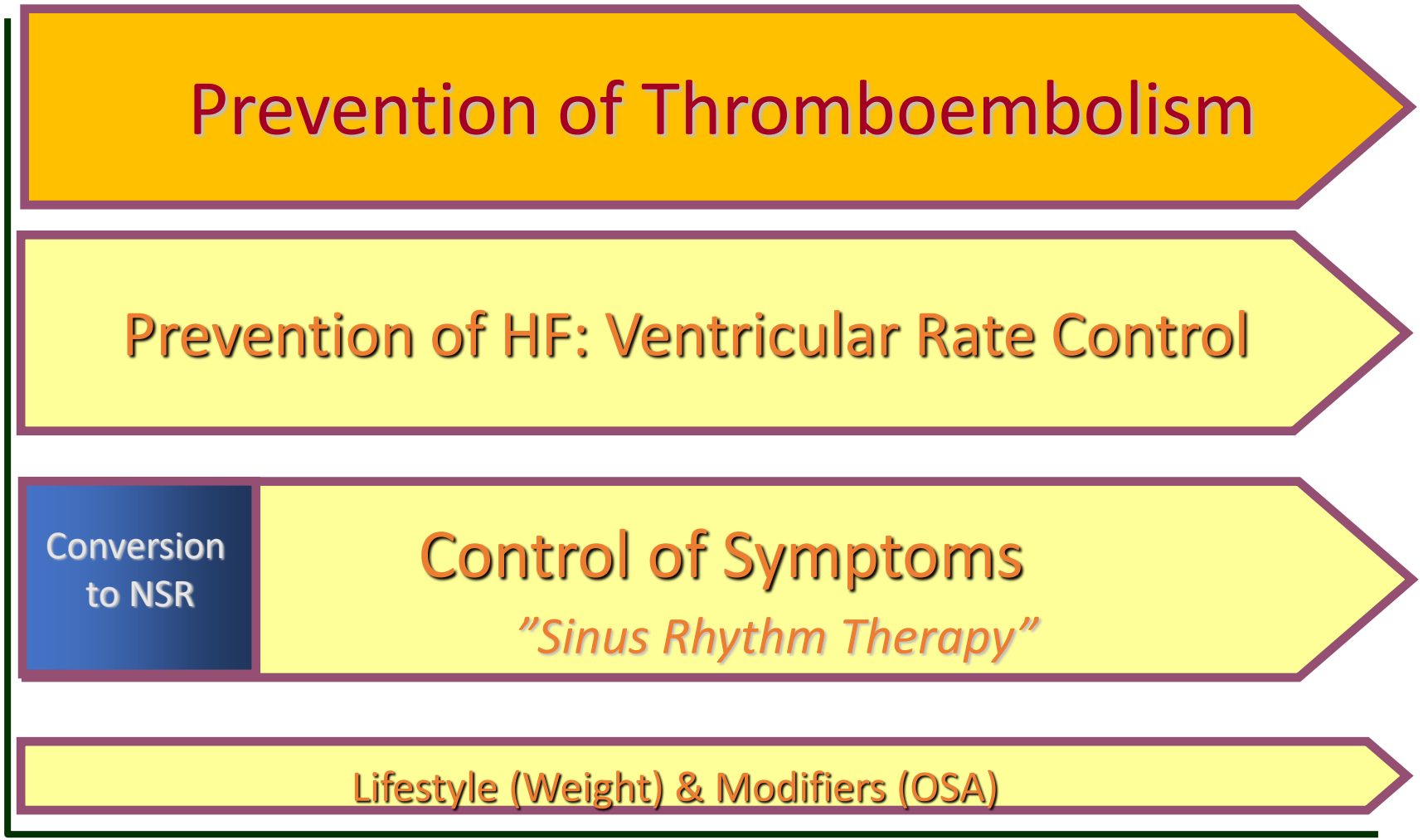
AF and HF: A Vicious Cycle



Verma A., et al. *Circulation* 2017;135:1548

What is the most important aspect in AF management?

Approach to Treatment of Atrial Fibrillation



What type of AF does this patient have?

1. Paroxysmal
2. Chronic
3. Persistent
4. Long standing persistent
5. Permanent

AF Definitions

- **Paroxysmal**: recurrent, terminates spontaneously within 7 days
- **Persistent**: episodes lasting > 7 days or require intervention for termination (cardioversion)
  - Long standing persistent: continuous AF > 12 months duration
- **Permanent**: mutual decision between patient and physician to cease further attempts to restore/ maintain normal sinus rhythm by any means

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- **AF**: AF in the absence of moderate – severe mitral stenosis or mechanical heart valve
- **Valvular AF**: AF in the setting of moderate – severe mitral stenosis (potentially requiring surgical intervention) or in the presence of an artificial (mechanical) heart valve
  - Warfarin is recommended

The term nonvalvular is no longer used in the new ACC/AHA/HRS Guidelines

1. January CT, et al. 2019Focused Update on Atrial Fibrillation. https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000000665.

AF and Stroke Risk

- Development of AF increases stroke risk 5 fold[1]
- Recurrence of stroke is 2x greater within 6 months in AF[2]
- AF promotes stasis of blood, induces structural changes in the LA and induces hypercoagulability[3]
- The LAA is the most common location for thrombus[4]

1. Holmes DR, et al. Atrial Fibrillation and Stroke Management: Present and Future. *Seminars in Neurology* 2010;30:528–536
2. Wolf PA et al, Duration of Atrial Fibrillation and the Imminence of Stroke: The Framingham Study. *Stroke* 1983; 14:664-667
3. Watson T, et al. Mechanisms of thrombogenesis in atrial fibrillation: Virchow's triad revisited. *Lancet* 2009;373:155
4. Mahajan R, et al. Importance of the underlying substrate in determining thrombus location in atrial fibrillation: implications for left atrial appendage. *Heart* 2012;98:1120

What is the patients annual stroke risk?

1. 1%-2%
2. 3%-5%
3. 6%-8%
4. 8%-10%

Assessing Stroke Risk in AF

Criteria		Poss. Point
Congestive heart failure Signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction	Yes / No	+1
Hypertension Resting BP > 140/90 mmHg on at least 2 occasions or current antihypertensive pharmacologic treatment	Yes / No	+1
Age 75 years or older	Yes / No	+2
Diabetes mellitus Fasting glucose > 125 mg/dL or treatment with oral hypoglycemic agent and/or insulin	Yes / No	+1
Stroke, TIA, or TE Includes any history of cerebral ischemia	Yes / No	+2
Vascular disease Prior MI, peripheral arterial disease, or aortic plaque	Yes / No	+1
Age 65 to 74 years	Yes / No	+1
Sex **C**ategory (female) Female gender confers higher risk	Yes / No	+1

Table 2 Stroke or thromboembolism/100 years at risk in relation to $CHADS_2$ and CHA_2DS_2-VASc scores in 90 490 patients without warfarin throughout follow-up

	n	Ischaemic stroke		Stroke/TIA/peripheral emboli	
		Unadjusted	Adjusted for Aspirin[1]	Unadjusted	Adjusted for aspirin[a]
$CHADS_2$ score					
0	13 258	0.6	0.6	0.9	0.9
1	23 041	3.0	3.4	4.3	4.9
2	25 813	4.2	4.7	6.1	6.8
3	15 527	7.1	8.0	9.9	11.1
4	8767	11.1	12.6	14.9	16.8
5	3315	12.5	14.1	16.7	18.9
6	769	13.0	14.6	17.2	19.4
CHA_2DS_2-VASc score					
0	5343	0.2	0.2	0.3	0.3
1	6770	0.6	0.6	0.9	1.0
2	11 240	2.2	2.5	2.9	3.3
3	17 689	3.2	3.7	4.6	5.3
4	19 091	4.8	5.5	6.7	7.8
5	14 488	7.2	8.4	10.0	11.7
6	9577	9.7	11.4	13.6	15.9
7	4465	11.2	13.1	15.7	18.4
8	1559	10.8	12.6	15.2	17.9
9	268	12.23	14.4	17.4	20.3
All	90 490	4.5	5.0	6.2	7.0

[a]Adjustment made for exposure to aspirin treatment, assuming that aspirin provides a 22% reduction in TE risk, to give an indication of 'untreated' rates. For abbreviations and details on risk schema, see text.

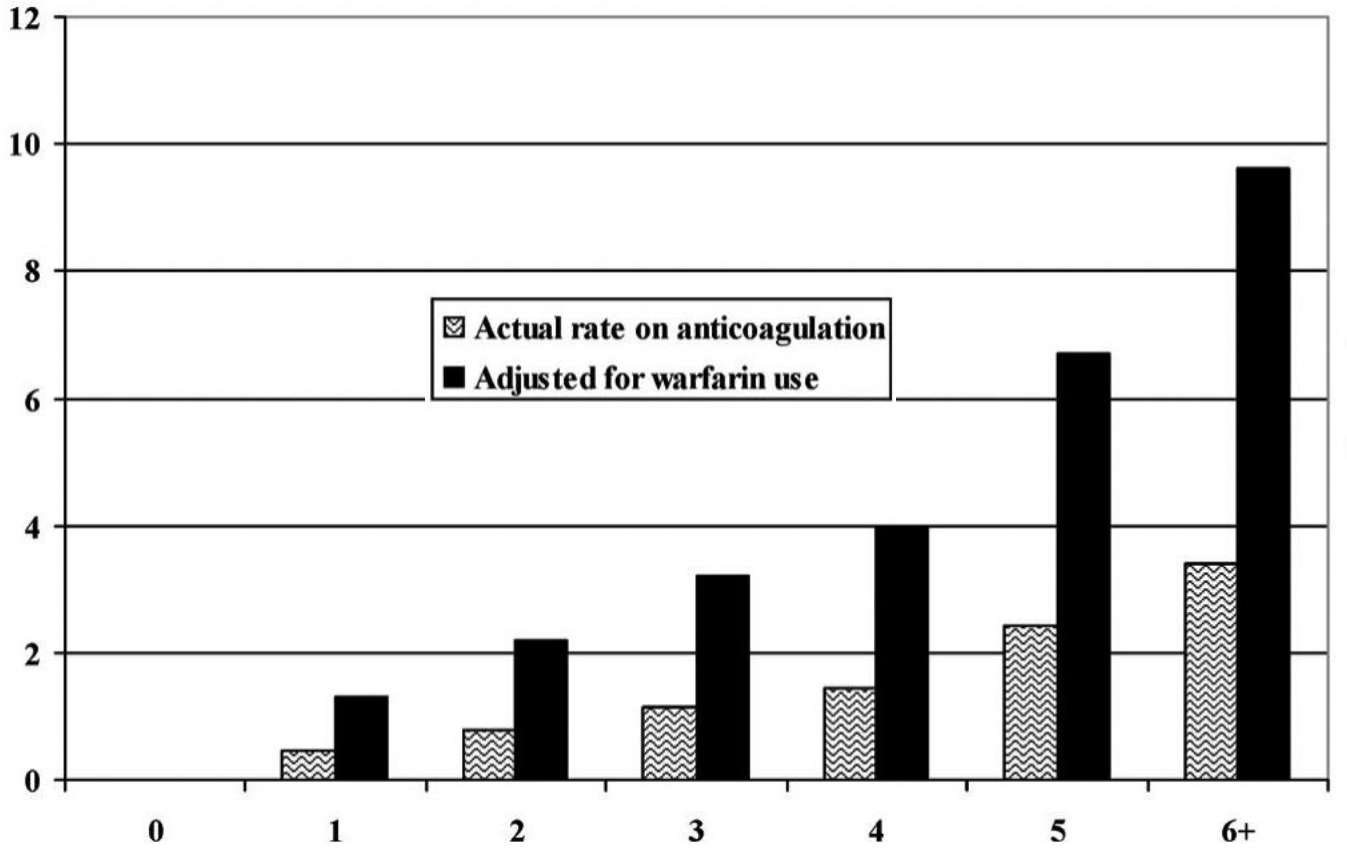
Friberg L and Lip G et al. European Heart Journal. 2012. 33: 1500-1510
January CT, et al. 2019 Focused Update on Atrial Fibrillation..

