What is the benefit of AF ablation beyond complete AF elimination?

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Disclosures

Consulting/ Honorarium – Biotronik SA and Germany

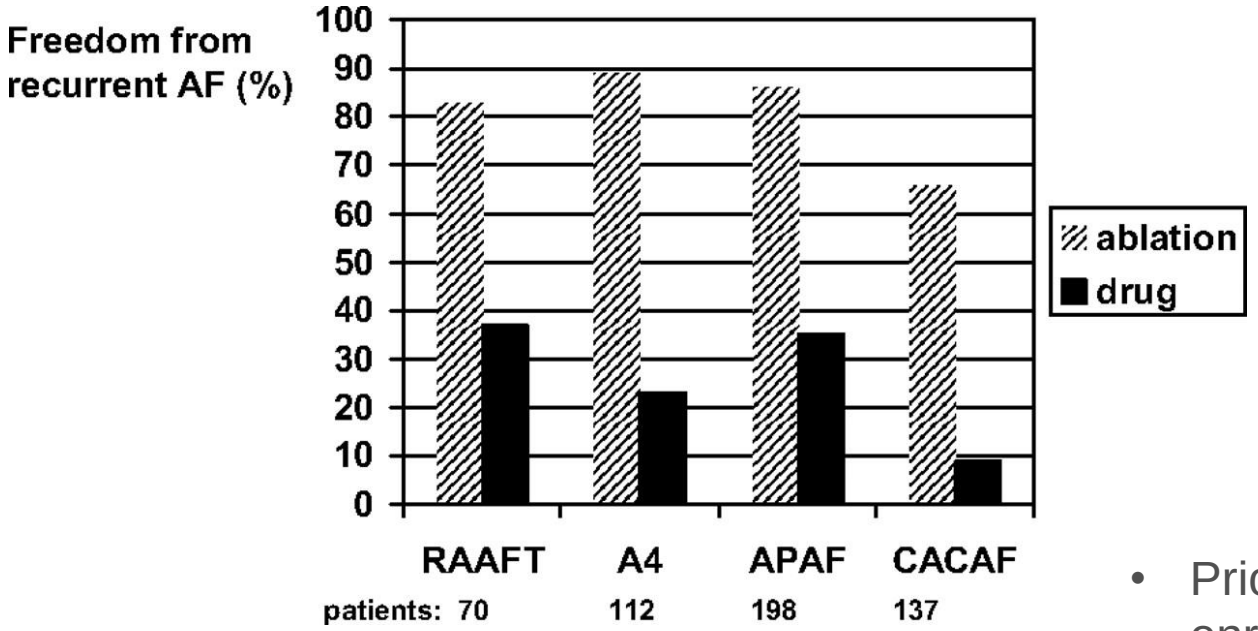
“ AF begets AF”
and the resultant co morbidities

Therefore the corollary must also be true

“ SR begets SR”
Reduction in complications

Background

- AF ablation improves symptoms
- Up until recent trials there was no evidence that AF ablation lowered the risk stroke or death
- PVI is not completely innocuous given the spectrum of recognized complication including atrio oesophageal fistula formation
- The benefit of ablation in the asymptomatic patient remained questionable
- Do we need to reconsider given the current technologies and ablation techniques



- Prior studies relatively small number of patients enrolled
- limited representation of patients with significant cardiac comorbidities
- largely paroxysmal AF
- exclusion of older patients
- patients were only followed for a period of 12 months
- studies were not powered to reveal possible beneficial effects of ablation on mortality, stroke, bleeding

Apples and Oranges, Volume: 118, Issue: 24, Pages: 2488-2490, DOI: (10.1161/CIRCULATIONAHA.108.823179

Relevance in pursuing SR?

- Several AAD trials suggested was little advantage of rate vs rhythm control
  - AFFIRM
  - RACE
  - STAF
  - PIAF
  - AF-CHF
- Arrhythmia drug therapy is also accompanied by side effects and has a proarrhythmia potential

Preceding Trials

Trials showing improvement in LV function, QOL, exercise capacity after catheter ablation for AF

- CAMERA – Catheter ablation vs Medical Rate Control in AF
- AATAC – Ablation vs Amiodarone for Treatment of Persistent AF in Patients with CHF and an Implanted Device
- PABA CHF – Pulmonary vein Antrum Isolation vs AVN Ablation with Biventricular Pacing for the for Treatment of AF in Patients with CHF
- MANTRA PAF – Medical Anti arrhythmia Treatment or RF ablation in PAF
- EAST – Early Treatment of AF for Stroke Prevention

First RCTs powered to investigate the effect of catheter ablation on AF vs conventional first line AAD therapy on hard parameters of mortality and stroke :

- CABANA - Compare Ablation to state of the art drug therapy for patients with new onset/ undertreated AF

