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Atrial fibrillation something more to learn?

Catheter ablation or antiarrhythmic drugs 20 years later

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Conflict of interest disclosure

- *Dr. De Ponti has received :*

-lecture fees from Biosense Webster and Biotronik

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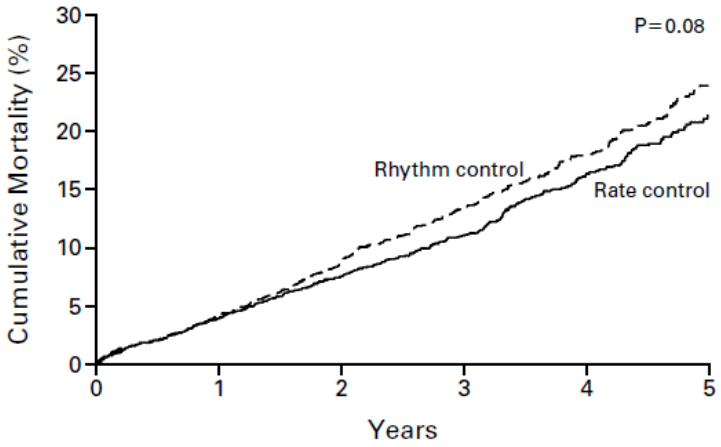
Comparison of rate control and rhythm control in pts with AF: AFFIRM study

RATE VERSUS RHYTHM CONTROL FOR ATRIAL FIBRILLATION



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)

Table 3. Adverse Events.*

Event	Overall (N=4060)	Rate-Control Group (N=2027)	Rhythm-Control Group (N=2033)	P Value
	no. of patients (%)			
Primary end point (death)	666 (26.3)	310 (25.9)	356 (26.7)	0.08†
Secondary end point (composite of death, disabling stroke, disabling anoxic encephalopathy, major bleeding, and cardiac arrest)	861 (32.3)	416 (32.7)	445 (32.0)	[illegible]
Torsade de pointes	14 (0.5)	2 (0.2)‡	12 (0.8)	0.007
Sustained ventricular tachycardia	15 (0.6)	9 (0.7)	6 (0.6)	[illegible]
Cardiac arrest followed by resuscitation				
Ventricular fibrillation or ventricular tachycardia	19 (0.6)	10 (0.7)	9 (0.5)	0.83
Pulseless electrical activity, bradycardia, or other rhythm	10 (0.3)	1 (<0.1)	9 (0.6)	0.01
Central nervous system event				
Total	211 (8.2)	105 (7.4)	106 (8.9)	0.93
Ischemic stroke§	157 (6.3)	77 (5.5)	80 (7.1)	0.79
After discontinuation of warfarin	69	25	44	
During warfarin but with INR <2.0	44	27	17	
Concurrent atrial fibrillation	67	42	25	
Primary intracerebral hemorrhage	34 (1.2)	18 (1.1)	16 (1.3)	0.73
Subdural or subarachnoid hemorrhage	24 (0.8)	11 (0.8)	13 (0.8)	0.68
Disabling anoxic encephalopathy	9 (0.3)	4 (0.2)	5 (0.4)	0.74
Myocardial infarction	140 (5.5)	67 (4.9)	73 (6.1)	0.60
Hemorrhage not involving the central nervous system	203 (7.3)	107 (7.7)	96 (6.9)	0.44
Systemic embolism	16 (0.5)	9 (0.5)	7 (0.4)	0.62
Pulmonary embolism	8 (0.3)	2 (0.1)	6 (0.5)	[illegible]
Hospitalization after base line	2594 (76.6)	1220 (73.0)	1374 (80.1)	<0.001

*Percentages were derived from a Kaplan–Meier analysis. P values were derived from the log-rank statistic.

Wyse et al. NEJM 2002

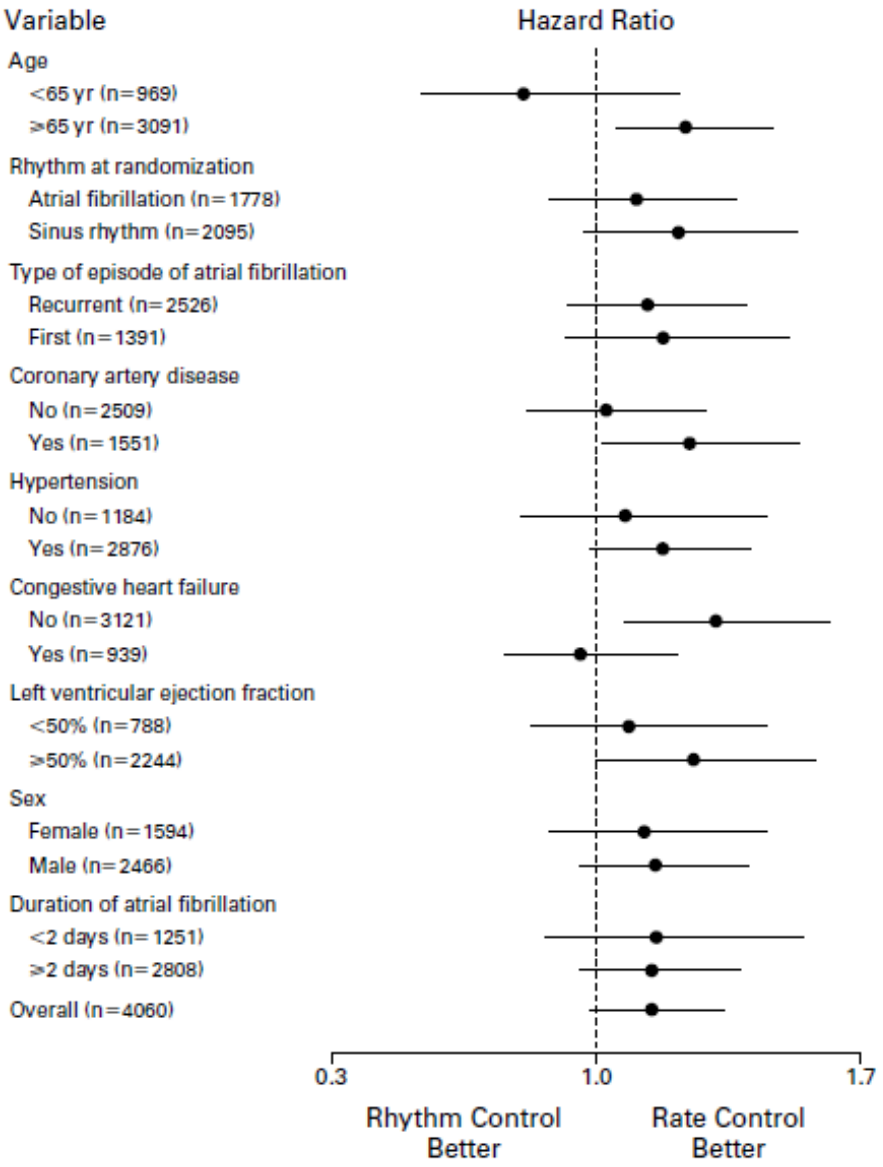
Comparison of rate control and rhythm control in pts with AF: AFFIRM study

TABLE 4. ADDITIONAL ADVERSE EVENTS OR CLINICAL FINDINGS PROMPTING DISCONTINUATION OF A DRUG.*

EVENT	OVERALL (N=4060)	RATE-CONTROL GROUP (N=2027)	RHYTHM-CONTROL GROUP (N=2033)	P VALUE†
	no. of patients (%)			
Congestive heart failure	79 (2.4)	37 (2.1)	42 (2.7)	0.58
Pulmonary event	132 (4.6)	24 (1.7)	108 (7.3)	<0.001
Gastrointestinal event	162 (5.0)	35 (2.1)	127 (8.0)	<0.001
Bradycardia	169 (5.1)	64 (4.2)	105 (6.0)	0.001
Prolongation of the corrected QT interval (>520 msec)	35 (1.1)	4 (0.3)	31 (1.9)	<0.001
Other	590 (19.8)	176 (14.0)	414 (25.4)	<0.001

*Percentages were derived from a Kaplan–Meier analysis.

†P values were based on the log-rank statistic.



Wyse et al. NEJM 2002

Relationship between SR, treatment, and survival in the AF follow-up investigation of rhythm management (AFFIRM) study

TABLE 2. Covariates Significantly Associated With Survival Results With Echocardiographic Data Included

Covariate	*P*	HR	HR: 99% Confidence Limits	
			Lower	Upper
Age at enrollment*	<0.0001	1.06	1.05	1.08
Coronary artery disease	<0.0001	1.56	1.20	2.04
Congestive heart failure	<0.0001	1.57	1.18	2.09
Diabetes	<0.0001	1.56	1.17	2.07
Stroke or transient ischemic attack	<0.0001	1.70	1.24	2.33
Smoking	<0.0001	1.78	1.25	2.53
Left ventricular dysfunction	0.0065	1.36	1.02	1.81
Mitral regurgitation	0.0043	1.36	1.03	1.80
Sinus rhythm	<0.0001	0.53	0.39	0.72
Warfarin use	<0.0001	0.50	0.37	0.69
Digoxin use	0.0007	1.42	1.09	1.86
Rhythm-control drug use	0.0005	1.49	1.11	2.01

*Per year of age.