Predicting Stroke Risk by CHA2DS2VASC

Table 4. Stroke or Other Thromboembolism Events per Patient Year Based on the CHA_2DS_2VASc Scoring System

CHA_2DS_2 VASc Score	N	No. of TE Events/PY	TE Rate During 1 Year (95% CI)	TE Rate During 1 Year, Adjusted for Warfarin use*
0	1	0/2	0.00	0.0
1	422	3/653	0.46 (0.10, 1.34)	1.3
2	1230	15/1913	0.78 (0.44, 1.29)	2.2
3	1730	31/2673	1.16 (0.79, 1.64)	3.2
4	1718	38/2665	1.43 (1.01, 1.95)	4.0
5	1159	42/1732	2.42 (1.75, 3.26)	6.7
6	679	36/1016	3.54 (2.49, 4.87)	9.8
7	294	15/436	3.44 (1.94, 5.62)	9.6
8	82	3/125	2.41 (0.53, 6.88)	6.7
9	14	1/18	5.47 (0.91, 27.0)	15.2
Total	7329	184/11233	*P* value for trend	$P<0.0001$

*Theoretical TE rates without therapy: assuming that warfarin provides a 64% reduction in TE risk, based on Hart et al.[34] CI indicates confidence interval.



Lip G et al. Stroke. 2010. 41: 2731-2738

Who should receive long-term anticoagulation?

Patient Profile	Recommendation (Class of Recommendation, Level of Evidence)
AF and CHA_2DS_2-VASc score = 0 in men or 1 in women	It is reasonable to omit oral anticoagulant therapy (IIa, B)
AF and CHA_2DS_2-VASc score ≥ 2 in men	Oral anticoagulants are recommended (I, A & B)
AF and CHA_2DS_2-VASc score ≥ 3 in women	Oral anticoagulants are recommended (I, A & B)

Dealer's Choice: What to do about CHA2DS2VASc 1?

January CT, et al. 2019 Focused Update on Atrial Fibrillation. https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000000665.

What is idealized rate control?

1. 60 bpm
2. 80 bpm
3. 100 bpm
4. 110 bpm

The NEW ENGLAND JOURNAL of MEDICINE

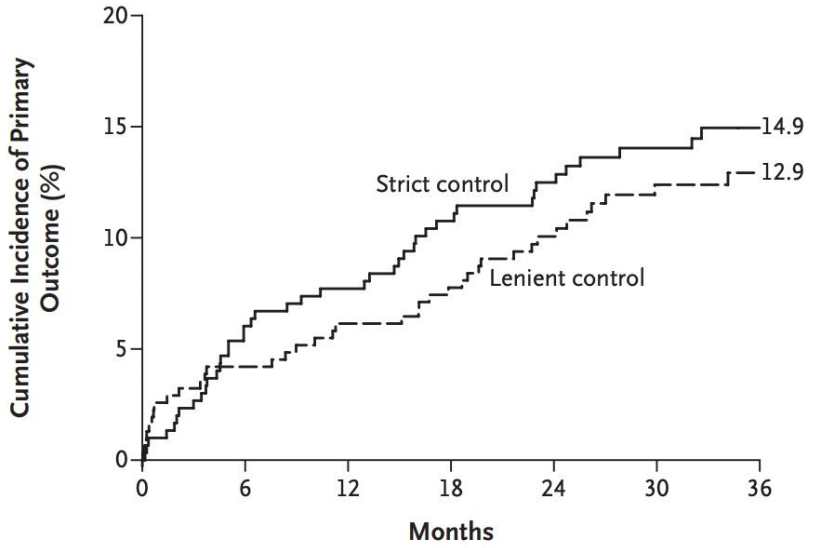
ESTABLISHED IN 1812 APRIL 15, 2010 VOL. 362 NO. 15

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*

624 patient with permanent AF

- 10% prior HF
- Randomization to 110 vs 80 bpm:
- Bb, CCB, Digoxin



No. at Risk

Strict control	303	282	273	262	246	212	131
Lenient control	311	298	290	285	255	218	138

Table 3. Cumulative Incidence of the Composite Primary Outcome and Its Components during the 3-Year Follow-up Period, According to Treatment Group.*

Outcome	Lenient Rate Control (N=311)	Strict Rate Control (N=303)	Hazard Ratio (90% CI)
	no. of patients (%)		
Composite primary outcome	38 (12.9)	43 (14.9)	0.84 (0.58–1.21)
Individual components			
Death from cardiovascular cause	9 (2.9)	11 (3.9)	0.79 (0.38–1.65)
From cardiac arrhythmia	3 (1.0)	4 (1.4)	
From cardiac cause other than arrhythmia	1 (0.3)	2 (0.8)	
From noncardiac vascular cause	5 (1.7)	5 (1.9)	
Heart failure	11 (3.8)	11 (4.1)	0.97 (0.48–1.96)
Stroke	4 (1.6)	11 (3.9)	0.35 (0.13–0.92)
Ischemic	3 (1.3)	8 (2.9)	
Hemorrhagic	1 (0.3)	4 (1.5)	
Systemic embolism	1 (0.3)	0	
Bleeding	15 (5.3)	13 (4.5)	1.12 (0.60–2.08)
Intracranial	0	3 (1.0)	
Extracranial	15 (5.3)	10 (3.5)	
Syncope	3 (1.0)	3 (1.0)	
Life-threatening adverse effect of rate-control drugs	3 (1.1)	2 (0.7)	
Sustained ventricular tachycardia or ventricular fibrillation	0	1 (0.3)	
Cardioverter–defibrillator implantation	0	1 (0.3)	
Pacemaker implantation	2 (0.8)	4 (1.4)	

Which AAD is best in HF?

1. Dronedarone
2. Flecainide
3. Amiodarone
4. Lidocaine

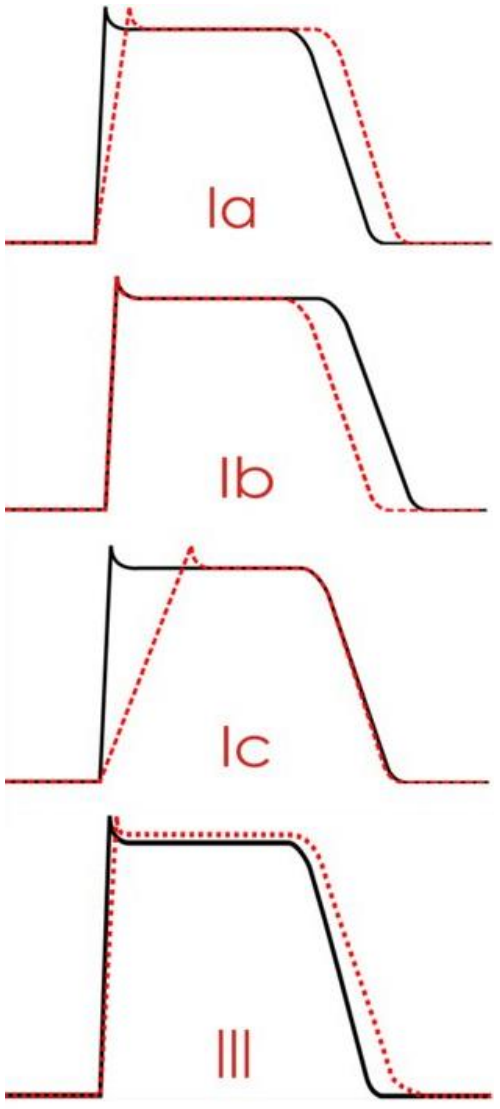
Anti-arrhythmic drugs for AF

Vaughan-Williams Classification

IA	IC	III
Quinidine	Flecainide	Sotalol
Procainamide	Propafenone	**Amiodarone**
Disopyramide		**Dofetilide**
		Dronedarone

II Beta Blockers

IV Calcium Channel Blockers



Antiarrhythmic Drug: Side Effects

- Quinidine: diarrhea, fever, rash, thrombocytopenia, granulomatous hepatitis, tinnitus, torsades
- Procainamide: vomiting, rash, lupus (~10%), agranulocytosis, torsades
- Disopyramide: anticholinergic effects; negative inotropic effects, VT, torsades
- Flecainide/propafenone : pro-arrhythmia – wide complex tachycardia- QRS prolongation
- **Sotalol/Ibutilide/Dofetilide: pro-arrhythmia - torsades**
- **Amiodarone: liver, lung, thyroid, skin, neurological and eye toxicity**

Does rhythm or rate control have survival advantage?

Atrial Fibrillation:
Rate Control versus Rhythm Control Trials

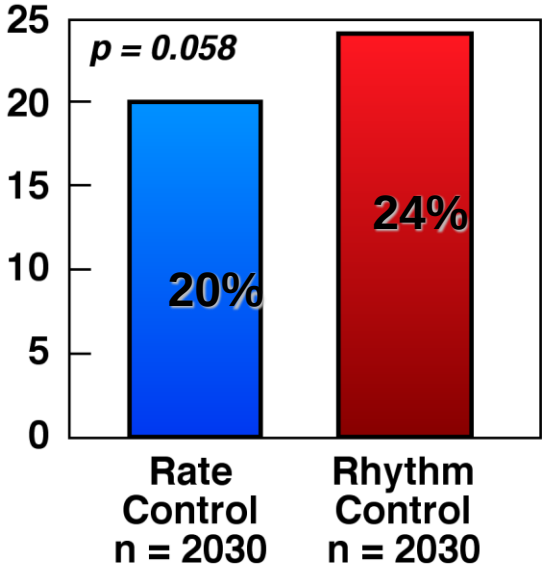
	PIAF	STAF	RACE	AFFIRM
n	252	200	522	4060
Follow-up (range)	1 year	19.6 months (0-36)	2.3 year	3.5 years (3.5-6)
Mean age (years)	61.5	65.8	68	69.7
Duration of AF	< 360 days	< 2 years	< 1 year	< 6 months
Important inclusion criteria	Symptomatic patients	Moderate risk of AF recurrence	1-2 previous DCC within 2 years	High risk of AF recurrence
Primary endpoint	Symptom improvement	Composite [a]	Composite [b]	Overall mortality
Rhythm control	55.1%	10%	22.6%	23.8% (at 5 years)
Rate control	60.8%	9%	17.2%	21.3% (at 5 years)
p (primary end point)	0.317	0.99	0.11	0.08

[a] Combination death, stroke or transient ischemic attack, cardiopulmonary resuscitation, or systemic embolism

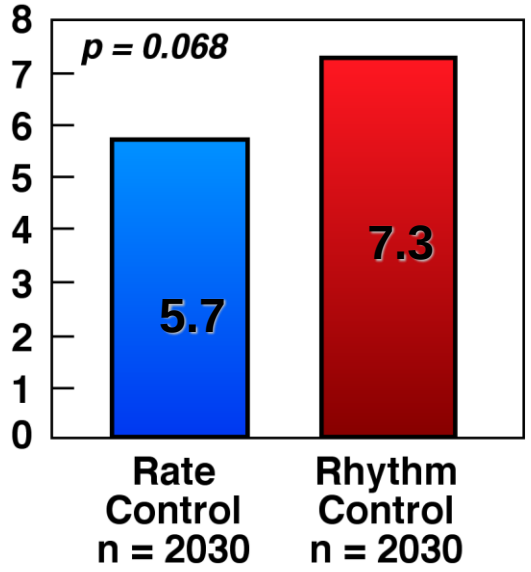
[b] Death from cardiovascular causes, heart failure, thromboembolic complications, bleeding, implantation of a pacemaker, and sever adverse effects of anti-arrhythmic drugs