- CASTLE AF - Catheter Ablation vs Standard conventional Treatment in Patients with Left ventricular dysfunction and AF

Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) Trial: Study Rationale and Design

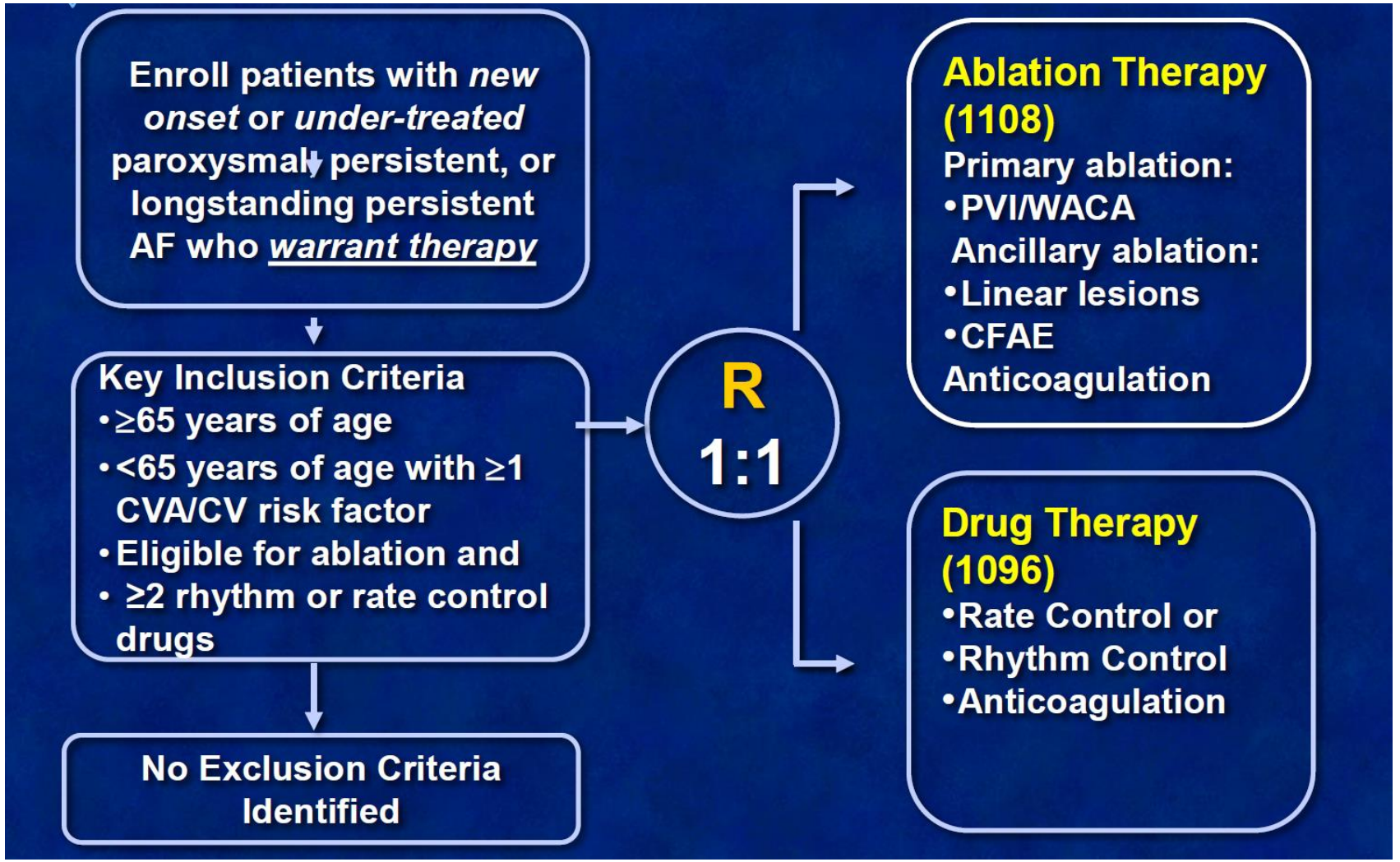
Douglas L. Packer, MD [a,*], Daniel B. Mark, MD, MPH [b], Richard A Robb, PhD [a], Kristi H. Monahan, RN [a], Tristram D. Bahnson, MD [b], Kathleen Moretz, RN [b], Jeanne E. Poole, MD [d], Alice Mascette, MD [c], Yves Rosenberg, MD [c], Neal Jeffries, PhD [c], Hussein R. Al-Khalidi, PhD [b], Kerry L. Lee, PhD [b], for the CABANA Investigators

