ACC Middle East Conference 2018

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جمعية القلب السعودية
Saudi Heart Association

Atrial Fibrillation Ablation

Recent Clinical Trials That Changed (or not) My Practice

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Update on Atrial Fibrillation Ablation

Atrial Fibrillation: What's New? Not Much

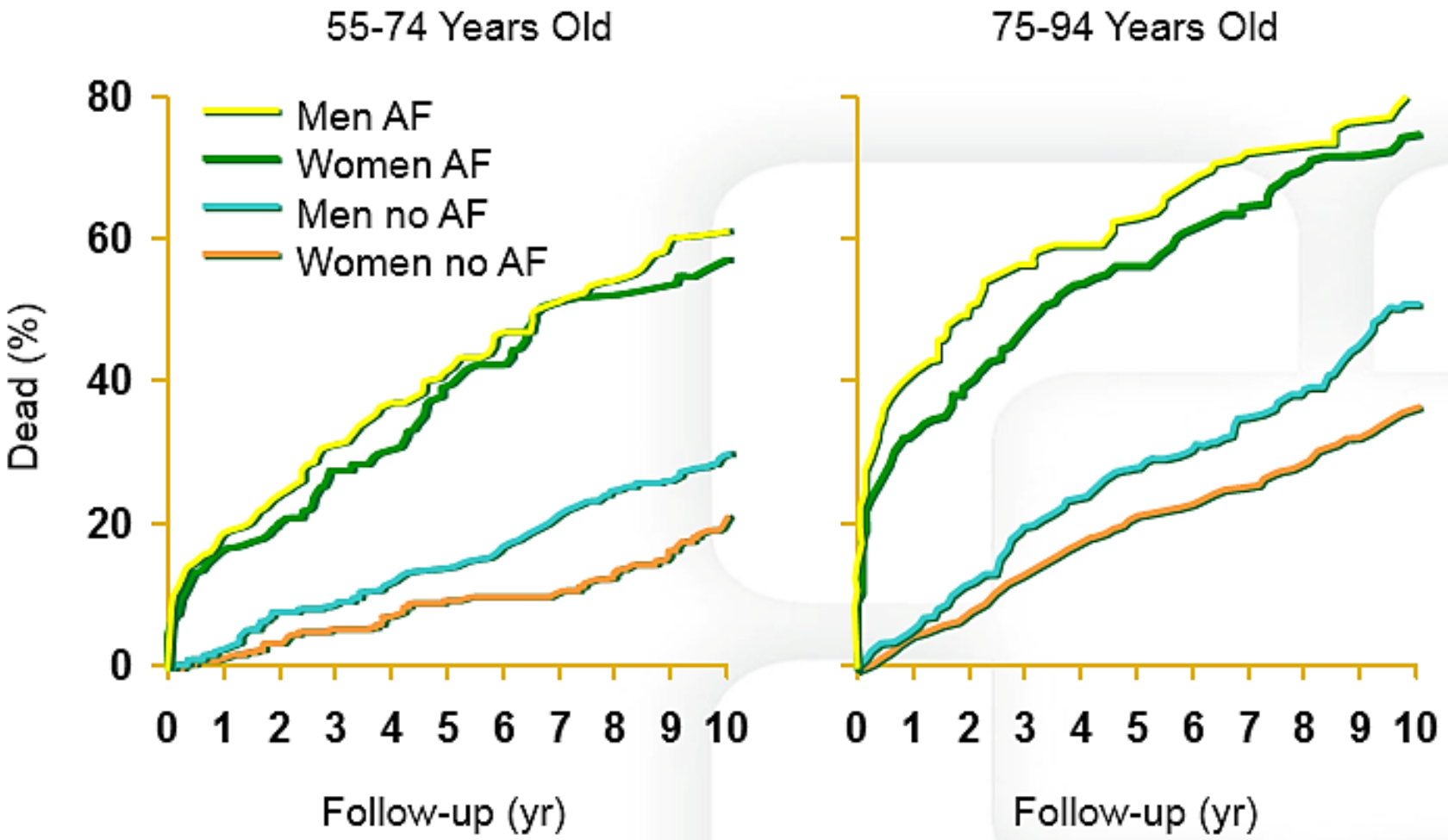
CASTLE AF
CABANA
Upstream therapy

AF Ablation: GOALS

- **Relief of symptoms**
- **Improved quality of life**
- Prevention of CHF
- Prevention of stroke
- Decrease disease progression
- Reduction of Mortality
- Reduction in cost of care