AFFIRM Trial Results

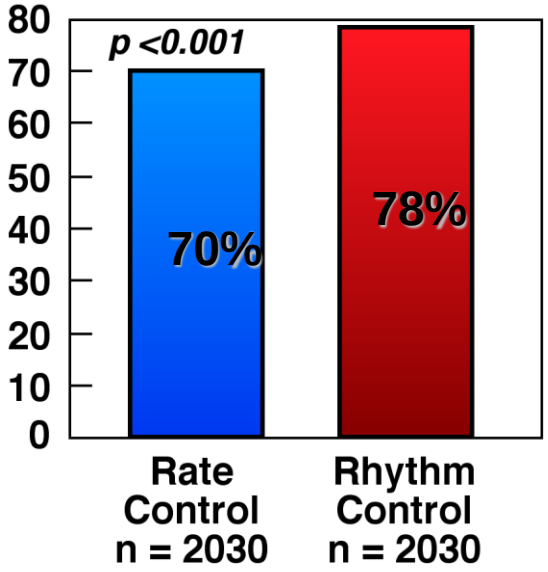
Mortality :
No difference



Strokes :
No difference



Hospitalizations*



4,060 patients; enrolled 1995-99; age > 65 yrs or <65 yrs with HTN, CHF; AF duration > 6 hours

PRIMARY ENDPOINT: Mortality; Secondary endpoints: stroke, QOL

RATE CONTROL: **Digoxin 51%, beta blockers 49%, Calcium channel blocker 41%, ablate and pace 5%**

RHYTHM CONTROL : **Amiodarone 39%, Sotalol 33%, Propafenone 10%, Procainamide 5%, Quinidine 5%.**

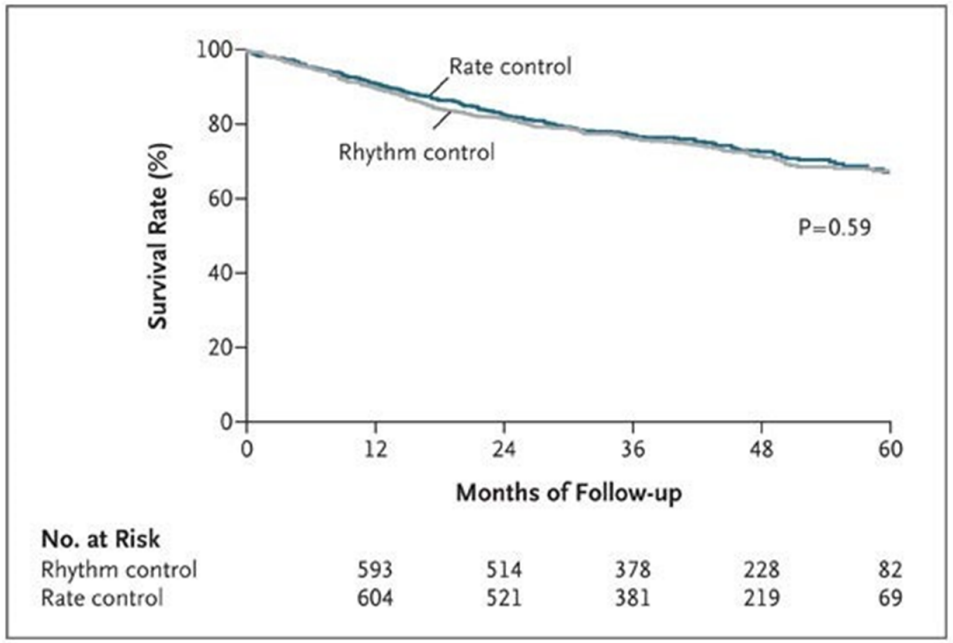
AFFIRM Investigators NEJM 2002; 347:1825-33

Table 1. Baseline Characteristics of the Patients.*

Variable	Rhythm-Control Group (N=682)	Rate-Control Group (N=694)
Male sex (%)	78	85
Age (yr)	66±11	67±11
Body-mass index†	27.8±5.4	28.0±5.1
Nonwhite race (%)‡	16	13
NYHA class III or IV (%)		
At baseline	32	31
During previous 6 mo	76	76
Predominant cardiac diagnosis (%)§		
Coronary artery disease	48	48
Valvular heart disease	5	5
Nonischemic cardiomyopathy	36	39
Congenital heart disease	1	1
Hypertensive heart disease	10	7
Coexisting conditions (%)		
Hypertension	49	46
Diabetes	22	20
Previous stroke or transient ischemic attack	11	8
Left ventricular ejection fraction (%)	27±6	27±6
Primary classification of atrial fibrillation (%)		
Paroxysmal	33	30
Persistent¶	67	70
≥6 Mo since first diagnosis of atrial fibrillation (%)	41	46
Atrial fibrillation on electrocardiography (%)	54	61
QRS duration (msec)	112±30	115±30
Previous electrical cardioversion (%)	34	37
Left atrial dimension (mm)	49±7	49±7
Previous hospitalization (%)		
For atrial fibrillation	51	55
For congestive heart failure (during previous 6 mo)	54	56
Concomitant drug therapy (%)		
Digoxin	64	65
Beta-blocker	80	78
Long-acting nitrate	17	17
Angiotensin-converting–enzyme inhibitor	86	86
Angiotensin-receptor blocker	11	11
Aldosterone antagonist	43	46
Oral anticoagulant	86	90
Aspirin	40	37
Lipid-lowering drug	44	42
Previous antiarrhythmic agent (%)	43	44
Implantable cardioverter–defibrillator (%)	7	7

* Plus–minus values are means ±SD. NYHA denotes New York Heart Association.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Race was self-reported.
§ Conditions in this category were determined by the investigator to be the predominant underlying cause of left ventricular systolic dysfunction.
¶ Atrial fibrillation was defined as persistent if the termination of most episodes required drug therapy or electrical cardioversion.

1376 patients with HF randomized to rate vs rhythm control



80% of patients treated with amiodarone

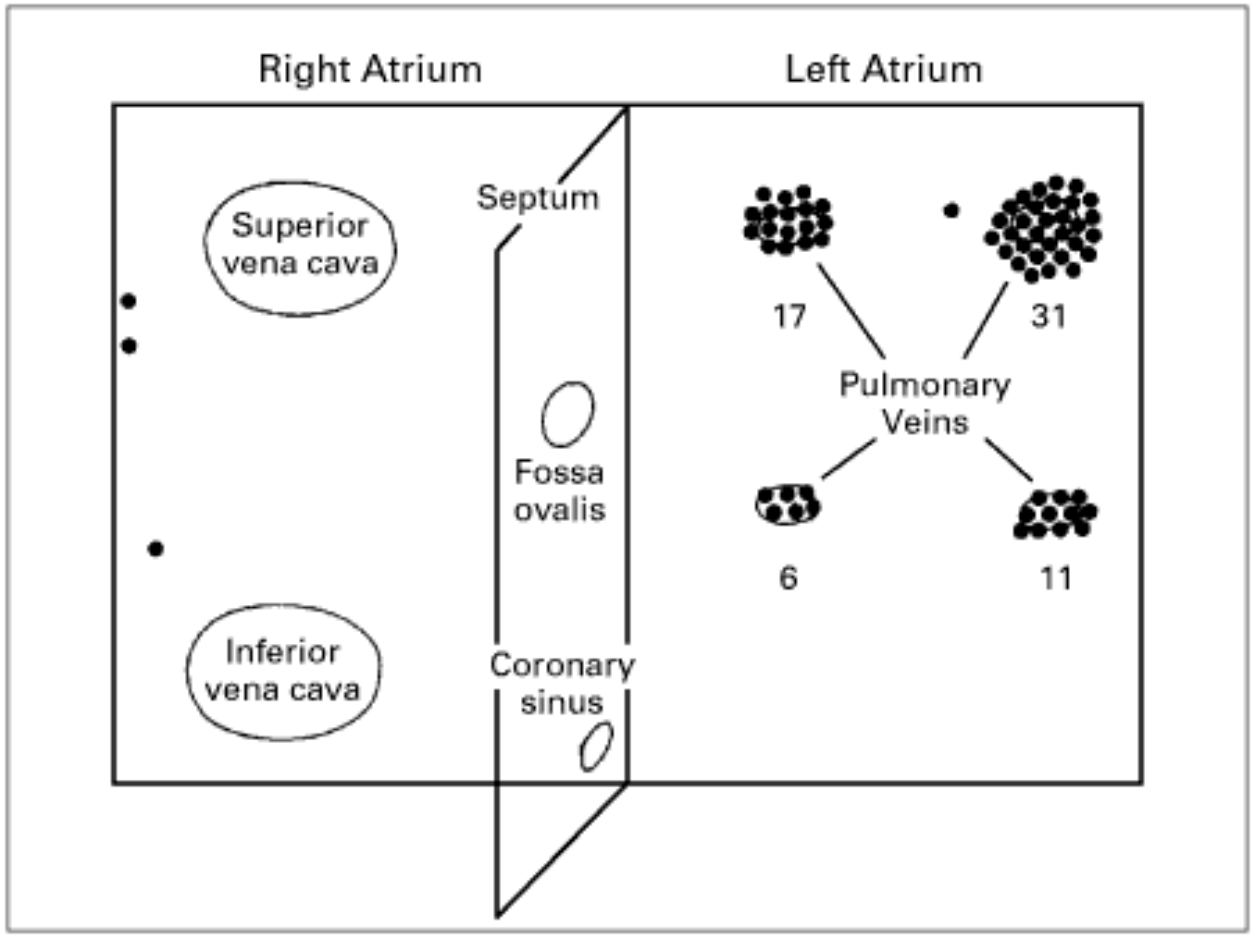
Amiodarone resulted in

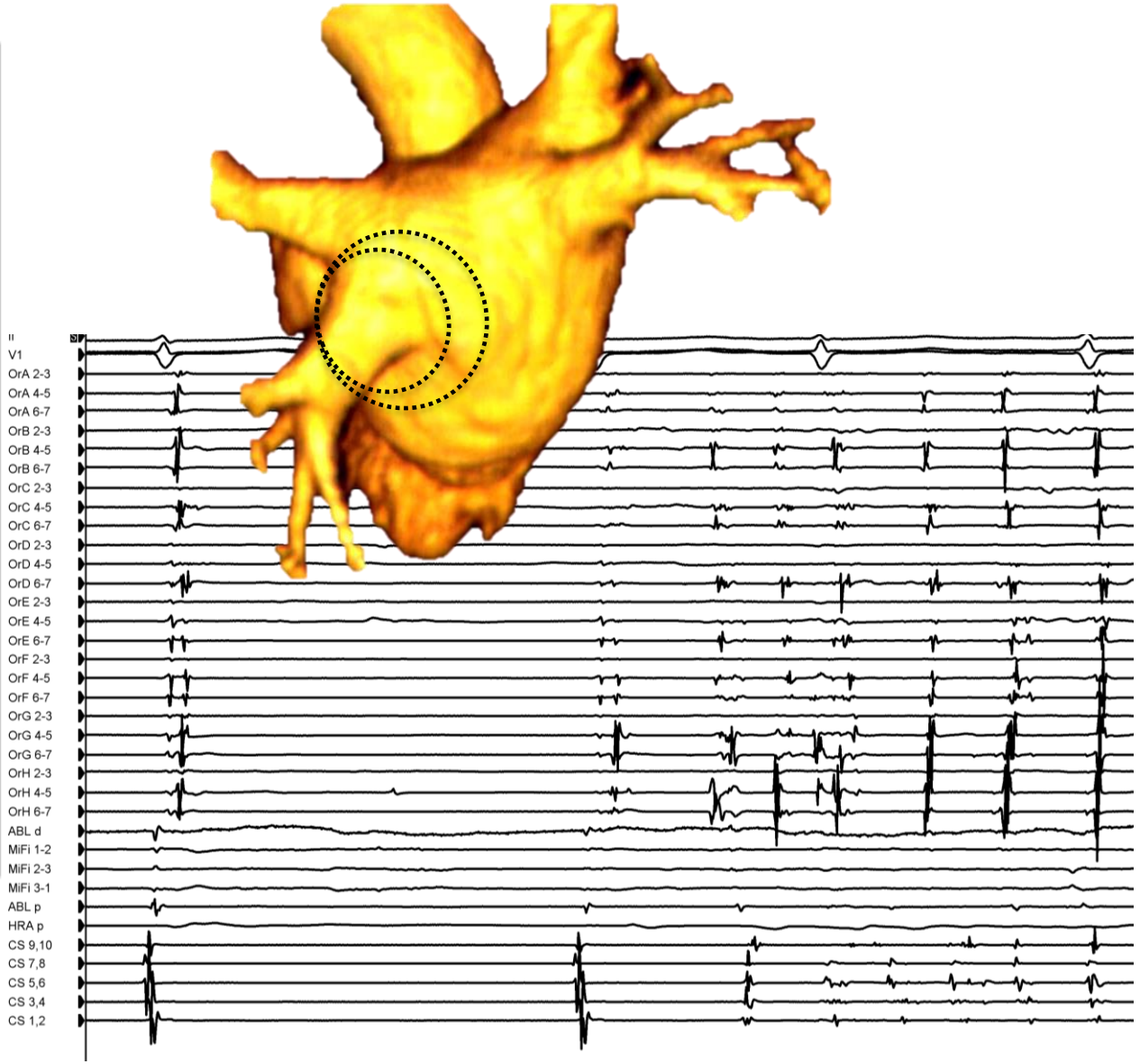
- ↑ maintenance of NSR
- No effect on mortality
- No effect on HF outcomes
- Intermittent ECGs were used to assess NSR
- CA not utilized
- Advanced AF population

Roy D, et al. *NEJM* 2008;358:2667-2677

Does the patient meet indication for catheter ablation?