Primary Endpoint

- All cause mortality
- Disabling stroke
- Serious bleeding
- Cardiac Arrest

Major secondary Endpoints

- cardiovascular hospitalization



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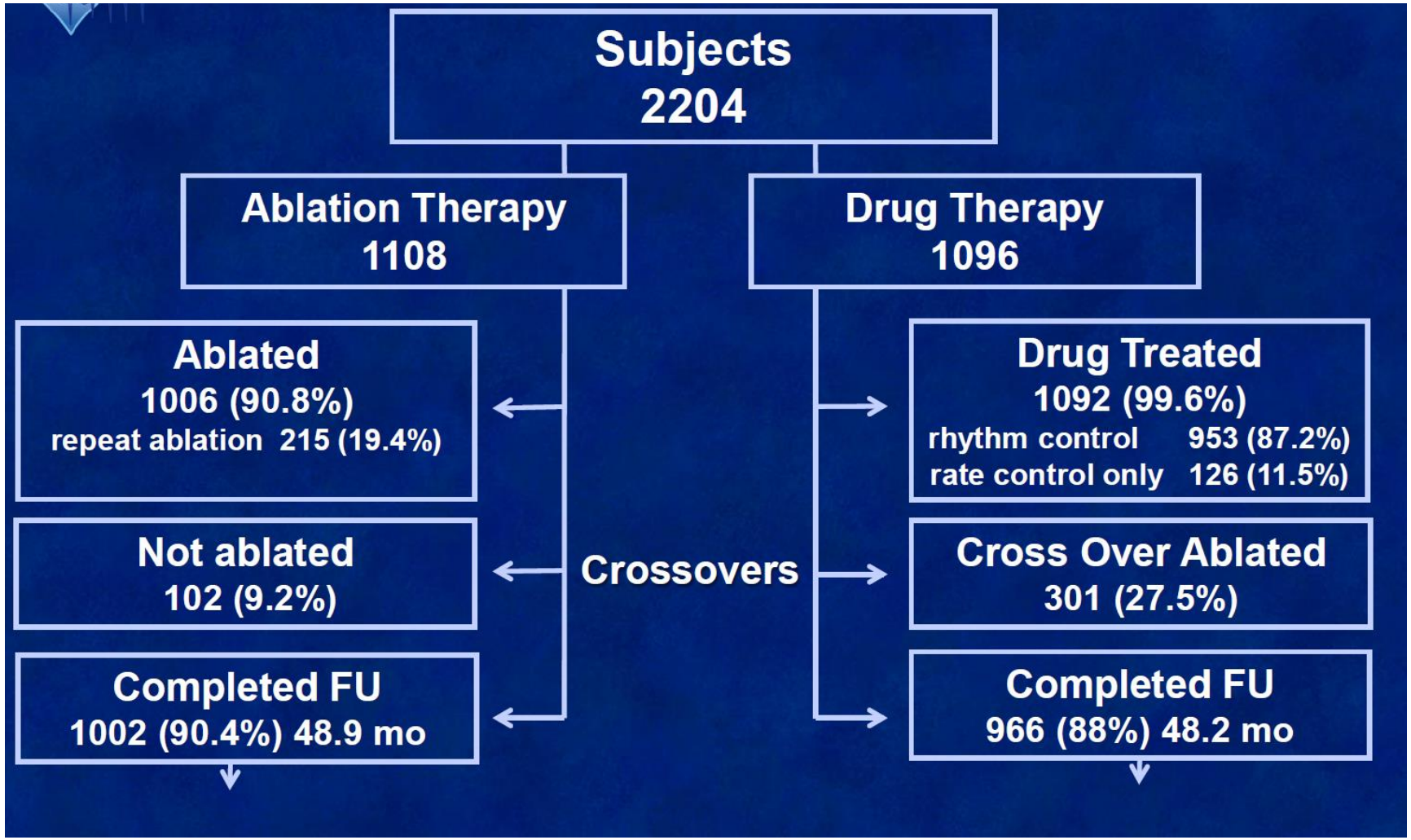