Corley et al., Circulation 2004

Rate vs. rhythm control: mainteance of sinus rhythm at the end of the study

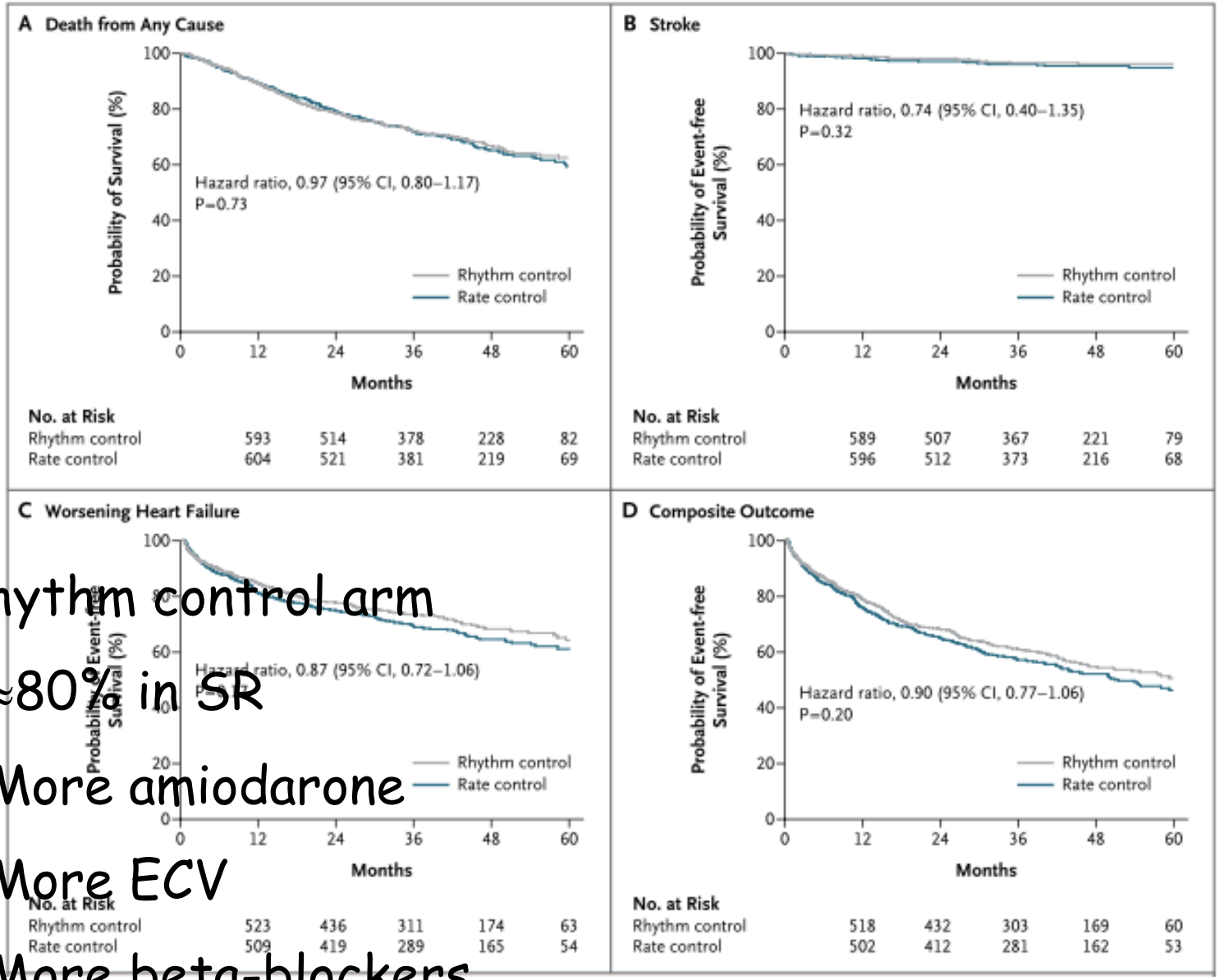
Table 1. Clinical Trials for AF Evaluating Rate Versus Rhythm

Trial	Population	Rate control	Rhythm control	Sinus rhythm at study end
AFFIRM[8] (n=4060)	Age>65 Other stroke risk factors	Digoxin (71%) BB (68%) CCB (46%)	Amiodarone (63%) Sotalol (41%) Propafenone (15%)	Rhythm (63%) Rate (35%)
HOT-CAFÉ[9,10] (n=205)	Persistent AF CCB (8%) Digoxin (43%)	BB (89%) Propafenone (37%) Sotalol (24%)	Amiodarone (57%)	Rhythm (64%) Rate (not specified)
PIAF[11] (n=252)	Persistent AF	BB (9%) Digoxin (7%) CCB (100%)	Amiodarone (100%)	Rhythm (56%) Rate (10%)
RACE[12] (n=522)	Persistent or recurrent AF/AFL	Not specified	Sotalol (initial agent)	Rhythm (39%) Rate (10%)
STAF[13] (n=200)	Persistent AF	BB (45%) CCB (22%) Digoxin (75%)	Amiodarone (42%) Sotalol (22%) Class 1 (12%)	Rhythm (38%) Rate (9%)
AF-CHF[14] (n=1376)	Persistent AF Ejection Fraction (<35%)	*BB (88%) *Amiodarone (7%) *CCB (3%)	*Amiodarone (82%) *Sotalol(2%) *Dofetilide (<1%)	Rhythm (73%) Rate (30-41%)

*Medication use at 12 months
Abbreviations: BB (beta adrenergic blocker), CCB (calcium channel blocker)

Bunch et al., J Gen Intern Med 2010

Rhythm control vs. rate control for AF & HF



In rhythm control arm

- ≈80% in SR
- More amiodarone
- More ECV
- More beta-blockers

Roy et al, NEJM 2008

Italian survey on atrial fibrillation management

Table 3
Clinical characteristics stratified by treatment strategy assignment

Characteristic	Rhythm Control (n = 2,643; 43.8%)	Rate Control (n = 3,310; 54.8%)
Age (yrs)		
15–50		
Male	141 (5.3)	36 (1.1)
Female	44 (1.7)	15 (0.5)
51–65		
Male	323 (12.2)	196 (5.9)
Female	204 (7.7)	134 (4.0)
66–75		
Male	406 (15.4)	408 (12.3)
Female	386 (14.6)	393 (11.9)
76–85		
Male	395 (15)	618 (18.7)
Female	469 (17.7)	758 (22.9)
>85		
Male	103 (3.9)	289 (8.7)
Female	172 (6.5)	463 (14)
Heart disease	1,906 (72.1)*	2,623 (79.2)

In rhythm control: 43.1% > 75 yrs

In rate control: 64.3% > 75 yrs

Zoni Berisso et al. Am J Cardiol 2013

Lifetime pattern of AF and the risk of stroke and death in a population-based cohort of men (from the Manitoba Follow-Up Study)

Risk of stroke by pattern of atrial fibrillation

							Interaction Model					
	Age-adjusted			Adjusted*			No Antithrombotic*,†			Antithrombotic*,†		
	HR	95%CI	P	HR	95%CI	P	HR	95%CI	P	HR	95%CI	P
Free of AF	1.00	Ref.		1.00	Ref.		1.00	Ref.		1.71	1.46-2.00	<0.0001
Newly diagnosed AF	1.85	1.19-2.88	0.006	1.71	1.10-2.66	0.02	1.96	1.07-3.58	0.03	0.74	0.31-1.78	0.50
Intermittent AF – In Sinus	1.35	0.95-1.92	0.09	1.02	0.72-1.45	0.9	1.77	1.10-2.84	0.02	0.38	0.19-0.75	0.006
Intermittent AF – In AF	1.07	0.34-3.32	0.9	0.68	0.22-2.13	0.5		*n/e*‡			*n/e*‡	
Sustained AF	2.20	1.58-3.06	<0.0001	1.85	1.33-2.59	0.0003	2.49	1.57-3.97	<0.0001	0.57	0.30-1.10	0.09
Antithrombotic therapy†		*N/A*		1.58	1.37-1.85	<0.0001		*N/A*		*N/A*		

N/A = Not applicable.

* *Adjusted for Age, Heart failure, Diabetes mellitus, Antihypertensive therapy, Cancer, Smoking.*

† *Antithrombotic therapy = Antiplatelet or anticoagulant.*

‡ n/e = not estimable due to insufficient event counts.

More atrial fibrillation more risk !!

Risk of death by pattern of atrial fibrillation

							Interaction Model					
	Age-adjusted			Adjusted*			No Antithrombotic*,†			Antithrombotic*,†		
	HR	95%CI	P	HR	95%CI	P	HR	95%CI	P	HR	95%CI	P
Free of AF	1.00	Ref.	-	1.00	Ref.	-	1.00	Ref.	-	0.52	0.47-0.58	<0.0001
Newly diagnosed AF	1.92	1.55-2.38	<0.0001	2.03	1.64-2.52	<0.0001	1.87	1.44–2.41	<0.0001	1.37	0.87-2.18	0.2
Intermittent AF – In Sinus	1.46	1.24-1.73	<0.0001	1.71	1.44-2.03	<0.0001	1.52	1.21-1.93	0.0005	1.31	0.93-1.85	0.1
Intermittent AF – In AF	1.90	1.25-2.90	0.003	2.41	1.58-3.68	<0.0001	2.61	1.48-4.61	0.0009	0.87	0.37-2.03	0.8
Sustained AF	2.08	1.78-2.44	<0.0001	2.48	2.11-2.92	<0.0001	2.40	1.95-2.94	<0.0001	1.12	0.81-1.54	0.5
Antithrombotic therapy†		*N/A*		0.55	0.49-0.60	<0.0001		*N/A*		*N/A*		

N/A = Not Applicable.