‘Focal’ Atrial Fibrillation Ablation

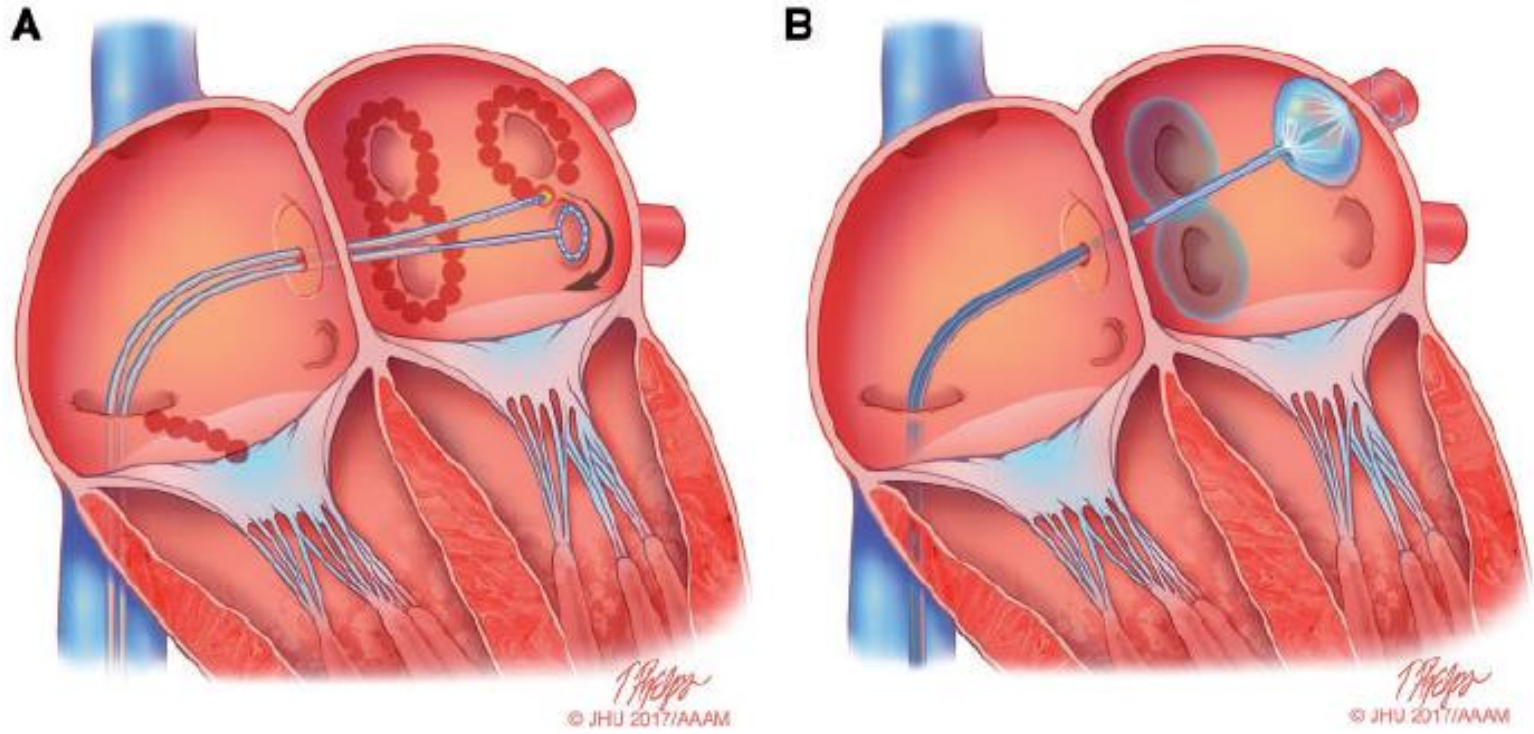




Haissaguerre et al. NEJM 1998,338:659-666

Catheter Ablation for AF

Energy sources may vary based on operator experience, preference, perceived complications and results, its clear that the goal is complete and verifiable pulmonary vein isolation with demonstration of entrance block.



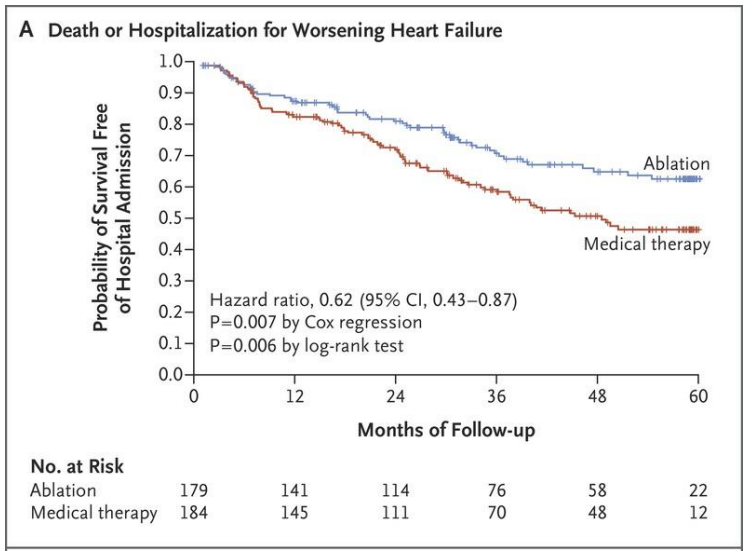
2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Europace* 2018 (20): 157-208

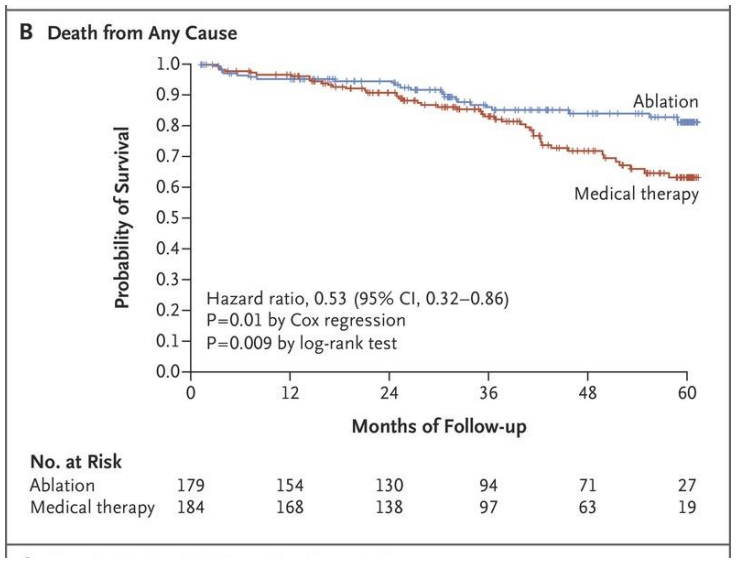
The NEW ENGLAND JOURNAL of MEDICINE

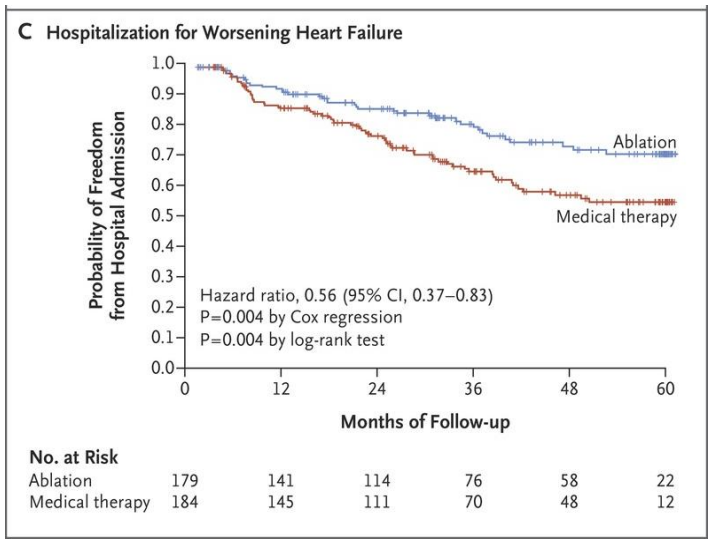
ESTABLISHED IN 1812 FEBRUARY 1, 2018 VOL. 378 NO. 5

Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

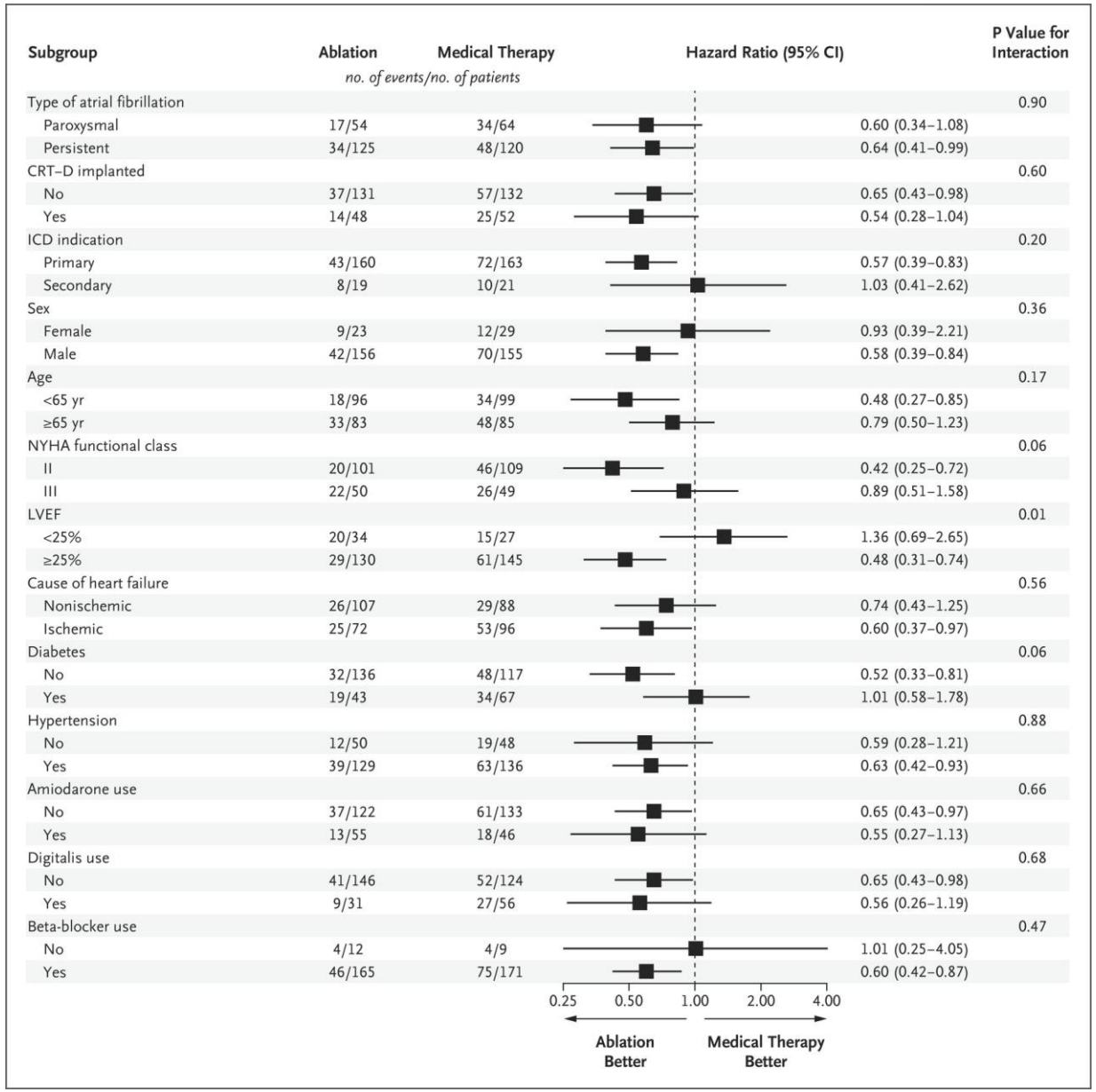






398 patients NYAH II-IV, EF<35% with ICD with px/pe AF were assigned to either CA or medical therapy