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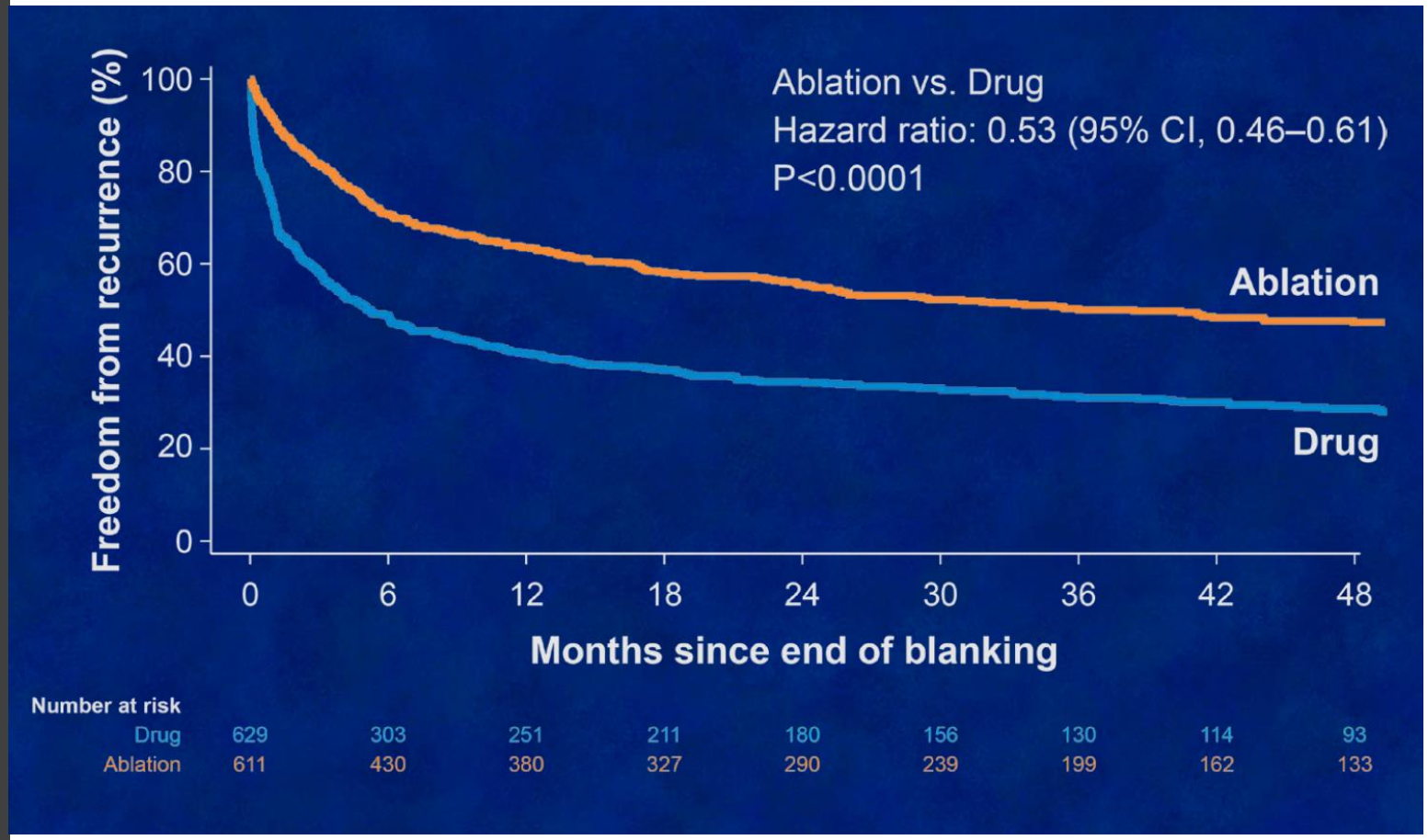
	Ablation	Drug Therapy
Sleep Apnea	23.6%	22.5%
Cardiomyopathy	8.9%	11.2%
Congestive Heart Failure	15.7%	14.9%
NYHA Class		
Class I	13.9%	11.6%
Class II/III	34.3%	36.7%
Prior CVA or TIA	10.6%	9.4%

AF Type	Ablation	Drug Therapy
Paroxysmal	42.4%	43.5%
Persistent	47.3%	47.3%
Longstanding Persistent	10.3%	9.2%
Years since onset of AF [Median (Q1,Q3)]	1.1 (0.3, 4.1	1.1 (0.3, 3.9)
CCS Severity of AF		
Class 0-1	34.6%	26.7%
Class 2	31.8%	32.4%
Class 3-4	43.5%	41.0%
Prior hospitalization for AF	40.6%	38.8%