Not a Cure…
Reduction of AF burden

Impact of Atrial Fibrillation on Mortality in Framingham Study

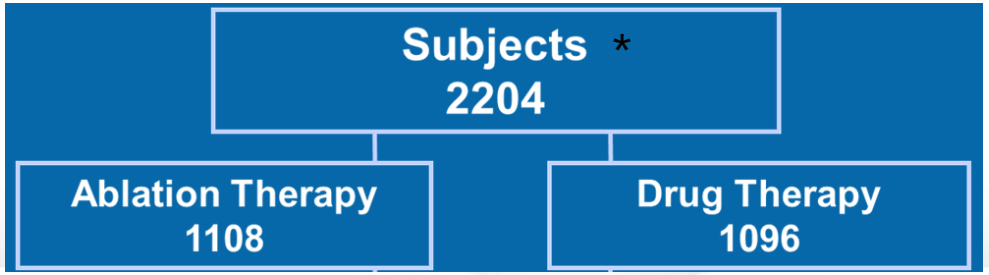


Benjamin et al: Circ 98:946, 1998

The long awaited news : Impact on Mortality

CABANA

Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation



Key Inclusion Criteria

- AF (Parox, persistent)
- ≥65 years of age
- <65 years + ≥1 CVA/CV risk factor
- Eligible for ablation and ≥2 rhythm or rate control drugs