CASTLE-AF: Results



Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction

The CAMERA-MRI Study

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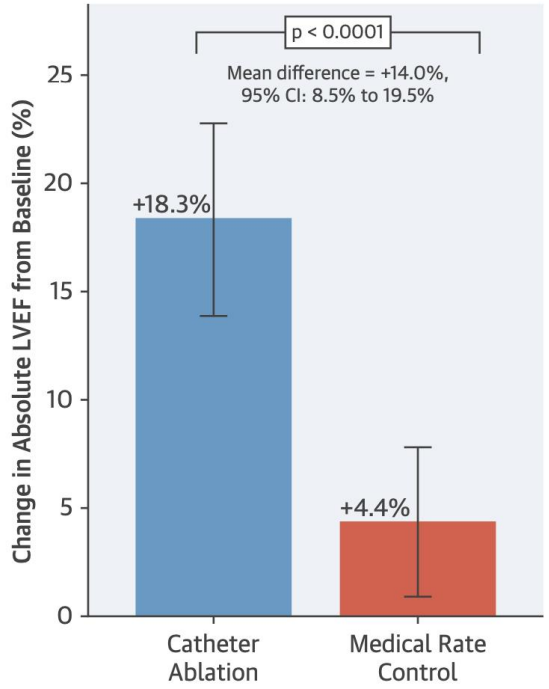
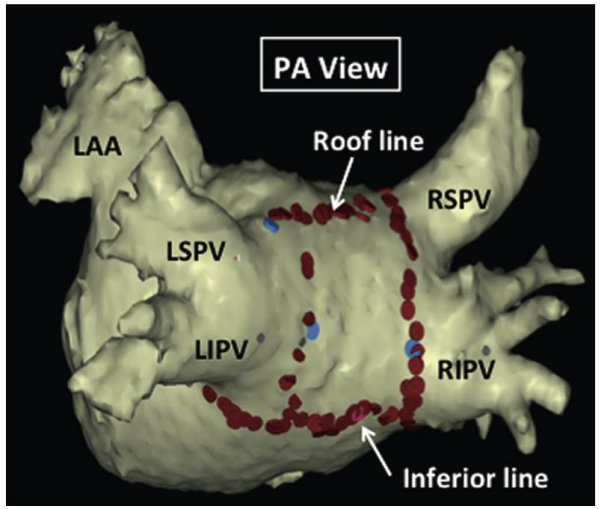
A Primary Endpoint: Change in LVEF at Baseline and 6 Months by Treatment Arm

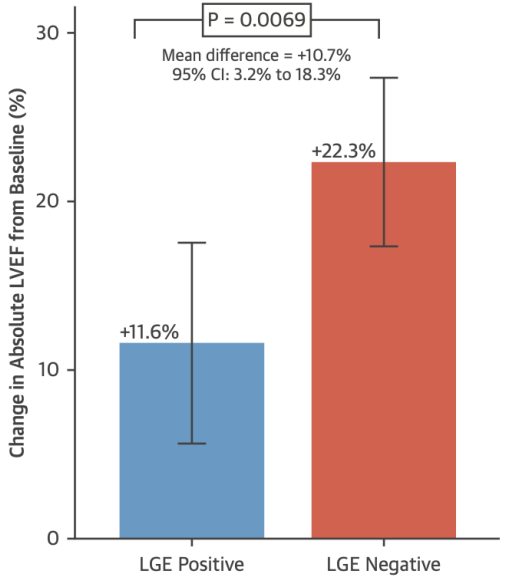


B Catheter Ablation Lesion Set in Left Atrium: Pulmonary Vein and Posterior Wall Isolation

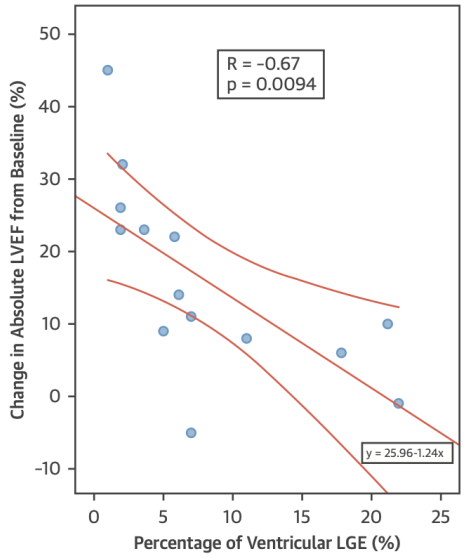


Prabhu, S. et al. J Am Coll Cardiol. 2017;70(16):1949-61.