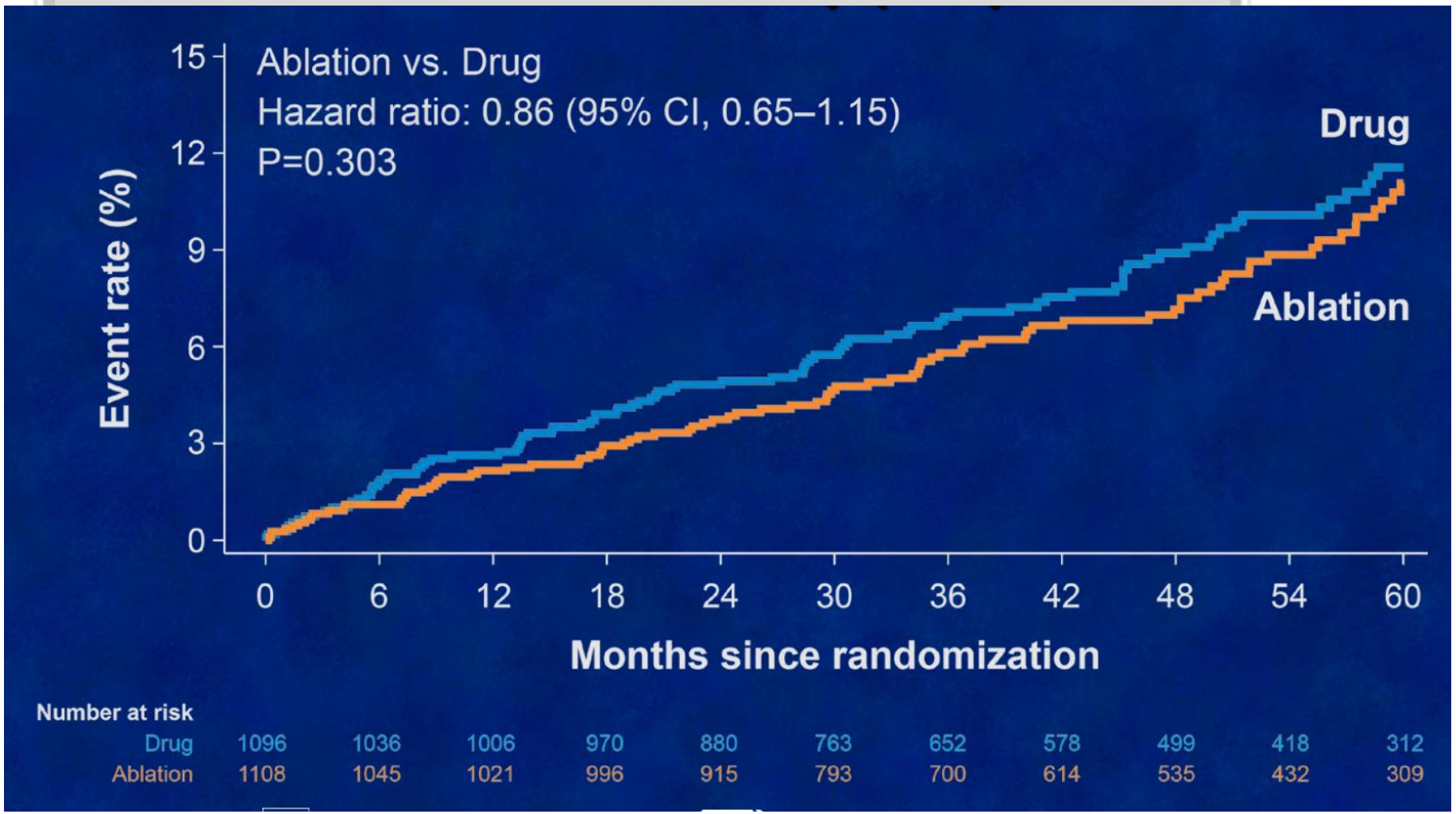
CABANA Trial

- There was a 47% reduction in recurrent AF with ablation compared to drug therapy

AF Recurrence



Results



- Negative study
- Ablation was not shown to be superior to AAD therapy for the primary end points of all cause mortality, disabling stroke and bleeding

Adverse effects related to catheter ablation and anti arrhythmia drug therapy in the CABANA Trial

Event	Ablation n = 1006 n (%)*
Catheter Insertion	39 (3.9)
Hematoma	23 (2.3)
Pseudo aneurysm	11 (1.1)
Atrial venous fistula	4 (0.4)
Pneumothorax	1 (0.1)
Sepsis	1 (0.1)
DVT	0
Pulmonary embolus	0
Catheter Manipulation Within the Heart	34 (3.4)
Pericardial effusion not requiring intervention	22 (2.2)
Cardiac tamponade with perforation	8 (0.8)
TIA	3 (0.3)
Coronary occlusion	0
Myocardial infarction	1 (0.1)
Complete heart block	0
Valvular damage	0
Ablation-related Events	18 (1.8)
Severe pericardial chest pain	11 (1.1)
Esophageal ulcer	5 (0.5)
Pulmonary Vein Stenosis > 75%	1 (0.1)
Phrenic nerve injury	1 (0.1)
Atrial esophageal fistula	0
Medication-related Events	0
Heparin induced bleeding	0

Event	Pts Receiving Drug n = 1092 n (%)*
Hyper- or hypothyroidism	17 (1.6)
Hypotension	3 (0.3)
Major proarrhythmic event (VT,VF)	9 (0.8)
Torsades des pointes	0
Atrial proarrhythmic event	1 (0.1)
Heart failure	0
Allergic reaction	7 (0.6)
Gastrointestinal abnormality	3 (0.3)
Moderate or severe diarrhea	0
Liver injury/failure	3 (0.3)
Pulmonary toxicity	1 (0.1)
Blindness	0
Kidney damage	0
Renal failure	0
Severe headache	0

* n (%) = number (percent) of patients who reported drug-related adverse event. Percent is calculated among all patients that have received drug.