* *Adjusted for Age, Heart Failure, Diabetes Mellitus, Antihypertensive therapy, Cancer, Smoking, Ischemic Heart Disease.*

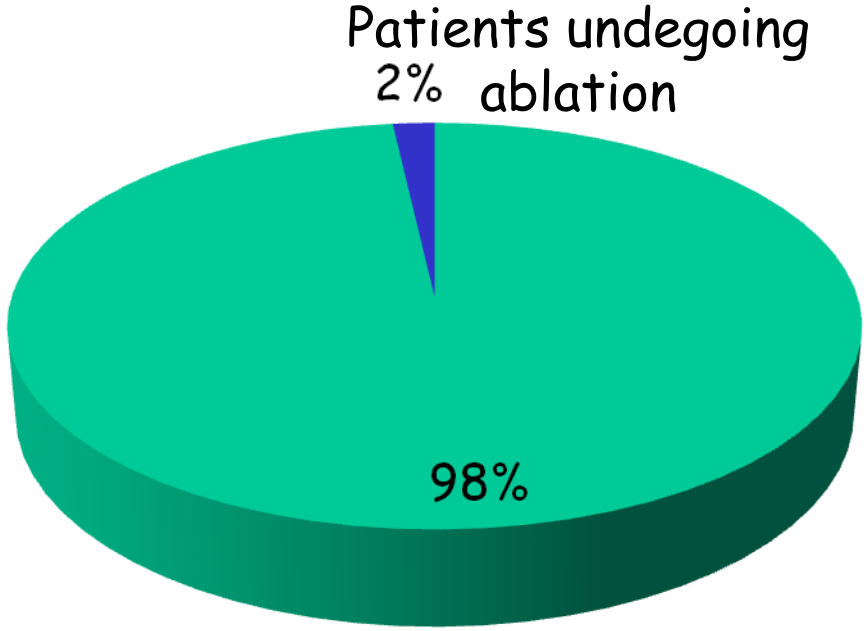
† *Antithrombotic therapy = Antiplatelet or anticoagulant.*

McIntire et al. Am J Cardiol 2018

Italian survey on atrial fibrillation management

Clinical characteristics of patients who underwent catheter ablation of atrial fibrillation substrate (n = 174)

Characteristic	n (%)
Gender	
Male	112 (64.4)
Female	62 (35.6)
Age (yrs)	
16–50	
Male	15 (8.6)
Female	4 (2.3)
51–65	
Male	46 (26.4)
Female	15 (8.6)
66–75	
Male	34 (19.5)
Female	25 (8.6)
>75	
Male	17 (9.8)
Female	18 (10.3)
Atrial fibrillation type	
Paroxysmal	34 (19.5)
Persistent	140 (80.5)
Heart disease	97 (55.7)
Previous cardioversion	
0	24 (13.8)
1–3	90 (51.7)
>3	52 (29.9)
Unknown	8 (4.6)
Symptoms leading to ablation	
Palpitations	144 (82.8)
Dyspnea	83 (47.7)
Asthenia	90 (51.7)
Other	3 (9.8)
Catheter ablation	
1	117 (67.2)
2	40 (23)
≥3	6 (3.4)
Unknown	11 (6.3)
Postablation antiarrhythmic drugs	
Propafenone	20 (11.5)
Flecainide	41 (23.6)
Amiodarone-dronedarone	46 (24.4)
Combinations	11 (6.3)
None	56 (32.2)
Postablation antithrombotic therapy	
No	40 (23)
Antiplatelet agents	38 (21.8)
Oral anticoagulation	96 (55.2)



Zoni Berisso et al. Am J Cardiol 2013

Management of AF: the BLITZ - AF

Table 1 Burden of atrial fibrillation/atrial flutter in the ER

	No of medical accesses in the ER	Hospital admissions	%
Total	364 134	60 332	16.6
For AF/af	3689	1024	27.8
%	1.0	1.7	

Table 4 Discharge

	Total (n = 4126)
In hospital events, *n* (%)	
Ischaemic stroke	14 (0.3)
TIA	6 (0.2)
Haemorrhagic stroke	4 (0.1)
Peripheral embolism	8 (0.2)
Pulmonary embolism	10 (0.2)
Major bleeding	23 (0.6)
Heart failure	319 (7.7)
Acute coronary syndrome	95 (2.3)
Atrial fibrillation recurrence	111 (2.7)
Other CV events	131 (3.2)
Other non-CV events	112 (2.7)
Deaths, *n* (%)	48 (1.2)
Ischaemic stroke	1 (2.1)
Haemorrhagic stroke	1 (2.1)
Heart failure	25 (52.1)
ACS	3 (6.3)
Other, CV	8 (16.7)
Other, non-CV	10 (20.8)

Table 3 Atrial fibrillation management

	Total (n = 4126)
Transthoracic echo, *n* (%)	3314 (80.3)
Transoesophageal echo, *n* (%)	673 (16.3)
Coronary angiography, *n* (%)	514 (12.5)
Coronary revascularization, *n* (%)	153 (3.7)
24 h Holter monitoring, *n* (%)	576 (14.0)
Electrophysiological study, *n* (%)	141 (3.4)
Cardioversion performed, *n* (%)[a]	1599 (38.8)
Electrical cardioversion, *n* (%)[a]	1000 (24.2)
Transthoracic	988 (98.8)
Transoesophageal	5 (0.5)
Internal, *n* (%)	8 (0.8)
Pharmacological cardioversion, *n* (%)[a]	674 (16.3)
Cardioversion planned, *n* (%)[a]	111 (2.7)
Electrical	107 (96.4)
Pharmacological	5 (4.5)
Ablation performed, *n* (%)	185 (4.5)
A-V node	27 (14.6)
Pulmonary vein	158 (85.4)
Ablation planned, *n* (%)	33 (0.8)
Device implant, *n* (%)	495 (12.0)
Left atrial appendage occlusion, *n* (%)	27 (0.7)

Gulizia et al. Europace 2018

In-hospital mortality in patients with atrial arrhythmias: the German experience

LA ablation in 21744/161502 pts (13.5%) increased over time

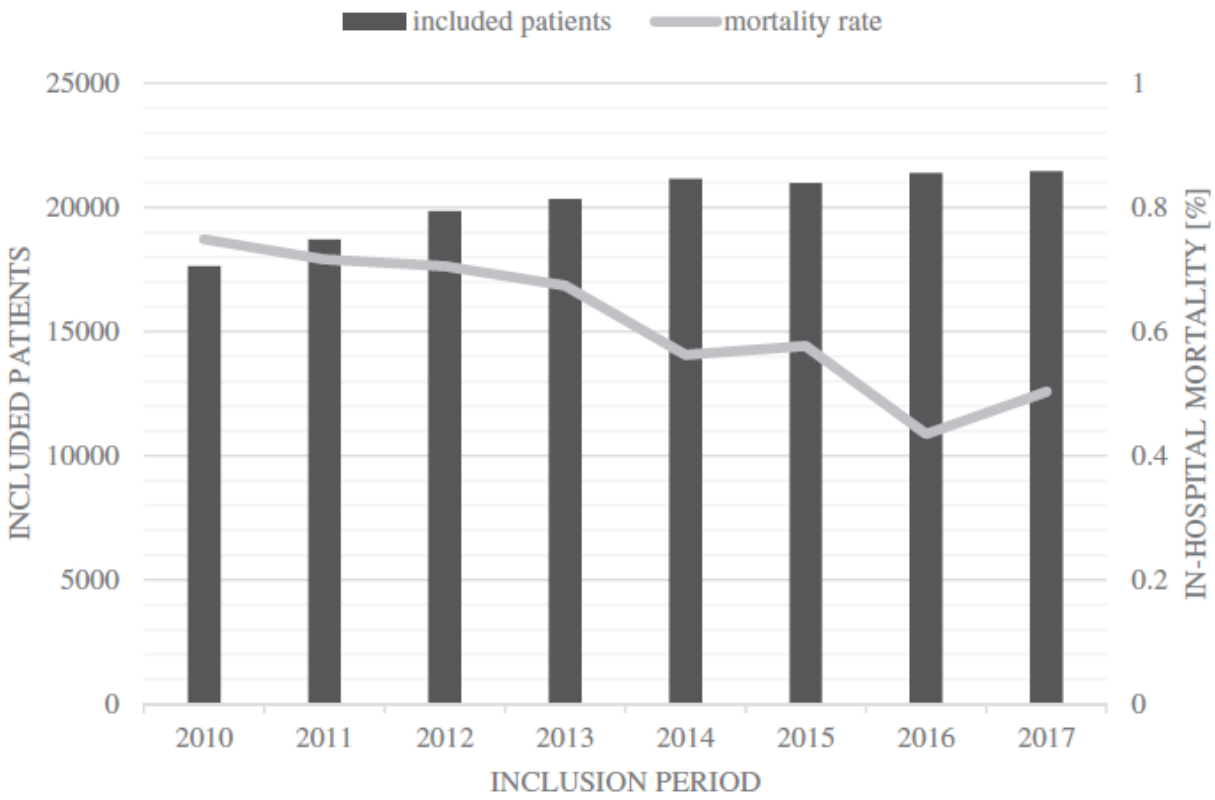


Figure 1 Numbers of included patients and mortality rates per year.

Konig et al. Eur Heart J 2018

Treatment of AF with CA or AADs: two meta-analysis

Table 4. Characteristics of Patients With AF Undergoing Catheter Ablation and Receiving AAD Therapy