A ΔLVEF Stratified by LGE Status in Patients Following Catheter Ablation



B Correlation Between % of Ventricular LGE and ΔLVEF Following Catheter Ablation

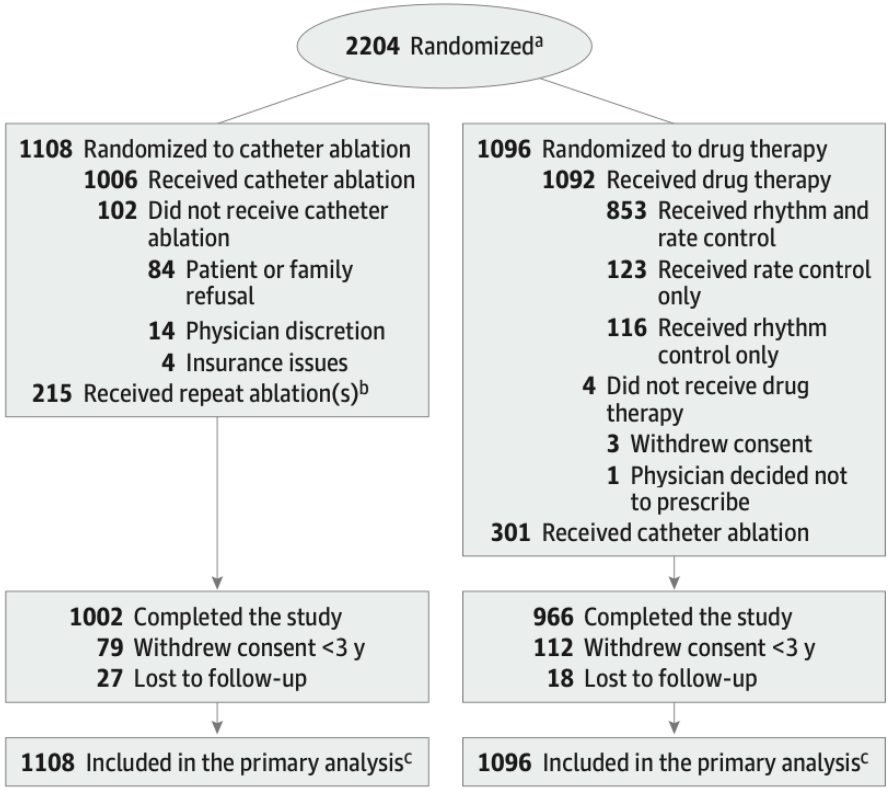


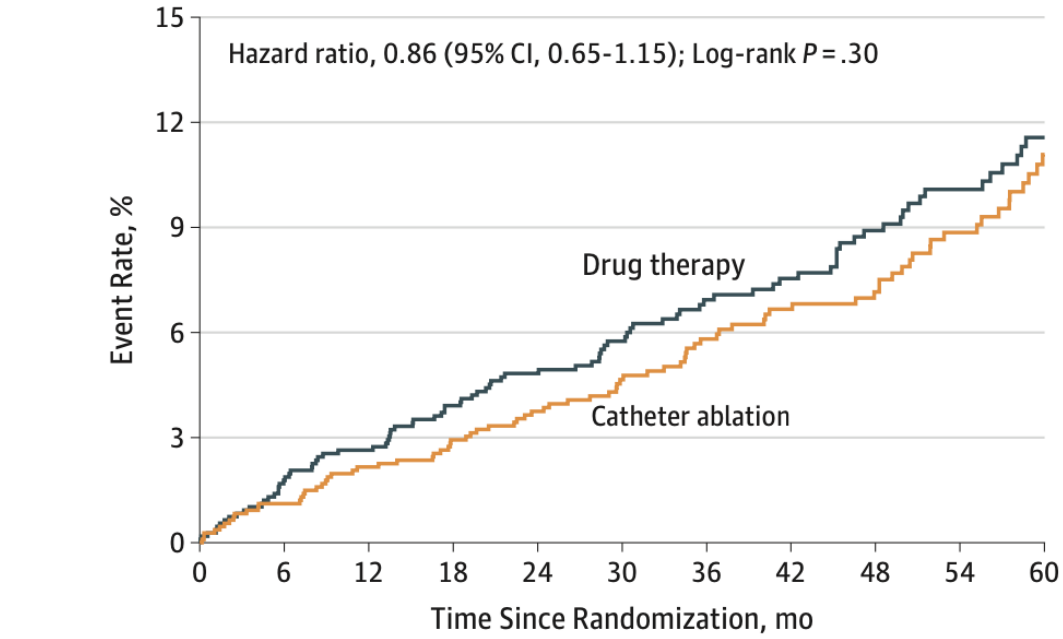
JAMA | Original Investigation

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

The CABANA Randomized Clinical Trial

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

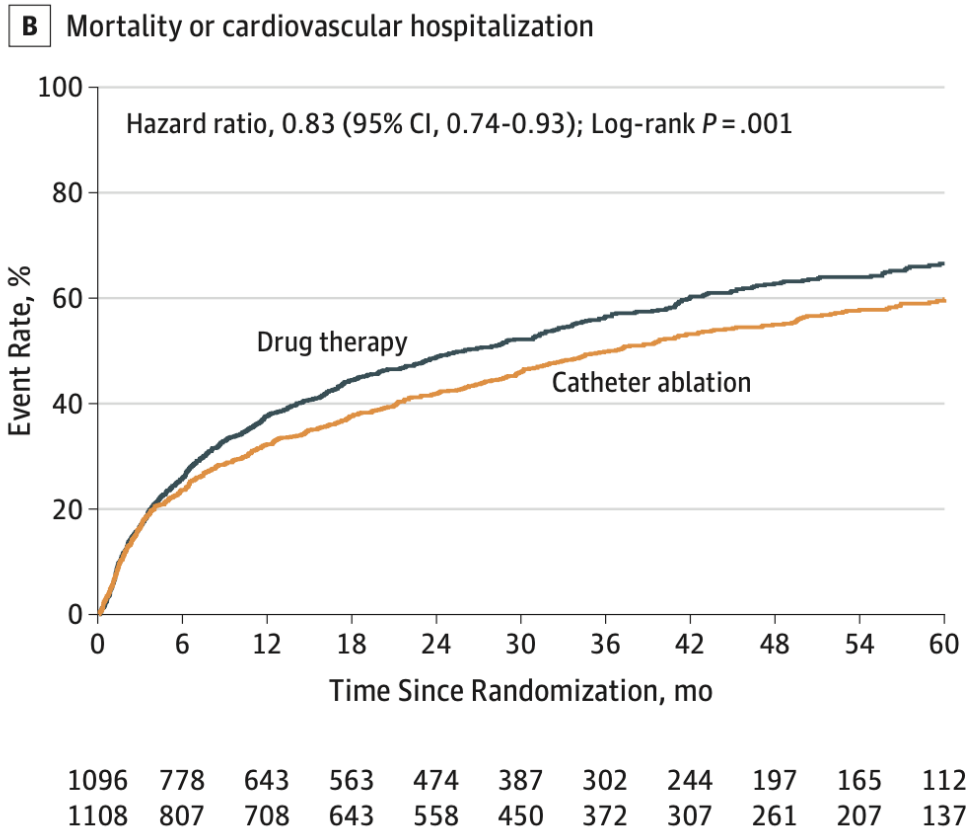


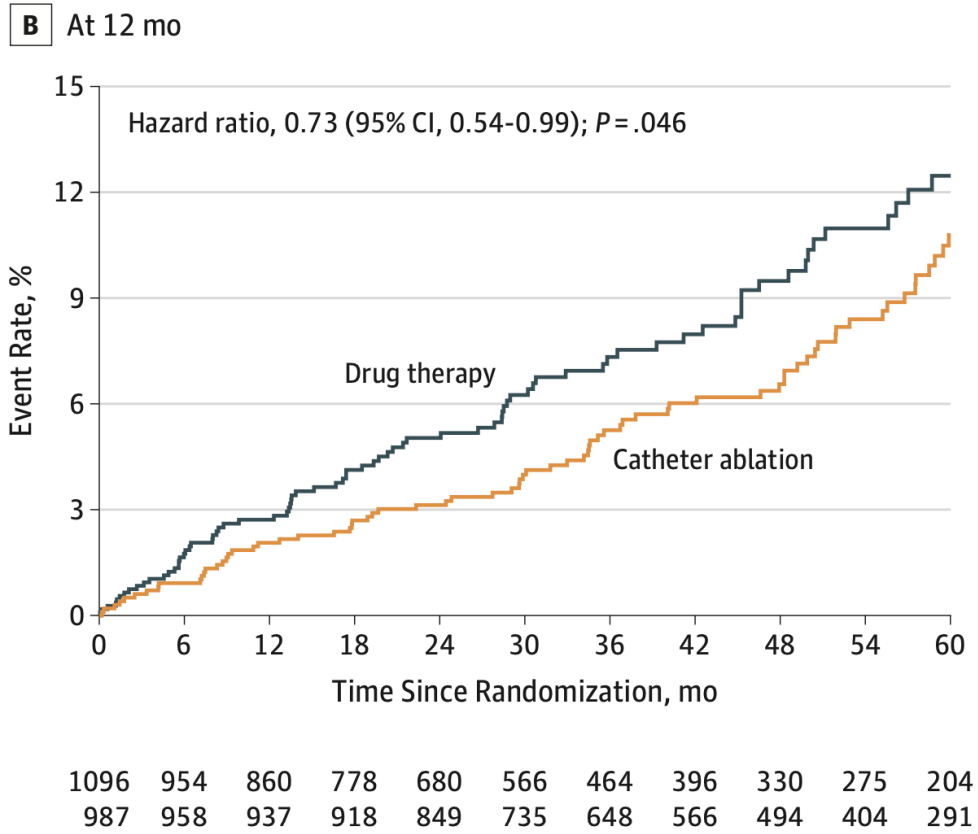


No. at risk											
Drug therapy	1096	1036	1006	970	880	763	652	578	499	418	312
Catheter ablation	1108	1045	1021	996	915	793	700	614	535	432	309

JAMA. April 2, 2019 Vol 321(13)

CABANA: Secondary Analyses





Per Protocol Analysis

9.2% of Catheter Ablation arm declined ablation
27.5% of Drug therapy arm crossed over to Ablation

Packer et al. JAMA. 2019. 321(13)

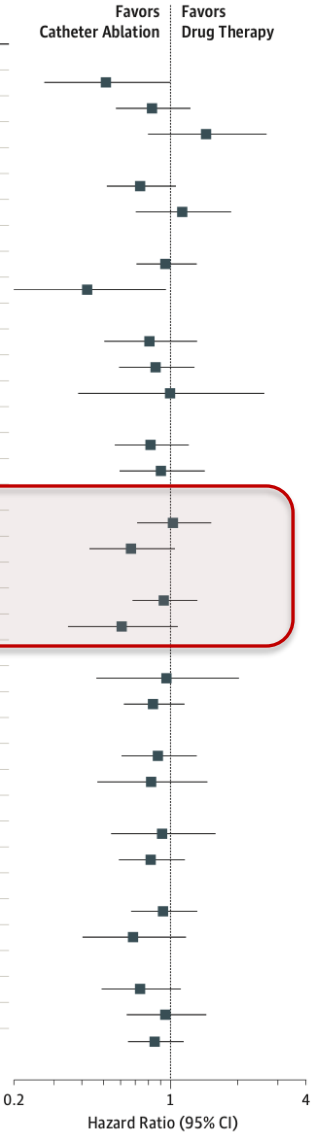
CABANA: HF Subgroup Analysis

Table 1. Baseline Demographics and Clinical Characteristics

Baseline Characteristic	No. (%) Catheter Ablation (n = 1108)	Drug Therapy (n = 1096)
Patients		
Age, median (Q1, Q3), y	68 (62, 72)	67 (62, 72)
<65	375 (33.8)	391 (35.7)
65-<75	577 (52.1)	553 (50.5)
≥75	156 (14.1)	152 (13.9)
Sex		
Male	695 (62.7)	690 (63.0)
Female	413 (37.3)	406 (37.0)
Race[a]		
White	1018 (92.0)	1007 (92.1)
Black or African American	39 (3.5)	38 (3.5)
Other[b]	50 (4.5)	48 (4.4)
Ethnicity		
Hispanic or Latino	30 (2.7)	32 (2.9)
Not Hispanic or Latino	1074 (97.3)	1062 (97.1)
Body mass index, median (Q1, Q3)[c]	30 (27, 34)	30 (26, 35)
AF severity (CCS class)[d]		
0 (Least severe)	105 (9.5)	118 (10.8)
1	166 (15.1)	173 (15.9)
2	350 (31.8)	353 (32.4)
3	401 (36.5)	382 (35.0)
4 (Most severe)	78 (7.1)	65 (6.0)
Heart function severity (NYHA class)[e]		
I (Least severe)	153 (13.9)	126 (11.6)
II/III (Most severe)	376 (34.3)	400 (36.7)

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

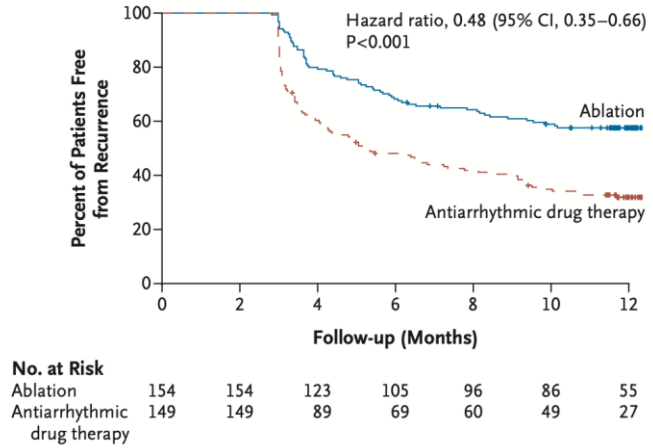
Source	No. of Events/Patients (Person-Years) Catheter Ablation	Drug Therapy	Hazard Ratio (95% CI)	Interaction *P* Value
Age, y				
<65	14/375 (1483)	27/391 (1498)	0.52 (0.27-1.00)	
≥65 and <75	50/577 (2159)	56/553 (2019)	0.84 (0.57-1.23)	.07
≥75	25/156 (514)	18/152 (529)	1.46 (0.80-2.67)	
Sex				
Male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



Late–Breaking RCTs: First-line AF ablation

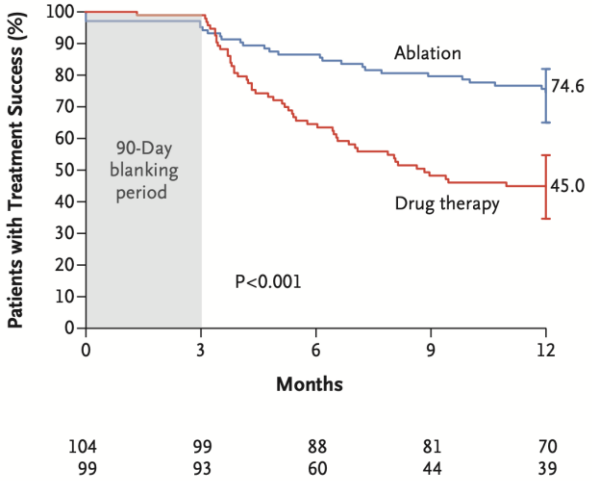
EARLY AF (Andrade et al) n = 303

- 73% male, 58 y/o, CHADS 1.9
- AAD: flecainide 76%
- 106 min procedure
- ***ILR within 24 hours in all***
- No crossovers
- **1 year: 57% vs 32% freedom AA**
  - *Symptomatic 89% vs 74% freedom*
  - *Burden 0% vs 0.13%*
- SAE: 3.2% *vs 4%*



STOP AF (Wazni et al) n = 203

- 63% male, 60 y/o, CHADS 2 (32%)
- AAD: flecainide `60%, amio 2%
- 139 min procedure
- **24h Holter 6/12, weekly telephone**
- 15 crossovers Med>Abl
- **1 year: 75% vs 45% freedom AA**
- SAE: 14% vs 14%