Primary Endpoint

- All-cause mortality, disabling stroke, serious bleeding, or cardiac arrest

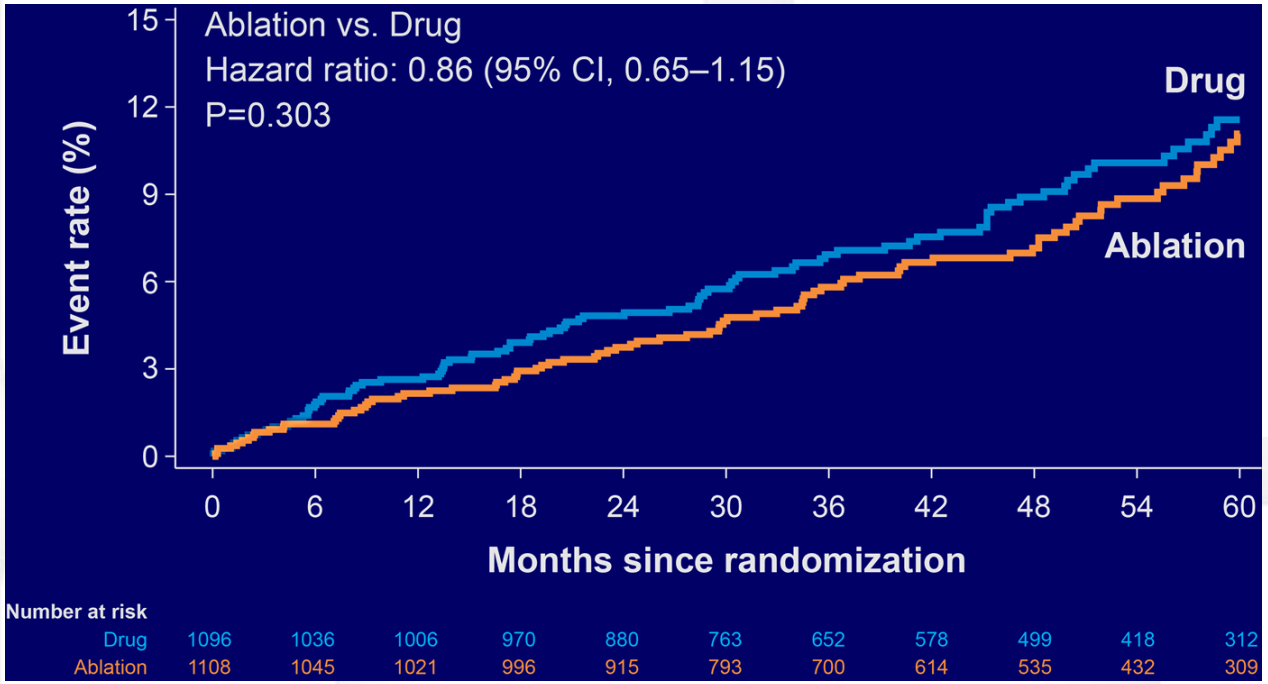
Major Secondary Endpoints

- All-cause mortality *
- Death (all-cause) or cardiovascular hospitalization
- AF recurrence

CABANA (Summary Results)

- Intention to treat (ablation vs. drug)
  - Primary endpoint: 8% vs. 9.2% , p = 0.3 (HR 0.86)

All-cause mortality
Disabling stroke
Serious bleeding
Cardiac arrest



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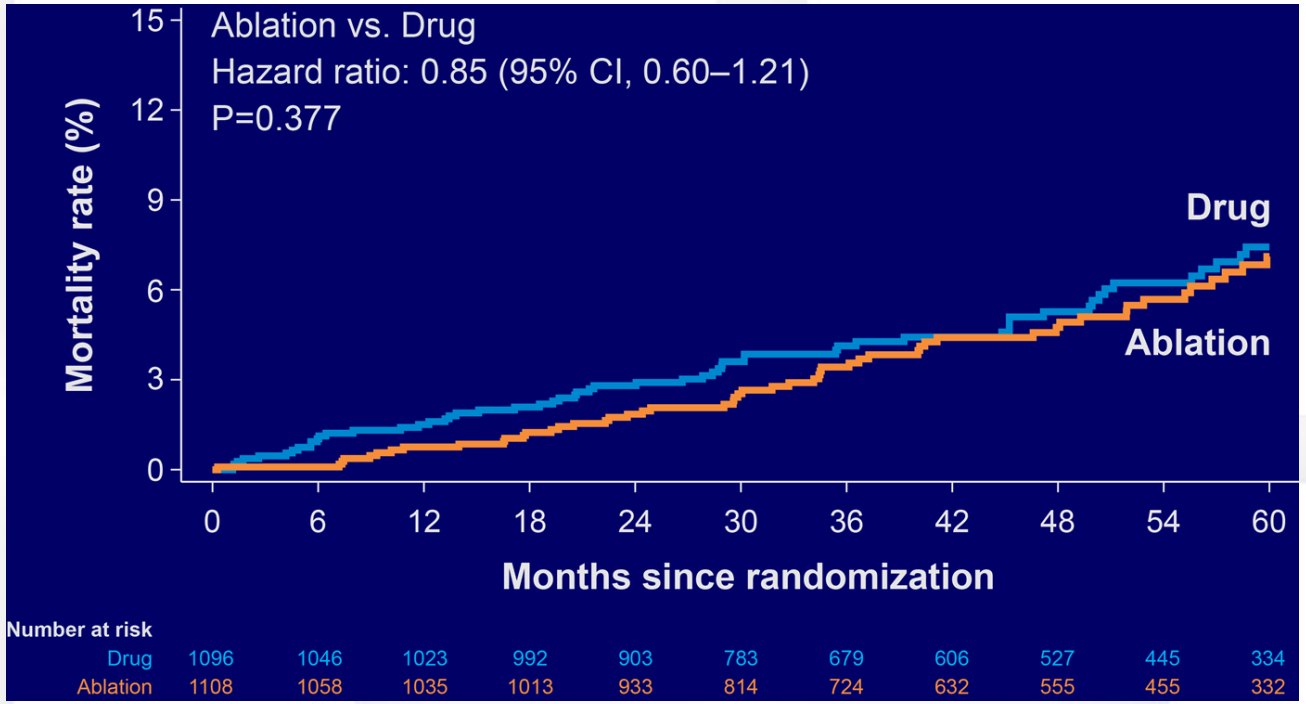
- Intention to treat (ablation vs. drug)
  - Primary endpoint: 8% vs. 9.2% , p = 0.3 (HR 0.86)
  - Death: (ITT) 5.2% vs. 6.1% p = 0.38