	Catheter Ablation			AAD		
Baseline Characteristic	t	n	Mean (Range)	t	n	Mean (Range)
Total patients						
Mean age, y	69	6936	55.5 (41–67)	57	6589	61.6 (38–70)
Mean No. drugs refractory	62	5206	2.6 (1–5)	8	535	1.7 (0–3)
Mean duration of arrhythmia, y	56	6096	6.0 (1–9)	19	1891	3.1 (0–11)
Mean LA size, mm	57	5899	41.6 (35–50)	33	3423	43.7 (33–49)
Mean LV ejection fraction, %	43	4655	57.7 (49–71)	34	3510	49.0 (25–67)
	t	n/N	%	t	n/N	%
Sex						
Male	69	4553/6321	72.0%	46	358/5662	64.6%
Female	69	1768/6321	28.0%	46	2004/5662	35.4%
Type of AF						
Paroxysmal	72	5189/7437	69.8%	35	2529/4481	56.4%
Persistent	67	970/6494	14.9%	34	1572/4475	35.1%
Permanent (long-standing)	62	843/6085	13.9%	40	376/5011	7.5%
Comorbid conditions						
Previous ablation	25	120/2888	4.2%	…	…	…
Ischemic heart disease	26	326/3247	10.0%	36	846/4660	18.2%
Nonischemic heart disease	3	12/272	4.4%	2	0/200	0.0%
Valvular heart disease	19	130/2327	5.6%	27	485/3022	16.0%
Structural heart disease	49	1341/4381	30.6%	10	522/1055	49.5%
Cardiomyopathy	3	39/254	15.4%	13	88/2361	3.7%
Dilated cardiomyopathy	11	218/1576	13.8%	8	96/1607	6.0%
ARVC/D	3	18/323	5.6%	…	…	…
CHF	4	34/216	15.7%	12	207/843	24.6%
Congenital heart disease	2	6/198	3.0%	…	…	…
Hypertrophic cardiomyopathy	11	52/1419	3.7%	1	0/127	0.0%
ICD	…	…	…	3	22/665	3.3%
Prior cardiac surgery (PCI/CABG)	3	0/767	0.0%	3	72/173	41.6%
Stroke	2	24/725	3.3%	…	…	…
Diabetes	8	60/1253	4.8%	7	214/1772	12.1%
Hypertension	31	937/3094	30.3%	40	1888/4912	38.4%
Medication history						
Anti-arrhythmics	41	3406/3585	95.0%	8	321/884	36.3%
Anticoagulants	1	45/45	100.0%	4	806/806	100.0%

t indicates No. of treatment groups reporting characteristic; n, No. of patients with this characteristic; LA, left atrium; LV, left ventricular; N, No. of patients evaluated in studies reporting characteristic; ARVC/D, arrhythmogenic right ventricular cardiomyopathy/dysplasia; CHF, congestive heart failure; PCI, percutaneous coronary intervention; ICD, implantable cardioverter-defibrillator; CABG, coronary artery bypass graft.

Calkins et al. Circ Arrhythm Electrophysiol 2009

Treatment of AF with CA or AADs: two meta-analysis

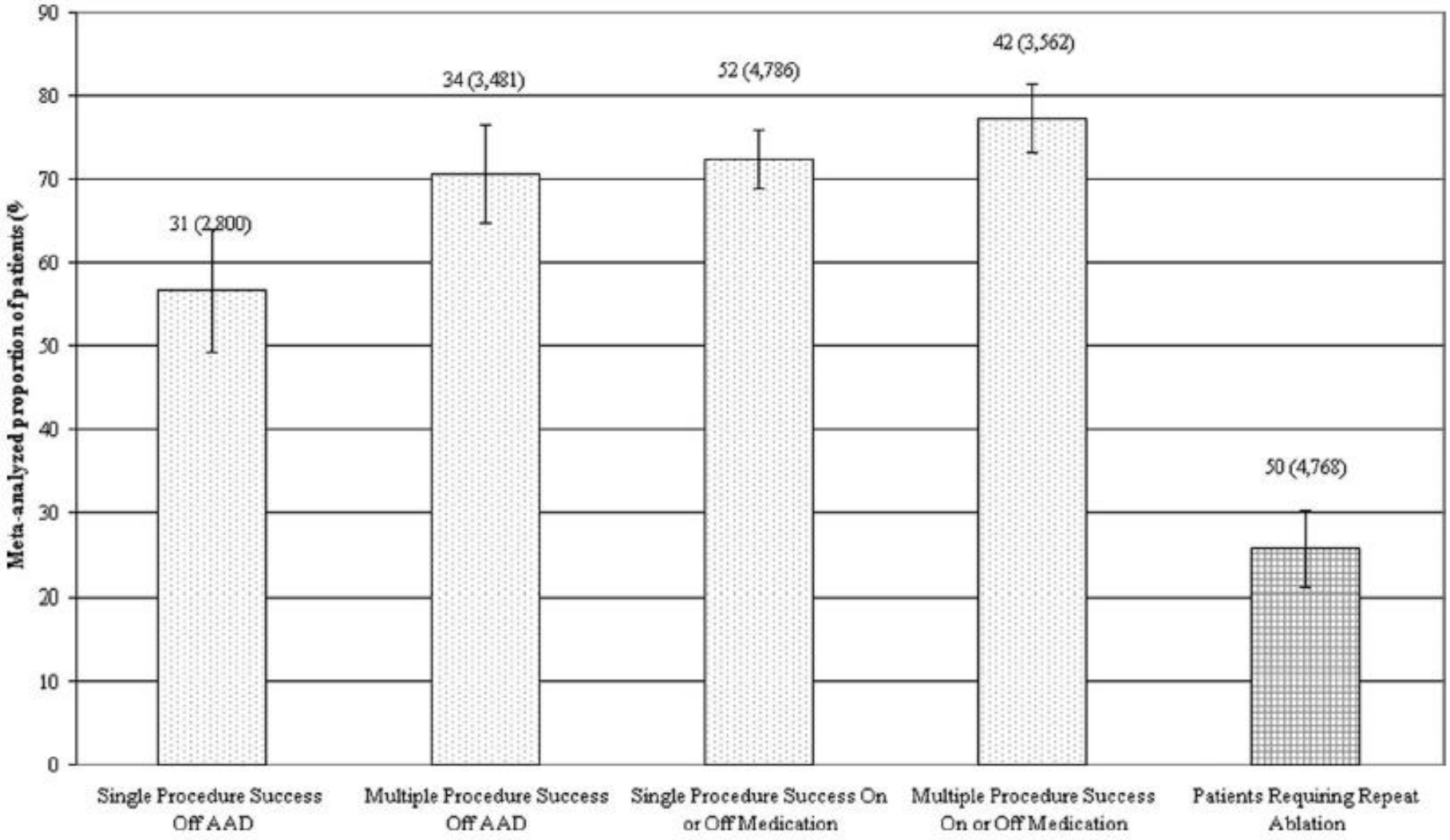


Figure 3. Efficacy of catheter ablation in patients with AF.

Calkins et al. Circ Arrhythm Electrophysiol 2009

Treatment of AF with CA or AADs: two meta-analysis

Table 5. Safety Outcomes for Patients With AF Undergoing Catheter Ablation

Outcomes	t	n/N	%
Mortality			
Death overall	65	42/5781	0.7
Procedure-related	64	0/5192	0.0
Vascular access complications			
Arteriovenous fistula	32	1/2885	0.0
Bleeding	33	1/2960	0.0
Hematoma	38	17/3719	0.5
Pneumothorax	34	0/2974	0.0
Femoral artery pseudoaneurysm	34	15/3032	0.5
Periprocedure events			
Stroke, ischemic	62	17/5665	0.3
TIA	60	13/5467	0.2
Cardiac tamponade	63	45/5723	0.8
PE	60	3/5496	0.1
DVT	56	1/4758	0.0
Other embolism	57	10/5347	0.2
LA-esophageal fistula	60	0/5496	0.0
Other fistula	58	3/5407	0.1
Pericardial effusion	64	36/5719	0.6
PV stenosis*	65	91/5831	1.6
AV block	60	1/5496	0.0
CHF exacerbation	60	0/5496	0.0
Need for a pacemaker	46	4/3902	0.1
Total No. of patients with events	28	97/1964	4.9

t indicates No. of treatment groups; n, No. of patients with this adverse event; N, No. of patients evaluated in studies reporting this adverse event; %, percent of patients with adverse event of interest; TIA, transient ischemic accident; PE, pulmonary embolism; DVT, deep vein thrombosis; LA, left atrial; PV, pulmonary vein; AV, atrioventricular; CHF, congestive heart failure.

*>70% Stenosis (early, <7 days after ablation; late, >7 days after ablation).

Table 6. Safety Outcomes for Patients With AF Receiving AAD Therapy

	Overall		
Safety Outcomes	t	n/N	%
Mortality			
Death overall	33	120/4291	2.8
Sudden death	21	18/2900	0.6
Treatment-related death	22	15/3179	0.5
Not treatment-related death	20	40/3023	1.3
Adverse events			
CV events	10	58/1572	3.7
Bradycardia	19	44/2349	1.9
GI	16	97/1499	6.5
Neuropathy	4	48/969	5.0
Thyroid dysfunction	5	19/576	3.3
Torsades	12	16/2238	0.7
Q-T* prolongation	12	5/2034	0.2
Total No. of patients with events	24	989/3318	29.8
Discontinuations			
Total	32	1035/4347	23.8
Due to AE	32	384/3682	10.4
Due to inefficacy	12	229/1694	13.5
Due to noncompliance	4	19/457	4.2

t indicates No. of treatment groups; n, No. of patients with this adverse event; N, No. of patients evaluated in studies reporting this adverse event; %, percentage of patients with adverse event of interest; CV, cardiovascular; GI, gastrointestinal; AE, adverse events.

*Interval of the Q and T waves.

Calkins et al. Circ Arrhythm Electrophysiol 2009

Effect of (g Therapy on Morta Among P The CABA

Douglas L. Packer, MD; eanne E. Poole, MD; Peter A. Noseworthy, M ny Pokushalov, MD; Alexander Romanov, M ilber, MD; Riccardo Cappato, MD; ccarelli, MD; James A. Reiffel, MD; J for the CABANA Investigators

IMPORTANCE Catheter ablation is effective in restoring sinus rhythm in atrial fibrillation (AF), but its effects on long-term mortality and stroke risk are uncertain.

OBJECTIVE To determine whether catheter ablation is more effective than conventional medical therapy for improving outcomes in AF.

DESIGN, SETTING, AND PARTICIPANTS The Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation trial is an investigator-initiated, open-label, multicenter, randomized trial involving 126 centers in 10 countries. A total of 2204 symptomatic patients with AF aged 65 years and older or younger than 65 years with 1 or more risk factors for stroke were enrolled from November 2009 to April 2016, with follow-up through December 31, 2017.

INTERVENTIONS The catheter ablation group (n = 1108) underwent pulmonary vein isolation, with additional ablative procedures at the discretion of site investigators. The drug therapy group (n = 1096) received standard rhythm and/or rate control drugs guided by contemporaneous guidelines.