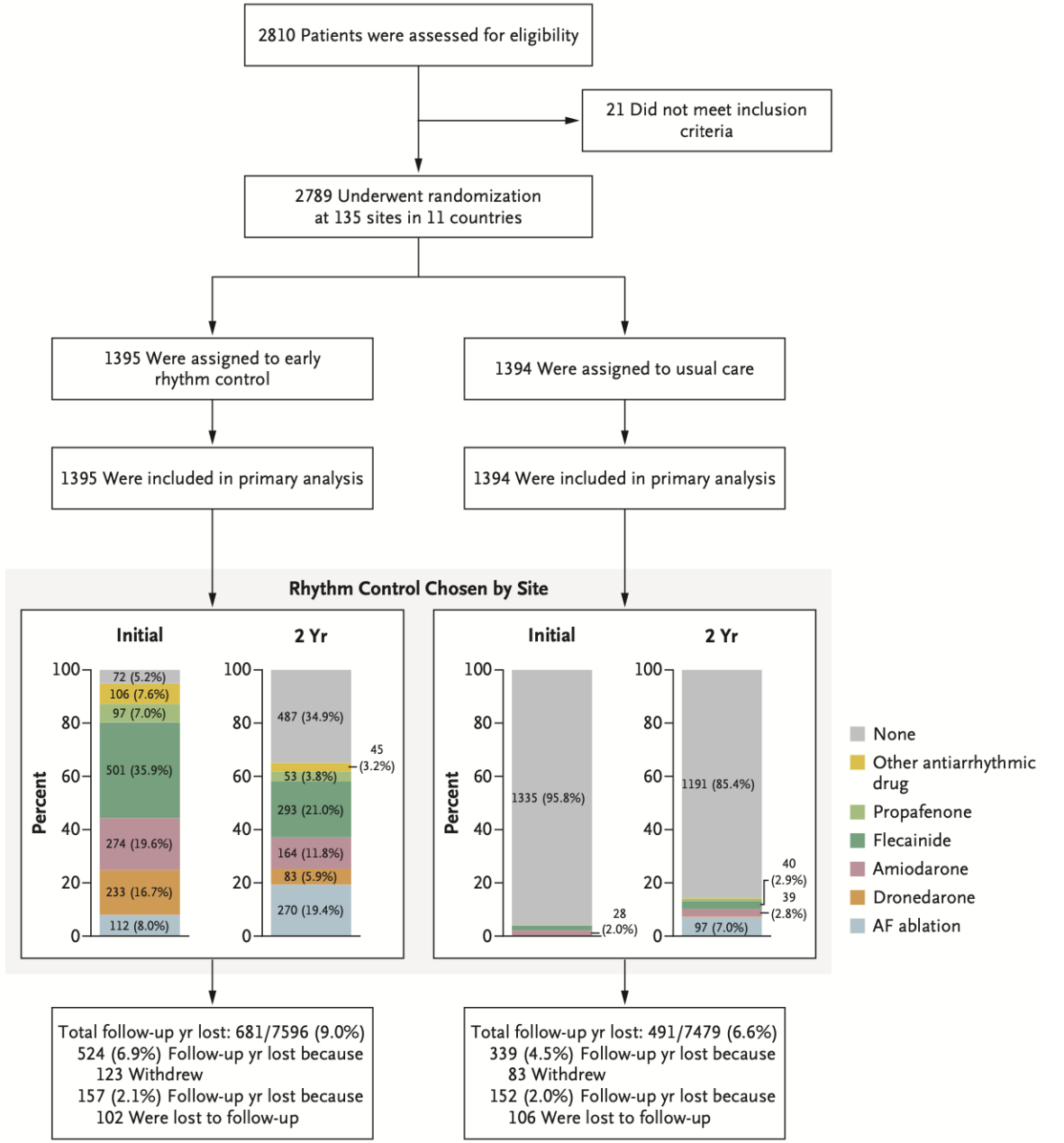
ORIGINAL ARTICLE

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

P. Kirchhof, A.J. Camm, A. Goette, A. Brandes, L. Eckardt, A. Elvan, T. Fetsch, I.C. van Gelder, D. Haase, L.M. Haegeli, F. Hamann, H. Heidbüchel, G. Hindricks, J. Kautzner, K.-H. Kuck, L. Mont, G.A. Ng, J. Rekosz, N. Schoen, U. Schotten, A. Suling, J. Taggeselle, S. Themistoclakis, E. Vettorazzi, P. Vardas, K. Wegscheider, S. Willems, H.J.G.M. Crijns, and G. Breithardt, for the EAST-AFNET 4 Trial Investigators*

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Early Rhythm Control (N=1395)	Usual Care (N=1394)
Age — yr	70.2±8.4	70.4±8.2
Female sex — no. (%)	645 (46.2)	648 (46.5)
Body-mass index†	29.2±5.4	29.3±5.4
Type of atrial fibrillation — no./total no. (%)		
First episode	528/1391 (38.0)	520/1394 (37.3)
Paroxysmal	501/1391 (36.0)	493/1394 (35.4)
Persistent	362/1391 (26.0)	381/1394 (27.3)
Sinus rhythm at baseline — no./total no. (%)	762/1389 (54.9)	743/1393 (53.3)
Median days since atrial fibrillation diagnosis (IQR)‡	36.0 (6.0–114.0)	36.0 (6.0–112.0)
Absence of atrial fibrillation symptoms — no./total no. (%)§	395/1305 (30.3)	406/1328 (30.6)
Previous cardioversion — no./total no. (%)	546/1364 (40.0)	543/1389 (39.1)
Concomitant cardiovascular conditions		
Previous stroke or transient ischemic attack — no. (%)	175 (12.5)	153 (11.0)
At least mild cognitive impairment — no./total no. (%)¶	582/1326 (43.9)	584/1341 (43.5)
Arterial hypertension — no. (%)	1230 (88.2)	1220 (87.5)
Blood pressure — mm Hg‖		
Systolic	136.5±19.4	137.5±19.3
Diastolic	80.9±12.1	81.3±12.0
Stable heart failure — no. (%)**	396 (28.4)	402 (28.8)
CHA_2DS_2-VASc score††	3.4±1.3	3.3±1.3
Valvular heart disease — no./total no. (%)	609/1389 (43.8)	642/1391 (46.2)
Chronic kidney disease of MDRD stage 3 or 4 — no. (%)‡‡	172 (12.3)	179 (12.8)
Medication at discharge — no./total no. (%)§§		
Oral anticoagulation with NOAC or VKA	1267/1389 (91.2)	1250/1393 (89.7)
Digoxin or digitoxin	46/1389 (3.3)	85/1393 (6.1)
Beta-blocker	1058/1389 (76.2)	1191/1393 (85.5)
ACE inhibitors or angiotensin II receptor blocker	953/1389 (68.6)	979/1393 (70.3)
Mineralocorticoid-receptor antagonist	90/1389 (6.5)	92/1393 (6.6)
Diuretic	559/1389 (40.2)	561/1393 (40.3)
Statin	628/1389 (45.2)	568/1393 (40.8)
Platelet inhibitor	229/1389 (16.5)	226/1393 (16.2)



Kirchof, P et al. NEJM. 2020.

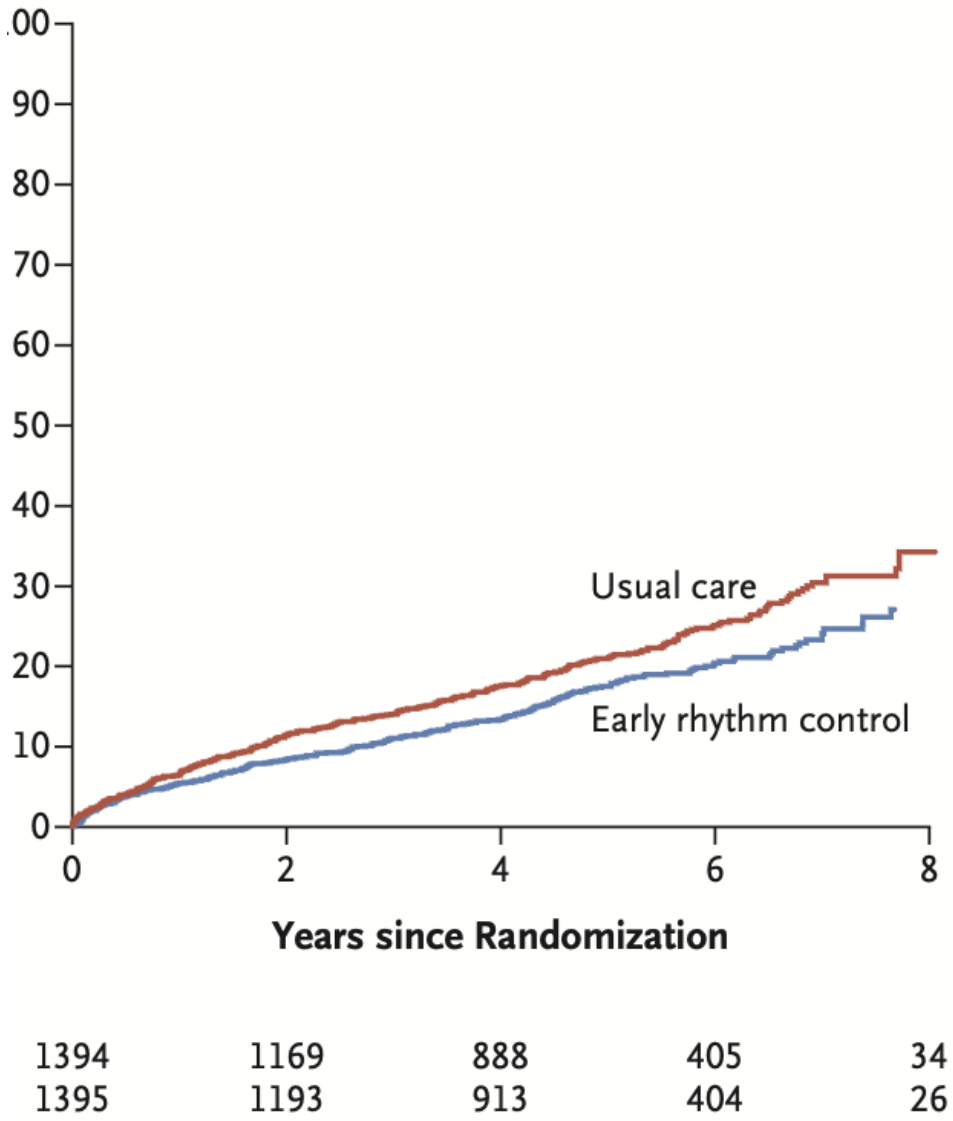


Table 2. Efficacy Outcomes.*

Outcome	Early Rhythm Control	Usual Care	Treatment Effect
First primary outcome — events/person-yr (incidence/100 person-yr)	249/6399 (3.9)	316/6332 (5.0)	0.79 (0.66 to 0.94)†
Components of first primary outcome — events/person-yr (incidence/100 person-yr)			
Death from cardiovascular causes	67/6915 (1.0)	94/6988 (1.3)	0.72 (0.52 to 0.98)‡
Stroke	40/6813 (0.6)	62/6856 (0.9)	0.65 (0.44 to 0.97)‡
Hospitalization with worsening of heart failure	139/6620 (2.1)	169/6558 (2.6)	0.81 (0.65 to 1.02)‡
Hospitalization with acute coronary syndrome	53/6762 (0.8)	65/6816 (1.0)	0.83 (0.58 to 1.19)‡
Second primary outcome — nights spent in hospital/yr	5.8±21.9	5.1±15.5	1.08 (0.92 to 1.28)§
Key secondary outcomes at 2 yr			
Change in left ventricular ejection fraction — %	1.5±9.8	0.8±9.8	0.23 (–0.46 to –0.91)¶
Change in EQ-5D score‖	–1.0±21.4	–2.7±22.3	1.07 (–0.68 to 2.82)¶
Change in SF-12 Mental Score**	0.7±10.6	1.6±10.1	–1.20 (–2.04 to –0.37)¶
Change in SF-12 Physical Score**	0.3±8.5	0.1±8.2	0.33 (–0.39 to 1.06)¶
Change in MoCA score	0.1±3.3	0.1±3.2	–0.14 (–0.39 to 0.12)¶
Sinus rhythm — no. of patients with feature/total no. (%)	921/1122 (82.1)	687/1135 (60.5)	3.13 (2.55 to 3.84)††
Asymptomatic — no. of patients with feature/total no. (%)‡‡	861/1159 (74.3)	850/1171 (72.6)	1.14 (0.93 to 1.40)††