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  - Serious stroke: 0.3% vs. 0.6% p = 0.19

	Ablation N = 1108	Drug N = 1096	Hazard Ratio (95% CI)	P-Value
Primary Outcome				
Composite:	89 (8.0%)	101 (9.2%)	0.86 (0.65, 1.15)	0.30
Death	58 (5.2%)	67 (6.1%)	0.85 (0.60, 1.21)	0.38
Disabling stroke	3 (0.3%)	7 (0.6%)	0.42 (0.11, 1.62)	0.19
Serious bleeding	36 (3.2%)	36 (3.3%)	0.98 (0.62, 1.56)	0.93
Cardiac arrest	7 (0.6%	11 (1.0%)	0.62 (0.24, 1.61)	0.33
Secondary Outcomes				
All-cause mortality	58 (5.2%)	67 (6.1%)	0.85 (0.60, 1.21)	0.38
Death or CV hospitalization	573 (51.7%)	637 (58.1%)	0.83 (0.74, 0.93)	0.001

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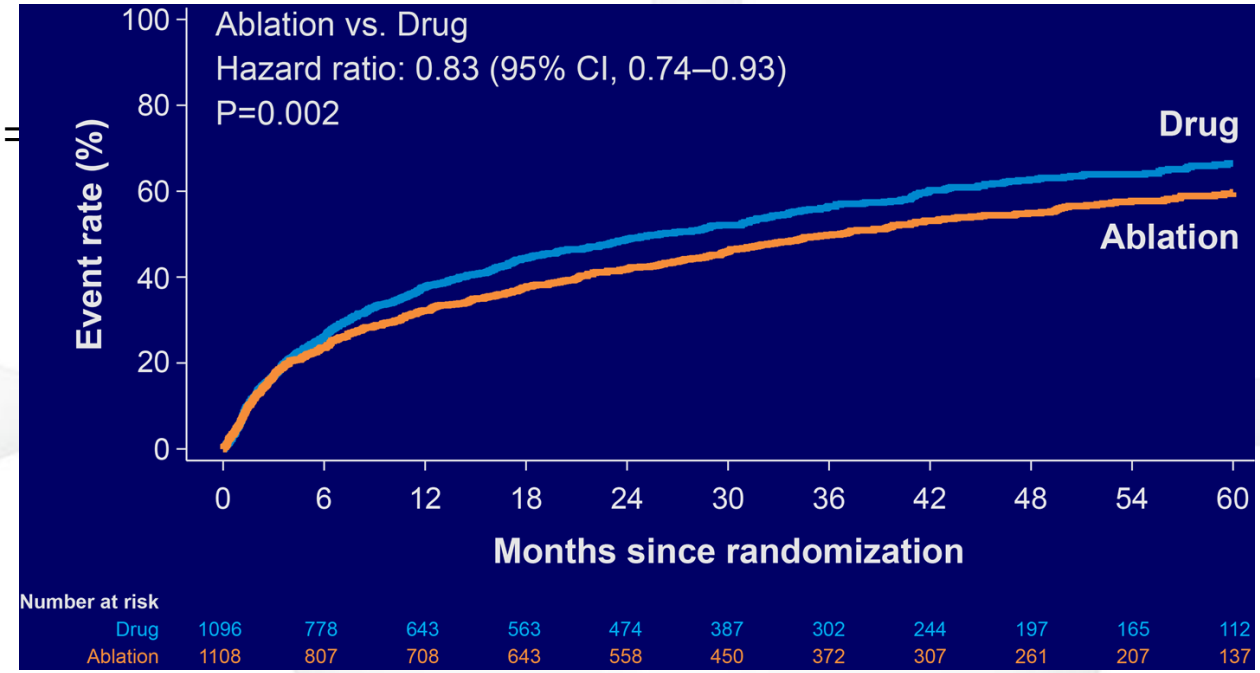
  - Serious stroke: 0.3% vs. 0.6% p = 0.19
- Secondary outcomes: (ablation vs. drug)
  - Death or CV hospitalization: 51.7% vs. 58.1%; p =