MAIN OUTCOMES AND MEASURES The primary end point was a composite of death, disabling stroke, serious bleeding, or cardiac arrest. Among 13 prespecified secondary end points, 3 are included in this report: all-cause mortality; total mortality or cardiovascular hospitalization; and AF recurrence.

RESULTS Of the 2204 patients randomized (median age, 68 years; 37.2% female; 42.9% had paroxysmal AF and 57.1% had persistent AF), 89.3% completed the trial. Of the patients assigned to catheter ablation, 1006 (90.8%) underwent the procedure. Of the patients assigned to drug therapy, 301 (27.5%) ultimately received catheter ablation. In the intention-to-treat analysis, over a median follow-up of 48.5 months, the primary end point occurred in 8.0% (n = 89) of patients in the ablation group vs 9.2% (n = 101) of patients in the drug therapy group (hazard ratio [HR], 0.86 [95% CI, 0.65-1.15]; $P = .30$). Among the secondary end points, outcomes in the ablation group vs the drug therapy group, respectively, were 5.2% vs 6.1% for all-cause mortality (HR, 0.85 [95% CI, 0.60-1.21]; $P = .38$), 51.7% vs 58.1% for death or cardiovascular hospitalization (HR, 0.83 [95% CI, 0.74-0.93]; $P = .001$), and 49.9% vs 69.5% for AF recurrence (HR, 0.52 [95% CI, 0.45-0.60]; $P < .001$).

CONCLUSIONS AND RELEVANCE Among patients with AF, the strategy of catheter ablation, compared with medical therapy, did not significantly reduce the primary composite end point of death, disabling stroke, serious bleeding, or cardiac arrest. However, the estimated treatment effect of catheter ablation was affected by lower-than-expected event rates and treatment crossovers, which should be considered in interpreting the results of the trial.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT00911508

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Effect of catheter ablation vs. AAD therapy on mortality, stroke, bleeding, and cardiac arrest in AF patients: the CABANA study

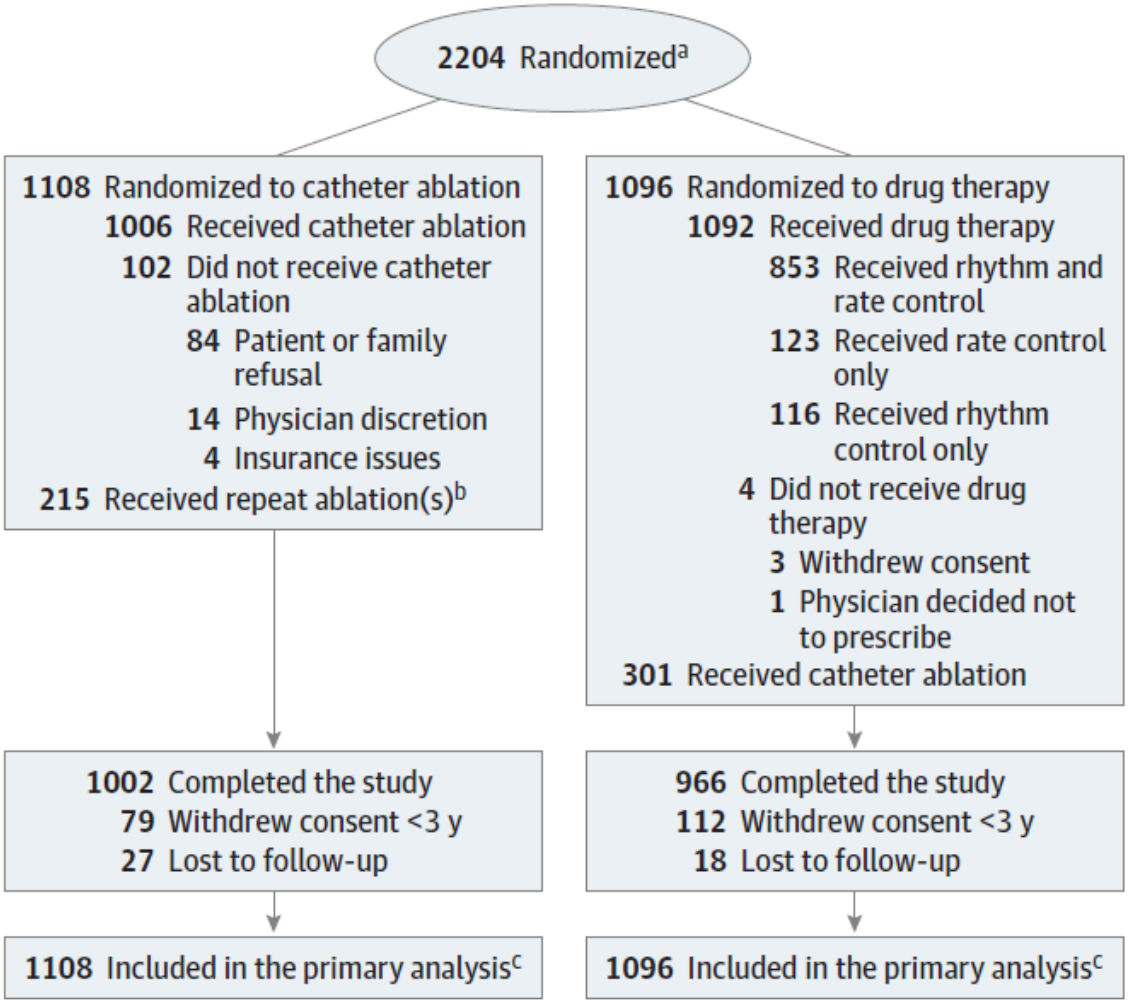
Eligible patients were aged 65 years and older

or

younger than 65 years with 1 or more risk factors for stroke (hypertension, heart failure, history of stroke, diabetes, or other heart problems)

had 2 or more episodes of paroxysmal AF or 1 episode of persistent AF in the prior 6 months

Figure 1. Randomization and Patient Flow in the CABANA Trial



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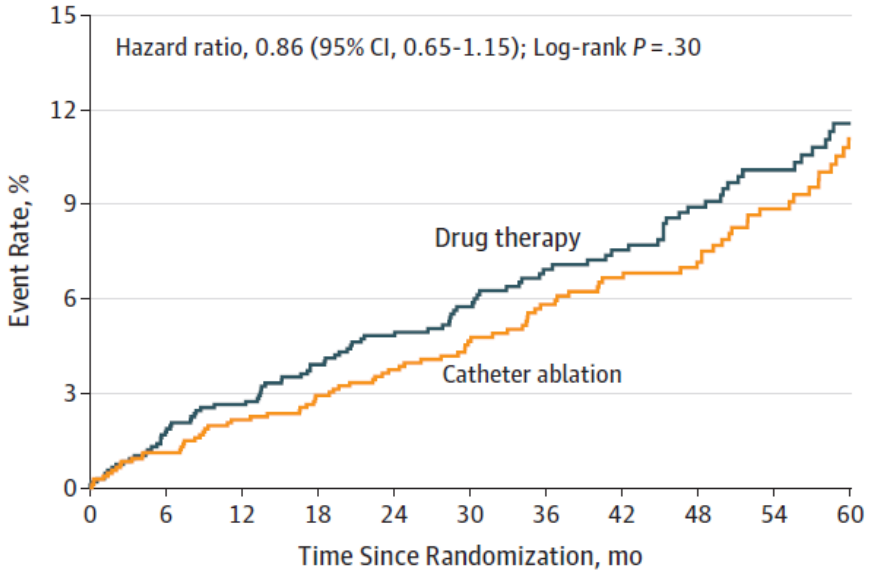
Effect of catheter ablation vs. AAD therapy on mortality, stroke, bleeding, and cardiac arrest in AF patients: the CABANA study

Figure 2. Kaplan-Meier Estimates of the Incidence of the Primary End Point



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

Kaplan-Meier estimates of the cumulative risk of death, disabling stroke, serious bleeding, or cardiac arrest (primary end point by intention-to-treat analysis). The median (25th, 75th percentile) length of patient follow-up was 4.1 years (2.5, 5.1) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group.

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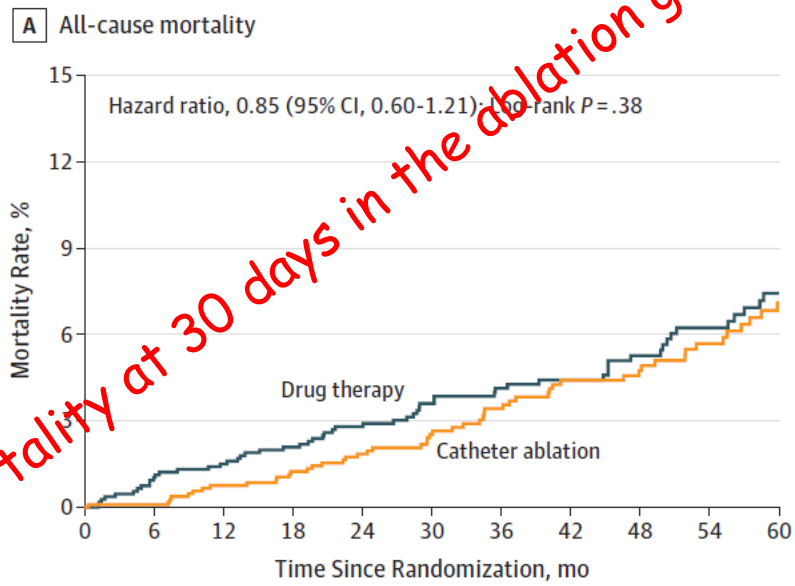
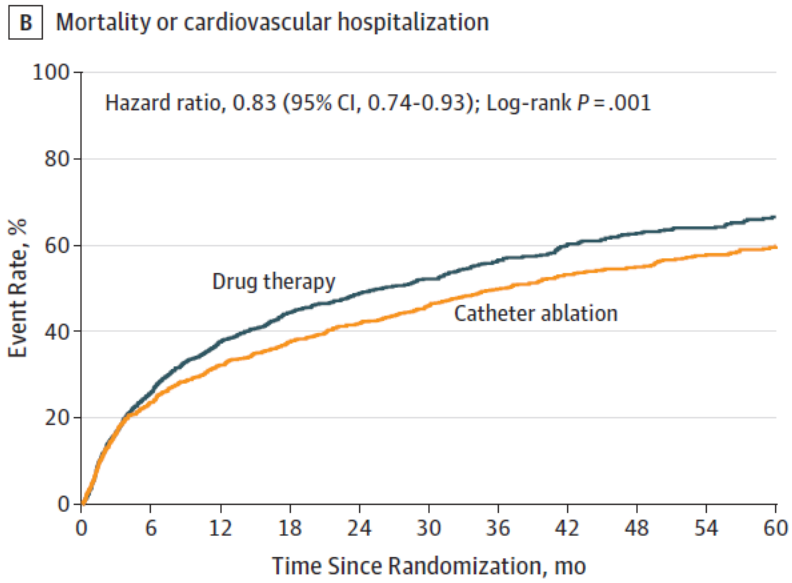
Effect of catheter ablation vs. AAD therapy on mortality, stroke, bleeding, and cardiac arrest in AF patients: the CABANA study