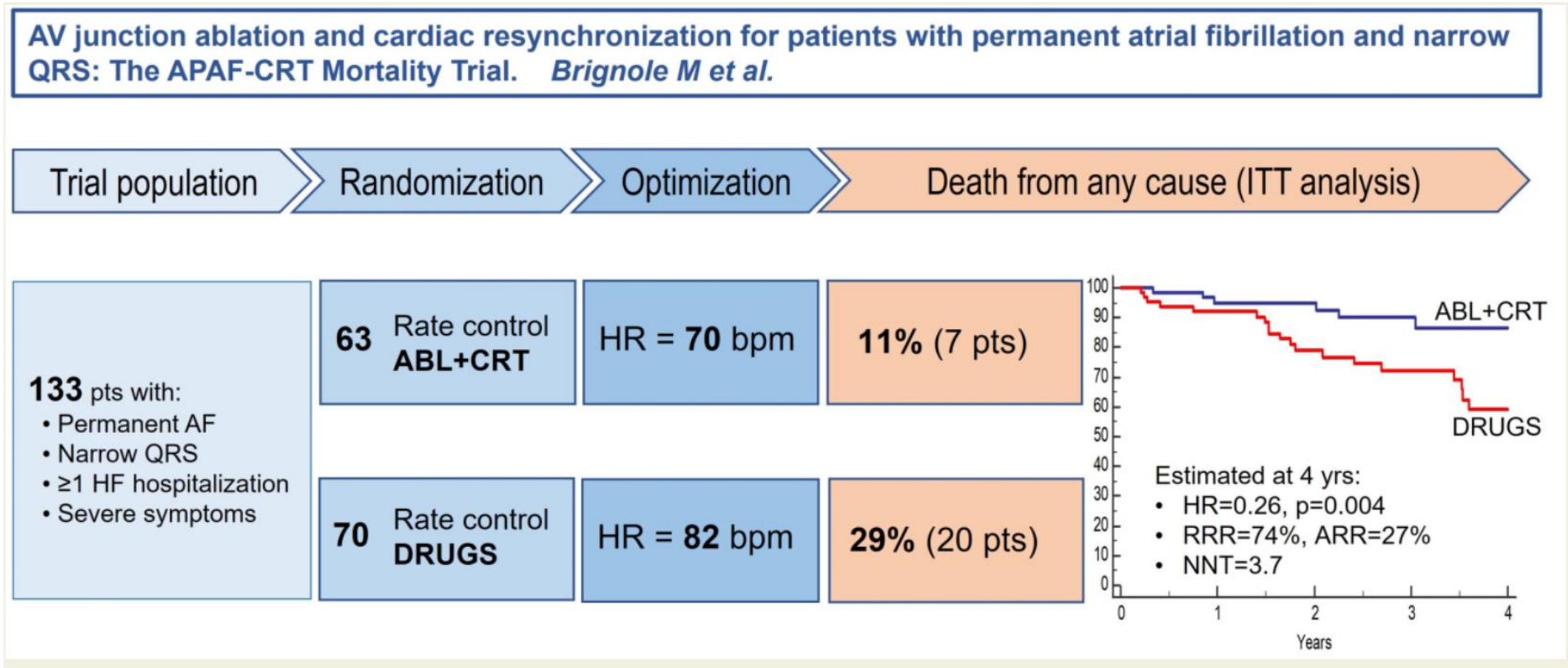
Early rhythm therapy reduced death, stroke, and hospitalization HF/ACS

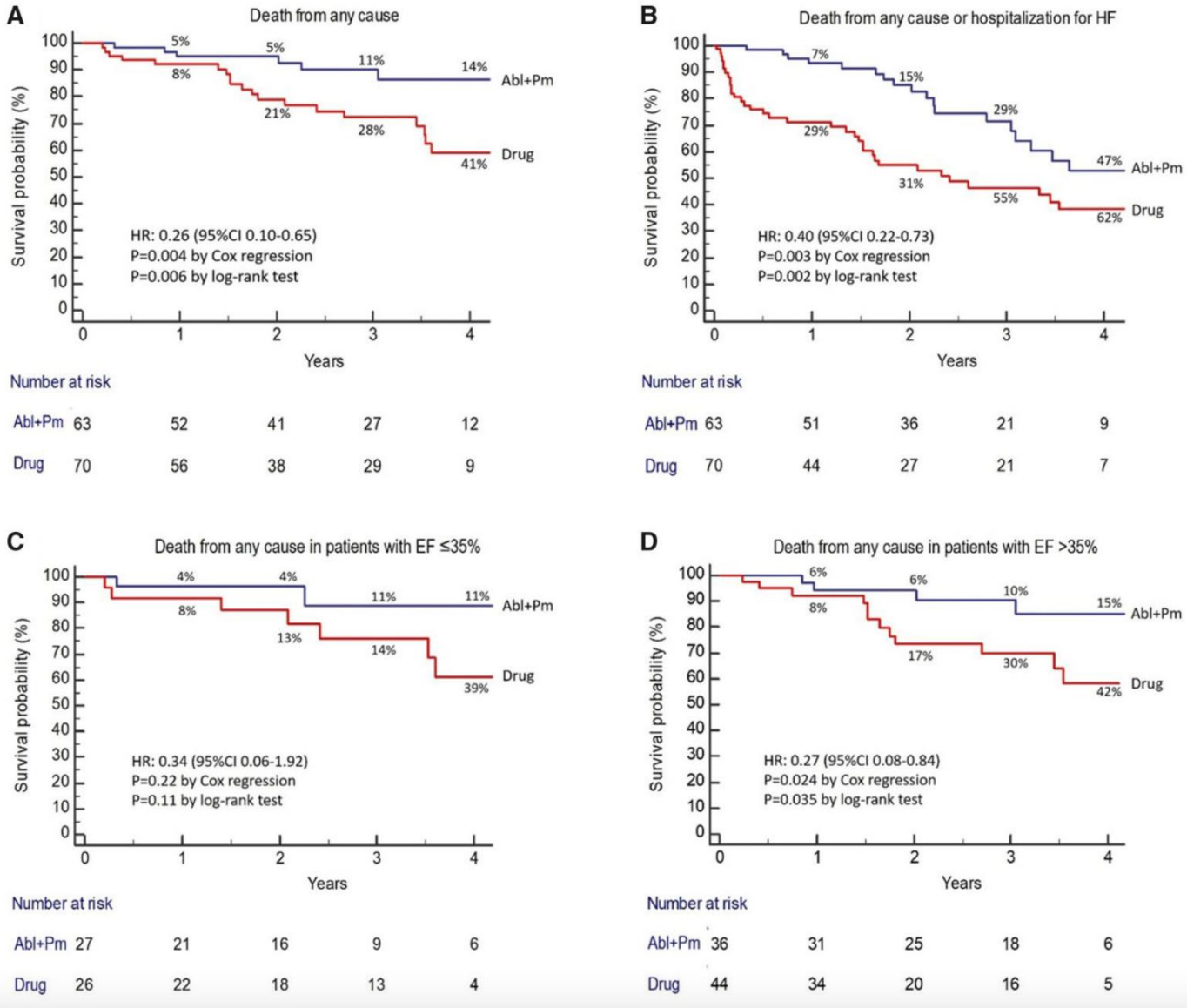
Kirchof, P et al. NEJM. 2020.

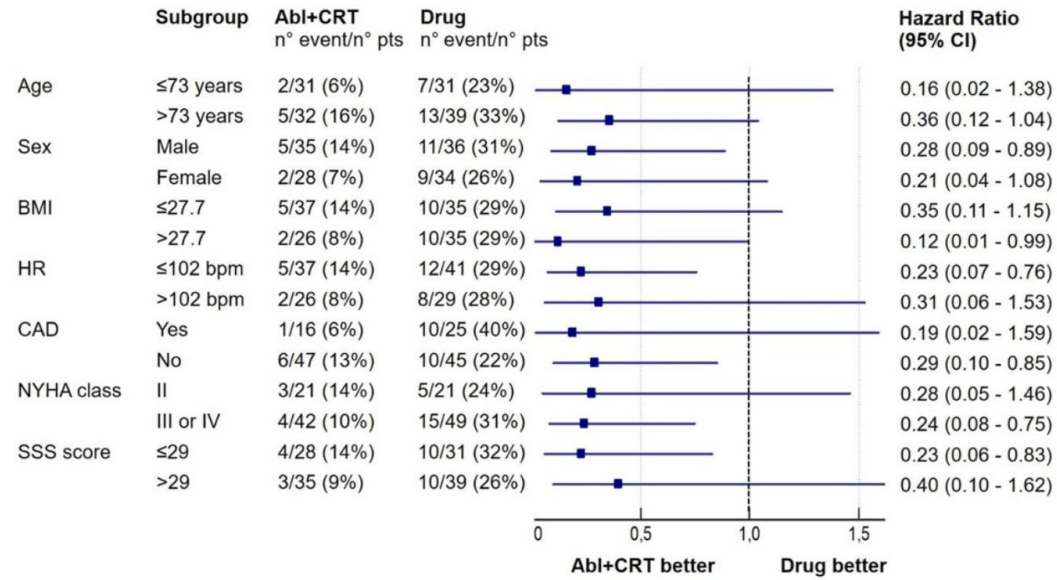
ESC European Society of Cardiology
European Heart Journal (2021) **42**, 4731–4739
doi:10.1093/eurheartj/ehab569
FASTTRACK CLINICAL RESEARCH
Arrhythmias

AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial

Michele Brignole [1,2]*, Francesco Pentimalli [3], Pietro Palmisano [4], Maurizio Landolina[5], Fabio Quartieri[6], Eraldo Occhetta[7], Leonardo Calò [8], Giuseppe Mascia [9], Lluis Mont[10], Kevin Vernooy [11], Vincent van Dijk[12], Cor Allaart[13], Laurent Fauchier [14], Maurizio Gasparini [15], Gianfranco Parati [2,16], Davide Soranna[17], Michiel Rienstra [18], and Isabelle C. Van Gelder[18]; for the APAF-CRT Trial Investigators†




A
Death from any cause
Survival probability (%)
Years
5%
5%
11%
14%
8%
21%
28%
41%
Abl+Pm
Drug
HR: 0.26 (95%CI 0.10-0.65)
P=0.004 by Cox regression
P=0.006 by log-rank test
Number at risk
Abl+Pm 63 52 41 27 12
Drug 70 56 38 29 9
B
Death from any cause or hospitalization for HF
Survival probability (%)
Years
7%
15%
29%
47%
29%
31%
55%
62%
Abl+Pm
Drug
HR: 0.40 (95%CI 0.22-0.73)
P=0.003 by Cox regression
P=0.002 by log-rank test
Number at risk
Abl+Pm 63 51 36 21 9
Drug 70 44 27 21 7
C
Death from any cause in patients with EF ≤35%
Survival probability (%)
Years
4%
4%
11%
11%
8%
13%
14%
39%
Abl+Pm
Drug
HR: 0.34 (95%CI 0.06-1.92)
P=0.22 by Cox regression
P=0.11 by log-rank test
Number at risk
Abl+Pm 27 21 16 9 6
Drug 26 22 18 13 4
D
Death from any cause in patients with EF >35%
Survival probability (%)
Years
6%
6%
10%
15%
8%
17%
30%
42%
Abl+Pm
Drug
HR: 0.27 (95%CI 0.08-0.84)
P=0.024 by Cox regression
P=0.035 by log-rank test
Number at risk
Abl+Pm 36 31 25 18 6
Drug 44 34 20 16 5


Subgroup
Abl+CRT n° event/n° pts
Drug n° event/n° pts
Hazard Ratio (95% CI)
Age ≤73 years 2/31 (6%) 7/31 (23%) 0.16 (0.02 - 1.38)
>73 years 5/32 (16%) 13/39 (33%) 0.36 (0.12 - 1.04)
Sex Male 5/35 (14%) 11/36 (31%) 0.28 (0.09 - 0.89)
Female 2/28 (7%) 9/34 (26%) 0.21 (0.04 - 1.08)
BMI ≤27.7 5/37 (14%) 10/35 (29%) 0.35 (0.11 - 1.15)
>27.7 2/26 (8%) 10/35 (29%) 0.12 (0.01 - 0.99)
HR ≤102 bpm 5/37 (14%) 12/41 (29%) 0.23 (0.07 - 0.76)
>102 bpm 2/26 (8%) 8/29 (28%) 0.31 (0.06 - 1.53)
CAD Yes 1/16 (6%) 10/25 (40%) 0.19 (0.02 - 1.59)
No 6/47 (13%) 10/45 (22%) 0.29 (0.10 - 0.85)
NYHA class II 3/21 (14%) 5/21 (24%) 0.28 (0.05 - 1.46)
III or IV 4/42 (10%) 15/49 (31%) 0.24 (0.08 - 0.75)
SSS score ≤29 4/28 (14%) 10/31 (32%) 0.23 (0.06 - 0.83)
>29 3/35 (9%) 10/39 (26%) 0.40 (0.10 - 1.62)
0
0,5
1,0
1,5
Abl+CRT better
Drug better