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Catheter Ablation for Atrial Fibrillation with Heart Failure

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- CASTLE AF trial was a multi centre open labelled RCT assessing whether catheter ablation lowers morbidity and mortality as compared with medical therapy (rate or rhythm control)
- Underlying LV dysfunction with medical treated HF

Patient selection

- Patients with paroxysmal or persistent atrial fibrillation/long standing persistent AF
- Medically treated heart failure NYHA grade 2, grade 3 or 4
- Left ventricular ejection fraction of 35% or less
- All patients were implanted with a Biotronik ICD or CRT–D with automatic daily remote monitoring activated

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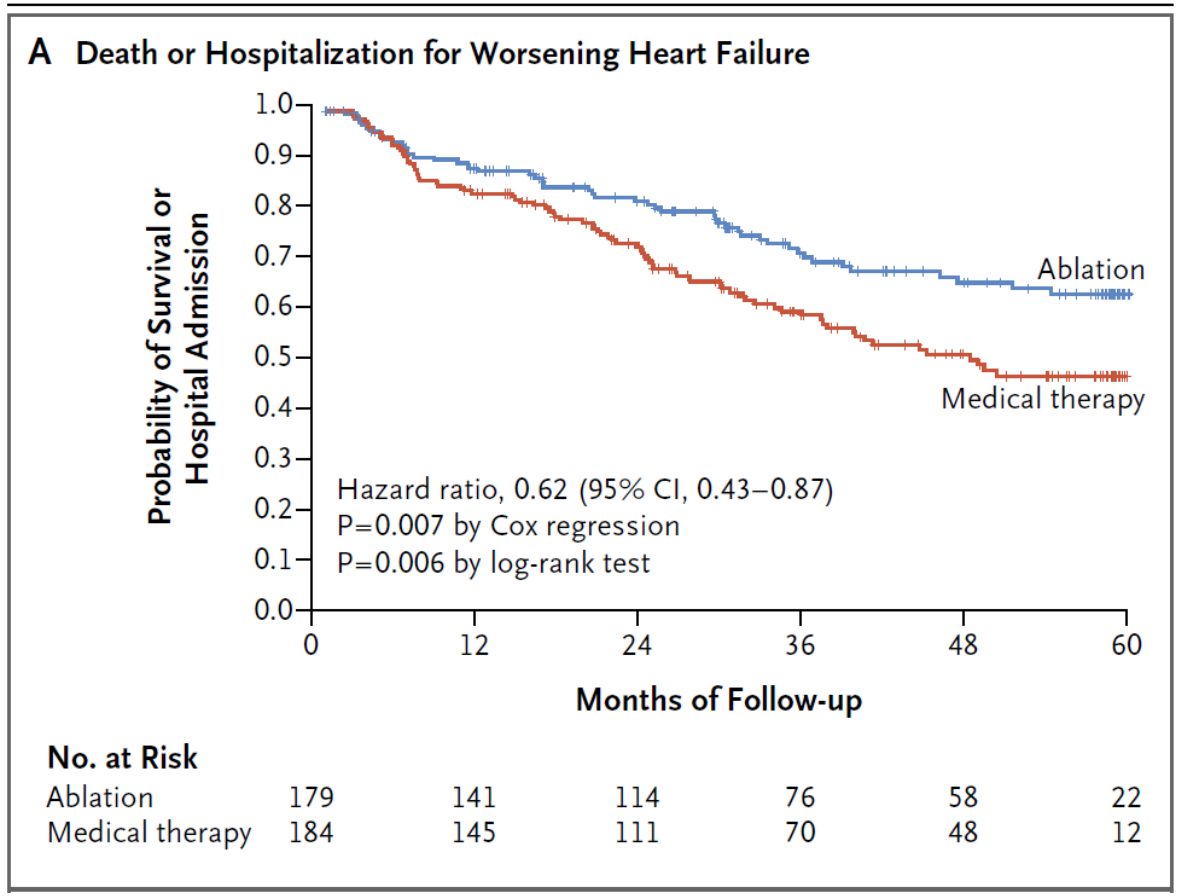
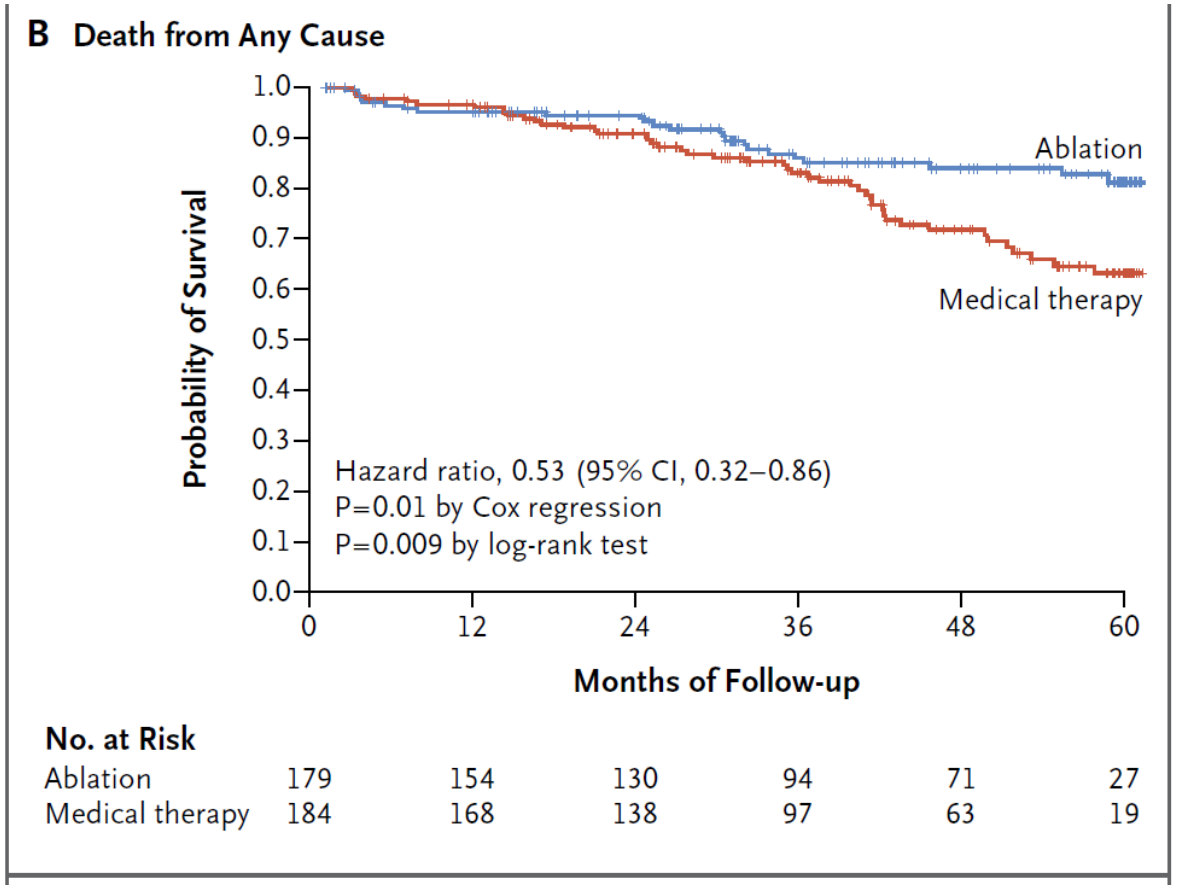
CASTLE AF study