Figure 3. Kaplan-Meier Estimates of All-Cause Mortality and Mortality or Cardiovascular Hospitalization by Intention-to-Treat Analysis





No. at risk

Drug therapy	1096	1046	1023	992	903	783	679	606	527	445	334
Catheter ablation	1108	1058	1035	1013	933	814	724	632	555	455	332

Drug therapy	1096	778	643	563	474	387	302	244	197	165	112
Catheter ablation	1108	807	708	643	558	450	372	307	261	207	137

A, The median (25th, 75th percentiles) length of patient follow-up was 4.1 years (2.5, 5.1) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group. B, The median (25th, 75th percentiles) length of patient follow-up was 4.1 years (2.5, 5.1) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group.

No mortality at 30 days in the ablation group!!!

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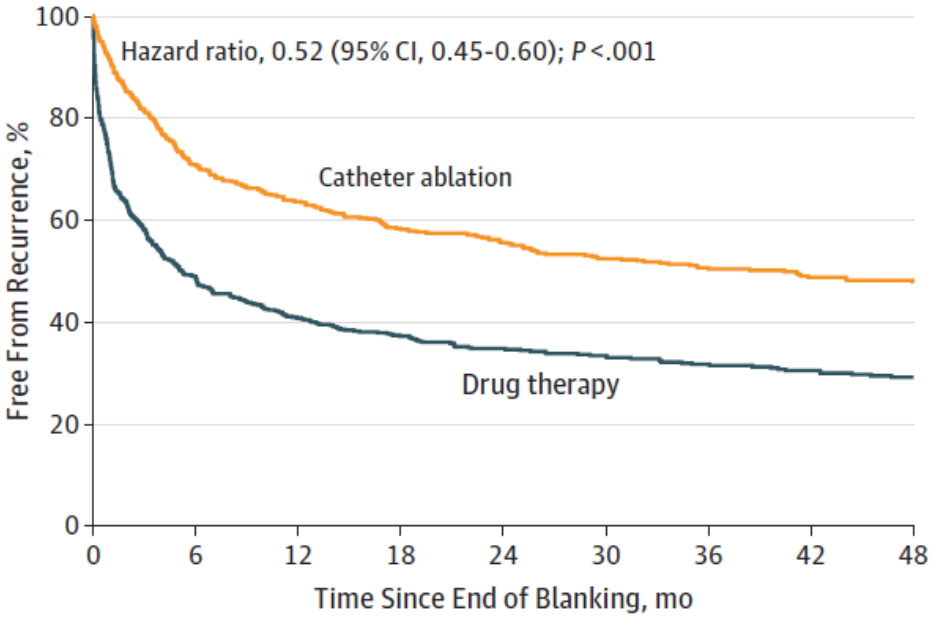
Effect of catheter ablation vs. AAD therapy on mortality, stroke, bleeding, and cardiac arrest in AF patients: the CABANA study

Figure 6. Recurrent Atrial Fibrillation After Blanking by Intention-to-Treat Analysis



No. at risk									
Drug therapy	629	304	252	212	181	157	131	115	94
Catheter ablation	611	432	381	328	291	241	201	163	134

Freedom from recurrence of atrial fibrillation following the blanking period in 1240 patients who used the study electrocardiogram event recorders (intention-to-treat analysis with death as a competing risk). The median (25th, 75th percentiles) length of patient follow-up was 4.3 years (2.8, 5.0) in the catheter ablation group and 4.3 years (2.7, 5.3) in the drug therapy group.

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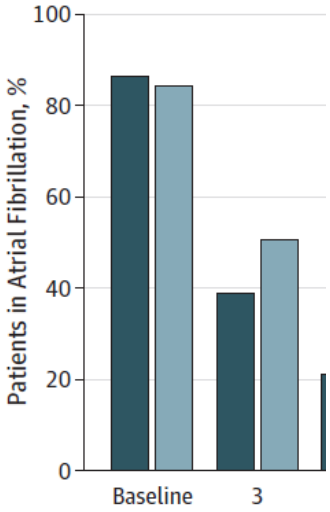
Effect of catheter ablation vs. AAD therapy on quality of life: the CABANA study

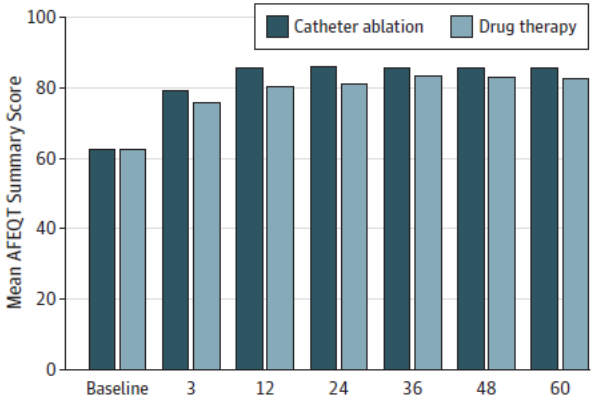
Figure 1. Patients Who Reported Being in Atrial Fibrillation Currently or Within the Past Month



No. of patients		
Catheter ablation	915	374
Drug therapy	885	493

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

A Mean AFEQT summary score



B Between-group AFEQT summary score difference

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

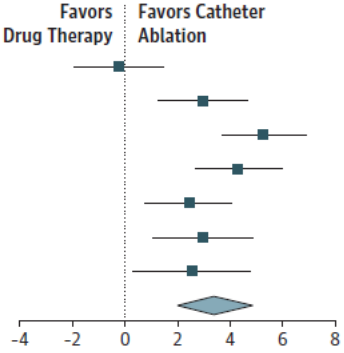
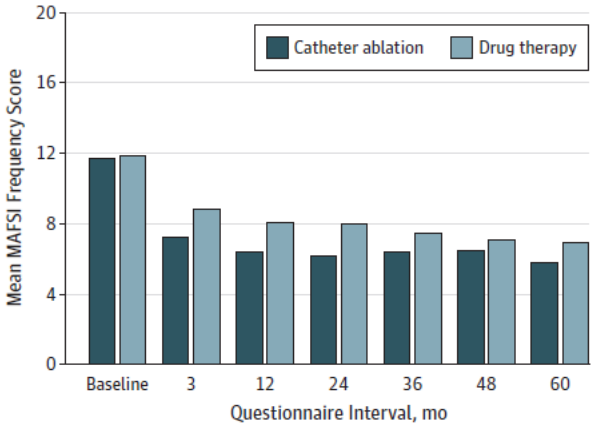


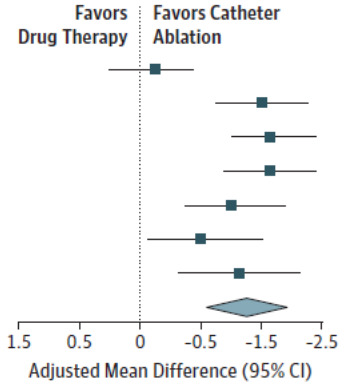
Figure 3. Mayo Atrial Fibrillation–Specific Symptom Inventory (MAFSI) Frequency Scores

A Mean MAFSI frequency score



B Between-group MAFSI frequency score difference

Interval, mo	No. of Patients Ablation (n = 1108)	No. of Patients Drug Rx (n = 1096)	Adjusted Mean Difference (95% CI)
Baseline	1069	1061	-0.2 (-0.7 to 0.4)
3	897	894	-1.6 (-2.2 to -1.0)
12	828	831	-1.7 (-2.3 to -1.2)
24	759	724	-1.7 (-2.3 to -1.1)
36	571	559	-1.2 (-1.9 to -0.6)
48	424	419	-0.8 (-1.6 to -0.1)
60	279	295	-1.3 (-2.1 to -0.5)
All	3758	3722	-1.4 (-1.9 to -0.9)