Characteristic	Treatment Type	
	Ablation	Medical Therapy
Left atrial diameter		
Total no. of patients evaluated	162	172
Median — mm	48.0	49.5
Interquartile range — mm	45.0–54.0	5.0–55.0
Left ventricular ejection fraction		
Total no. of patients evaluated	164	172
Median — %	32.5	31.5
Interquartile range — %	25.0–38.0	27.0–37.0
CRT-D implanted — no. (%)§	48 (27)	52 (28)
ICD implanted — no. (%)§	131 (73)	132 (72)
Dual-chamber	128 (72)	123 (67)
Single-lead device with "floating" atrial sensing dipole	3 (2)	9 (5)
Indication for ICD implantation — no. (%)		
Primary prevention	160 (89)	163 (89)
Secondary prevention	19 (11)	21 (11)
History of amiodarone use — no./total no. (%)¶		
Failure	78/175 (45)	82/176 (47)
Unacceptable side effects	21/175 (12)	24/176 (14)

RESULTS of the CASTLE AF

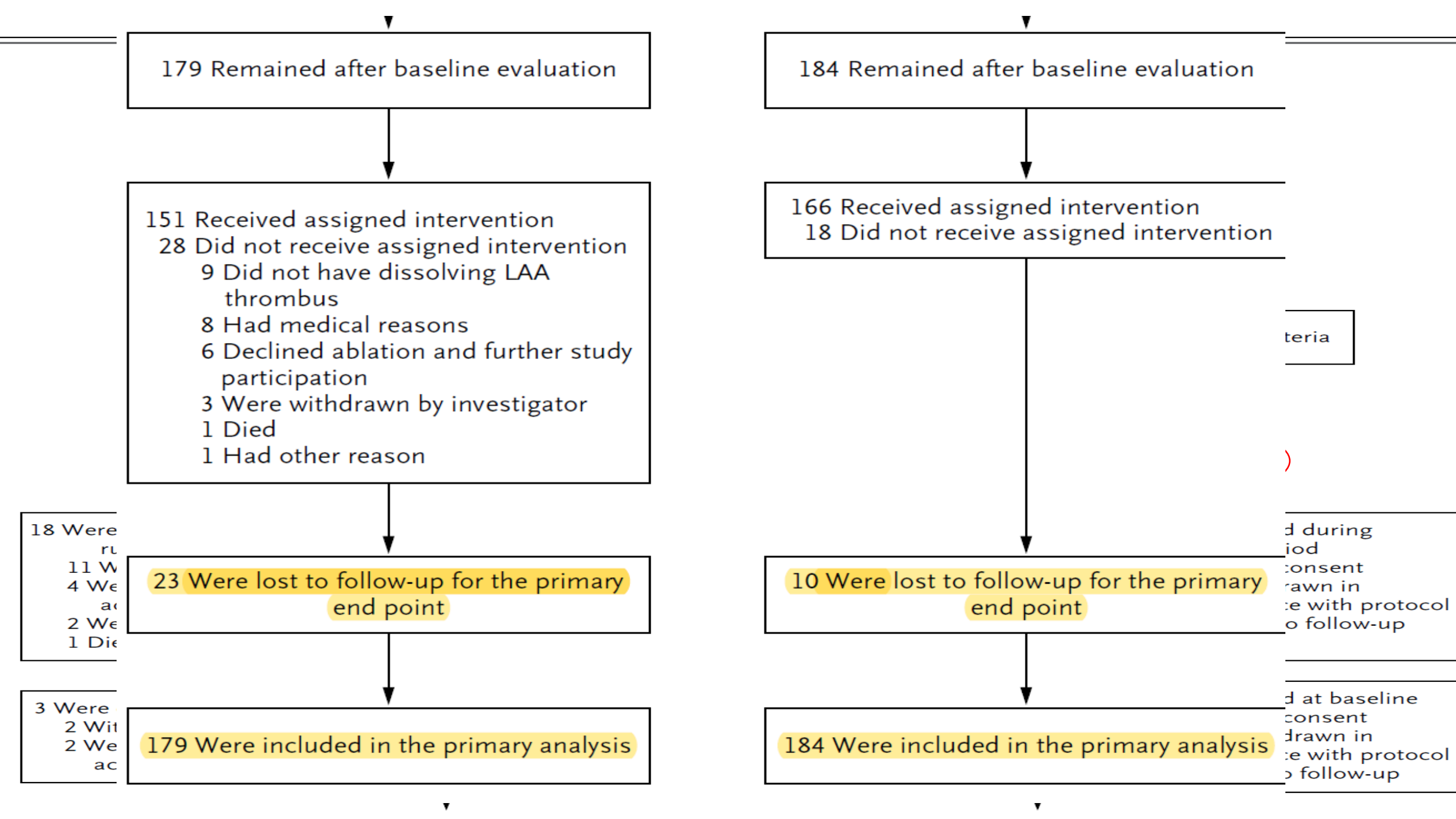
- There were 24 deaths in the ablation group and 46 deaths in the medical group (13.4% and 25.0 % respectively, P = 0.01)
- There were 37 patients with heart failure related admissions in the ablation group and 66 patient's in the medical therapy group (rates of 20.7% and 35.9% respectively, P = to 0.004)





Complications

- 3 patients in the ablation group had pericardial effusion one requiring pericardiocentesis
- 3 patients had severe bleeding requiring blood transfusion related to the femoral puncture sites, one with pseudoaneurysm which was surgically corrected
- Asymptomatic pulmonary vein stenosis was diagnosed in 1 patient


179 Remained after baseline evaluation
151 Received assigned intervention
28 Did not receive assigned intervention
9 Did not have dissolving LAA thrombus
8 Had medical reasons
6 Declined ablation and further study participation
3 Were withdrawn by investigator
1 Died
1 Had other reason
23 Were lost to follow-up for the primary end point
179 Were included in the primary analysis
184 Remained after baseline evaluation
166 Received assigned intervention
18 Did not receive assigned intervention
10 Were lost to follow-up for the primary end point
184 Were included in the primary analysis

Considerations in the CASTLE AF Trial

- Small number of patients that were finally included in the analysis for the ablation and drug therapy groups

- It took about 8 years to select 363 patients from among 3013 patient in the CASTLE AF Trial with Mortality benefit only emerging after 3 years

- All patients had an ICD or CRT–D which may have affected overall mortality in both groups

Is there a benefit of AF ablation beyond complete AF elimination?

- Catheter ablation for patients with the paroxysmal or persistent atrial fibrillation is superior to drug therapy for rhythm control
- Catheter ablation for patients with AF and heart failure also have a lower incidence of recurrence of atrial fibrillation and also benefit from all cause mortality reduction, hospitalization for CV risks and disabling strokes
- However the data suggests that patients undergoing ablation with underlying HF should be selectively chosen