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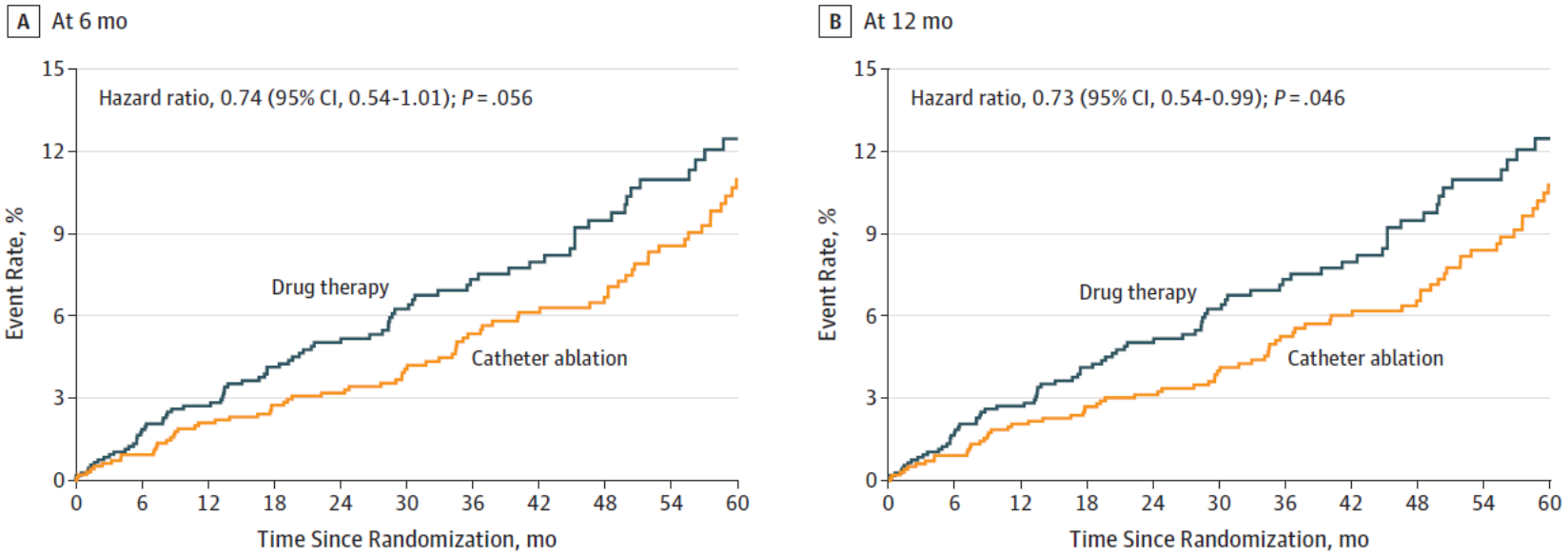
Effect of catheter ablation vs. AAD therapy on mortality, stroke, bleeding, and cardiac arrest in AF patients: the CABANA study

Figure 5. Kaplan-Meier Estimates of the Primary End Point by Per-Protocol Analysis



No. at risk

Drug therapy	1096	954	860	778	680	566	464	396	330	275	204
Catheter ablation	970	941	920	901	835	721	636	555	483	397	287

Drug therapy	1096	954	860	778	680	566	464	396	330	275	204
Catheter ablation	987	958	937	918	849	735	648	566	494	404	291

Kaplan-Meier estimates of the cumulative risk of death, disabling stroke, serious bleeding, or cardiac arrest (primary end point) by 6-month (A) and 12-month (B) per-protocol analysis. Figure includes patients randomized to catheter ablation who were ablated within 6 months (A) or 12 months (B) after randomization. It also includes all patients randomized to drug therapy, with follow-up censored at crossover to ablation. A, The median (25th, 75th percentiles) length of patient follow-up was 4.1 years (2.6, 5.2) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group. B, The median (25th, 75th percentiles) length of patient follow-up was 4.2 years (2.6, 5.2) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group.

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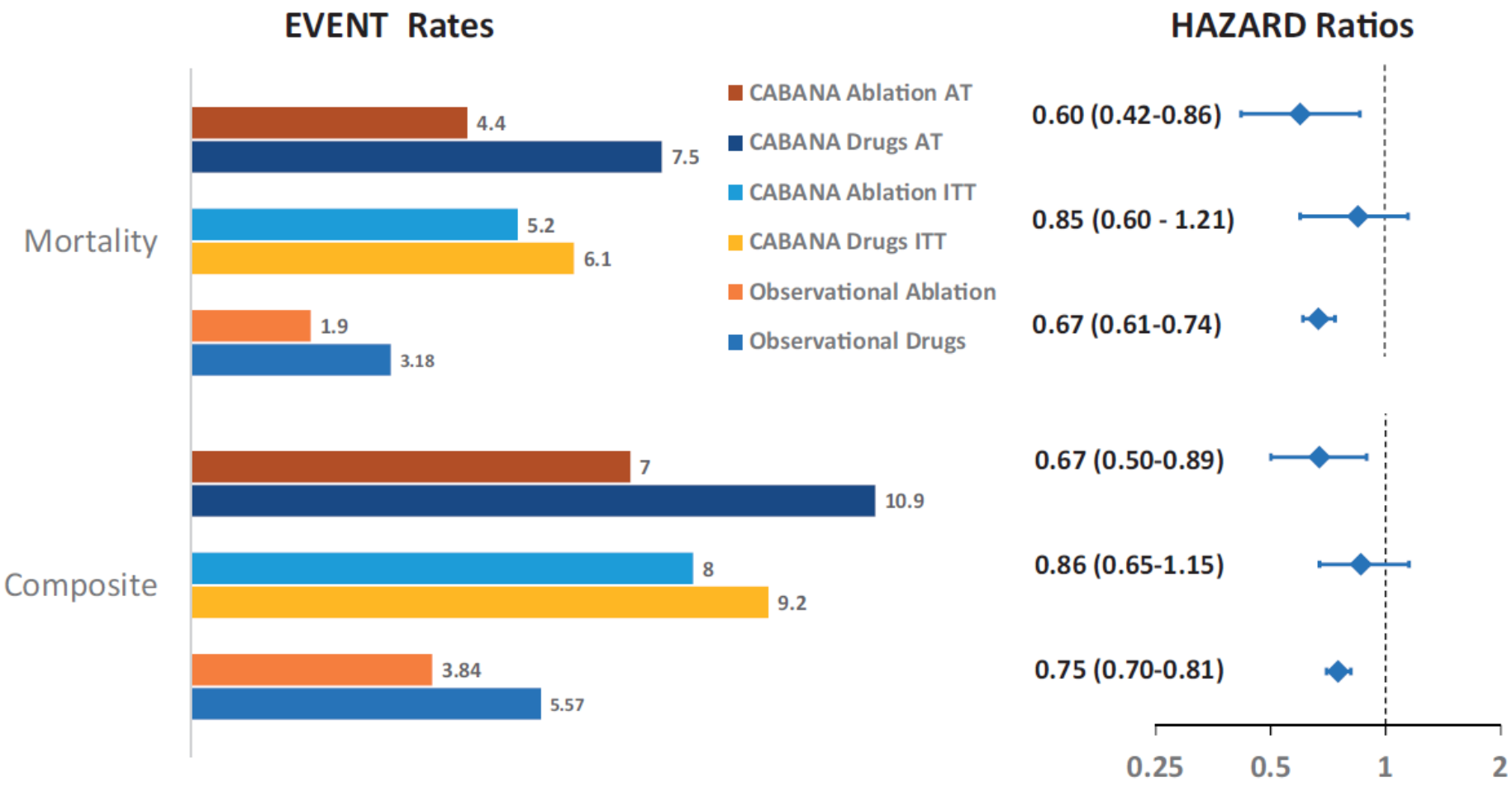
About the CABANA study



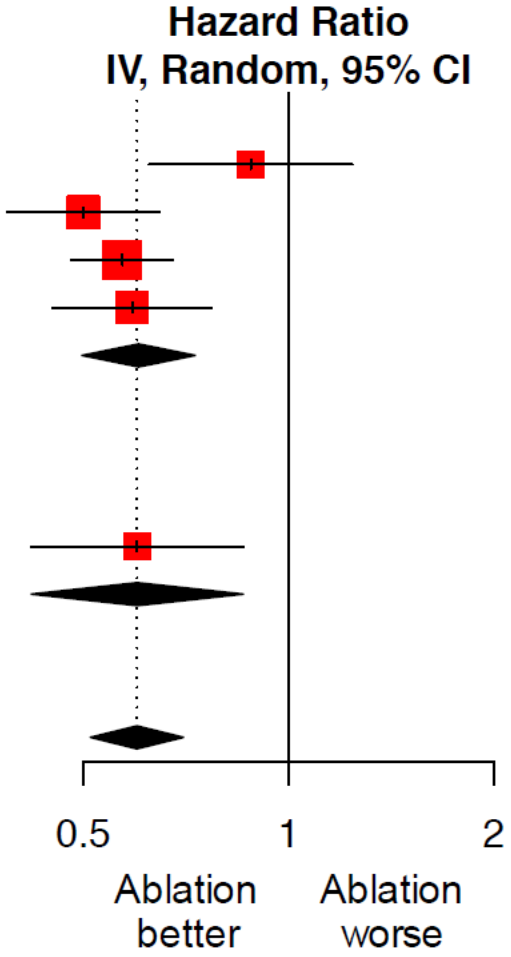
Camm Eur Heart J 2019

Impact of atrial fibrillation ablation on mortality, stroke and hospitalization for heart failure: a meta-analysis

Figure 3

Mortality (CABANA Treatment Received Analysis)

Study or Subgroup	TE	SE	Weight	Hazard Ratio IV, Random, 95% CI
Type = Matched database				
Chang 2014	−0.13	0.1748	14.6%	0.88 [0.62; 1.24]
Friberg 2016	−0.69	0.1317	20.9%	0.50 [0.39; 0.65]
Saliba 2017	−0.56	0.0866	30.8%	0.57 [0.48; 0.68]
Srivatsa 2018	−0.53	0.1370	20.0%	0.59 [0.45; 0.77]
Total (95% CI)			**86.3%**	**0.60 [0.50; 0.73]**
Heterogeneity: $Tau^2 = 0.0213$; $Chi^2 = 6.97$, df = 3 (P = 0.07); $I^2 = 57\%$				
Type = RCT				
CABANA (Treatment received)	−0.51	0.1828	13.7%	0.60 [0.42; 0.86]
Total (95% CI)			**13.7%**	**0.60 [0.42; 0.86]**
Heterogeneity: not applicable				
Total (95% CI)			**100.0%**	**0.60 [0.51; 0.70]**
Heterogeneity: $Tau^2 = 0.0134$; $Chi^2 = 6.98$, df = 4 (P = 0.14); $I^2 = 43\%$				
Residual heterogeneity: Tau^2 = NA; $Chi^2 = 6.97$, df = 3 (P = 0.07); $I^2 = 57\%$				

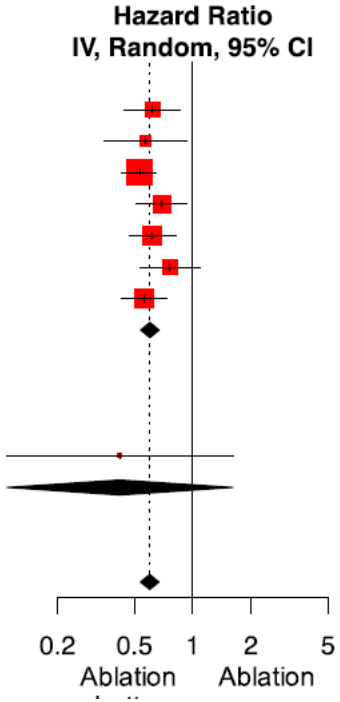


Saglietto et al. J Cardiovasc Electrophysiol submitted

Impact of atrial fibrillation ablation on mortality, stroke and hospitalization for heart failure: a meta-analysis

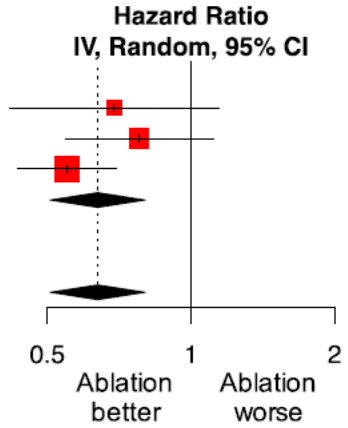
b) Stroke

Study or Subgroup	TE	SE	Weight	Hazard Ratio IV, Random, 95% CI
Type = Matched database				
Reynolds 2012	−0.48	0.1710	10.7%	0.62 [0.44; 0.87]
Chang 2014	−0.56	0.2520	4.9%	0.57 [0.35; 0.93]
Karasoy 2015	−0.63	0.1054	28.2%	0.53 [0.43; 0.65]
Friberg 2016	−0.37	0.1533	13.3%	0.69 [0.51; 0.93]
Saliba 2017	−0.48	0.1420	15.5%	0.62 [0.47; 0.82]
Srivatsa 2018	−0.27	0.1815	9.5%	0.76 [0.53; 1.08]
Noseworthy 2019	−0.58	0.1350	17.2%	0.56 [0.43; 0.73]
Total (95% CI)			99.3%	0.60 [0.54; 0.67]
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 4.31$, df = 6 (P = 0.64); $I^2 = 0\%$				
Type = RCT				
CABANA (ITT)	−0.87	0.6861	0.7%	0.42 [0.11; 1.61]
Total (95% CI)			0.7%	0.42 [0.11; 1.61]
Heterogeneity: not applicable				
Total (95% CI)			**100.0%**	**0.60 [0.54; 0.67]**
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 4.57$, df = 7 (P = 0.71); $I^2 = 0\%$				
Residual heterogeneity: Tau^2 = NA; $Chi^2 = 4.31$, df = 6 (P = 0.64); $I^2 = 0\%$				



c) Hospitalization for heart failure

Study or Subgroup	TE	SE	Weight	Hazard Ratio IV, Random, 95% CI
Type = Matched database				
Reynolds 2012	−0.37	0.2570	17.6%	0.69 [0.42; 1.14]
Chang 2014	−0.25	0.1814	30.6%	0.78 [0.55; 1.11]
Srivatsa 2018	−0.60	0.1206	51.7%	0.55 [0.43; 0.70]
Total (95% CI)			100.0%	0.64 [0.51; 0.80]
Heterogeneity: $Tau^2 = 0.0121$; $Chi^2 = 2.76$, df = 2 (P = 0.25); $I^2 = 28\%$				
Total (95% CI)			**100.0%**	**0.64 [0.51; 0.80]**
Heterogeneity: $Tau^2 = 0.0121$; $Chi^2 = 2.76$, df = 2 (P = 0.25); $I^2 = 28\%$				
Residual heterogeneity: Tau^2 = NA; $Chi^2 = 2.76$, df = 2 (P = 0.25); $I^2 = 28\%$				



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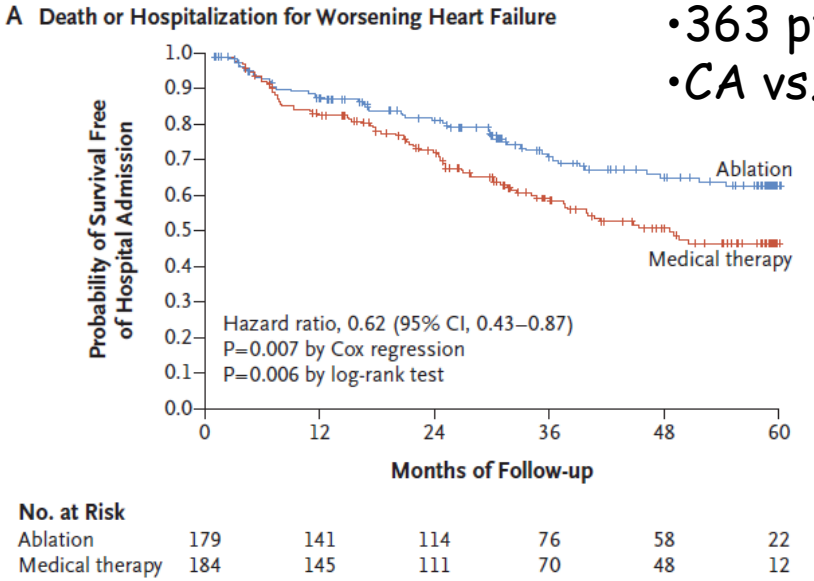
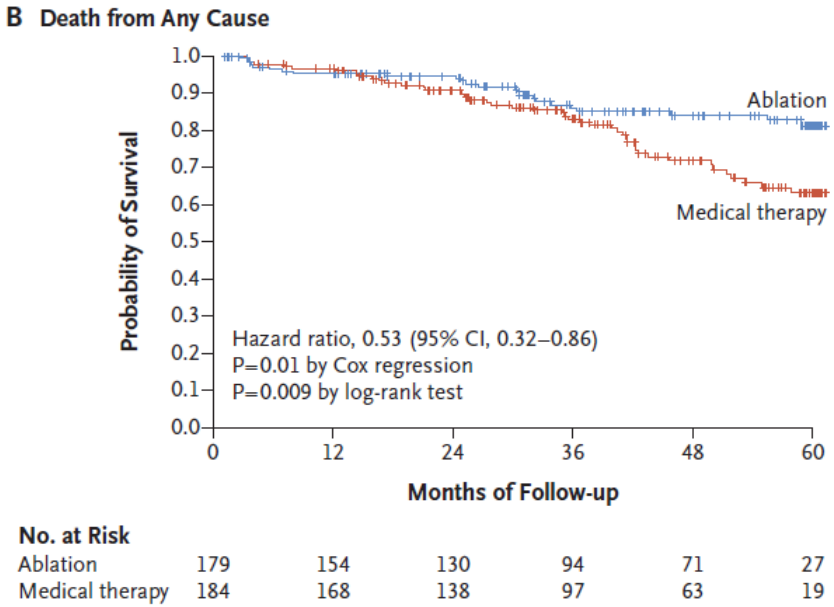
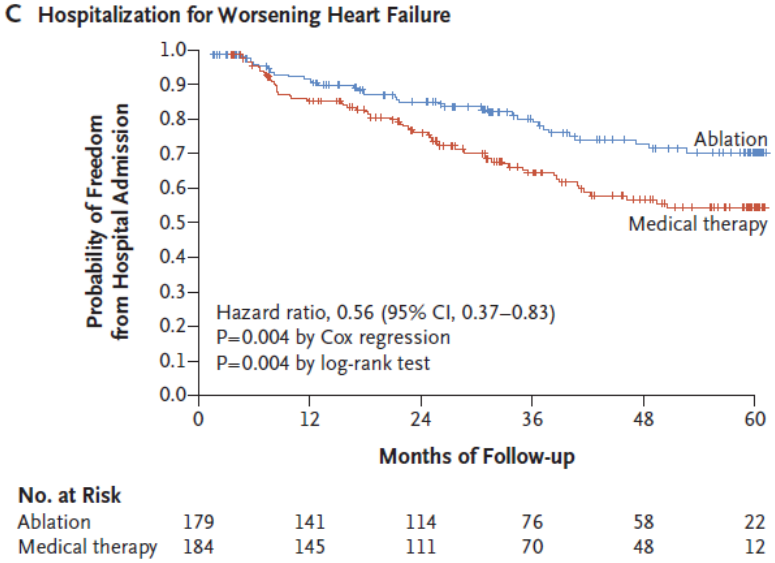
Catheter ablation for atrial fibrillation with heart failure CASTE-AF

- 363 pts, refractory AF, LVEF≤35%, med age 64 yrs
- CA vs. medical therapy (rhythm or rate control)







Marrouche et al. NEJM 2018

Conclusive remarks (1)

- In the past decades, data from RCTs showed that using antiarrhythmic drug therapy there was no significant difference between rate and rhythm control for atrial fibrillation both in the general population and in patients with heart failure
- Over the years, the use of catheter ablation has increased and it appears associated with a decreased in-hospital mortality
- In general, in Italy catheter ablation is less used than in other countries

Conclusive remarks (2)

- Althoug it is a complex study, the CABANA shows that, compared to antiarrhythmic drugs, catheter ablation decreases mortality/hospitalization and improves quality of life
- These data in favor of catheter ablation are corroborated by a wide body of evidence from propensity matched cohorts undergoing ablation or standard therapy showing that mortality, stroke and hospitalization rates are lower in pts undergoing ablation
- The benefit of catheter ablation is particularly evident in selected patients with heart failure