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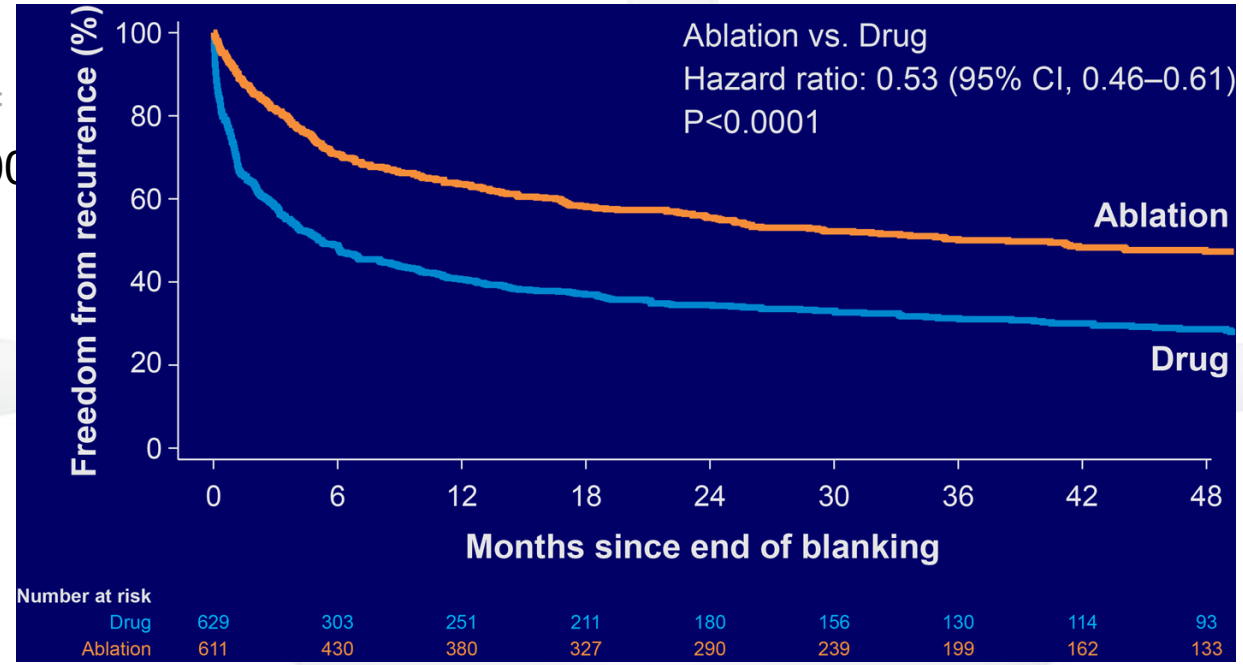
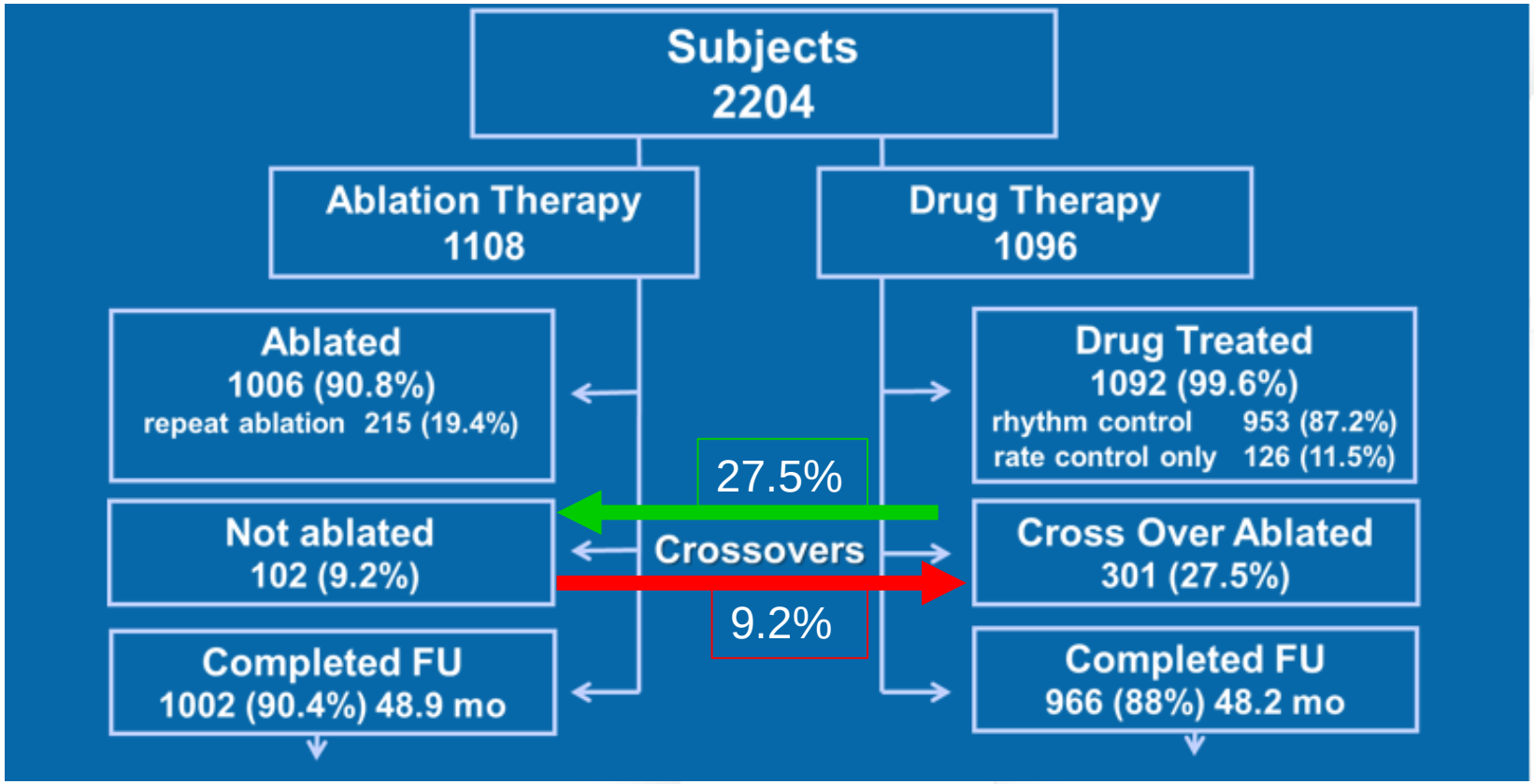
  - Death or CV hospitalization: 51.7% vs. 58.1%; p =
  - Time to first AF recurrence: HR 0.53, p < 0.0



CABANA: Patient Randomization



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  - Death: (ITT) 5.2% vs. 6.1% p = 0.38
  - Serious stroke: 0.3% vs. 0.6% p = 0.19
- Secondary outcomes: (ablation vs. drug)
  - Death or CV hospitalization: 51.7% vs. 58.1%; p = 0.002
  - Time to first AF recurrence: HR 0.53, p < 0.0001
- On treatment analysis (for ablation(1307) vs. drug therapy(897)):
  - Primary endpoint : 7.0% vs. 10.9% HR:0.67 p = 0.006;
  - All-cause mortality: 4.4% vs. 7.5% HR:0.6 p = 0.005;
  - Death or CV hospitalization: 41.2% vs. 74.9% HR:0.83 p = 0.002

CABANA (Adverse Events)

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

Ablation

Drugs

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.

- Tamponnade with ablation: 0.8%; Ablation-related events: 1.8%

CABANA: So, where does this leave us?

Ablation vs. Drugs

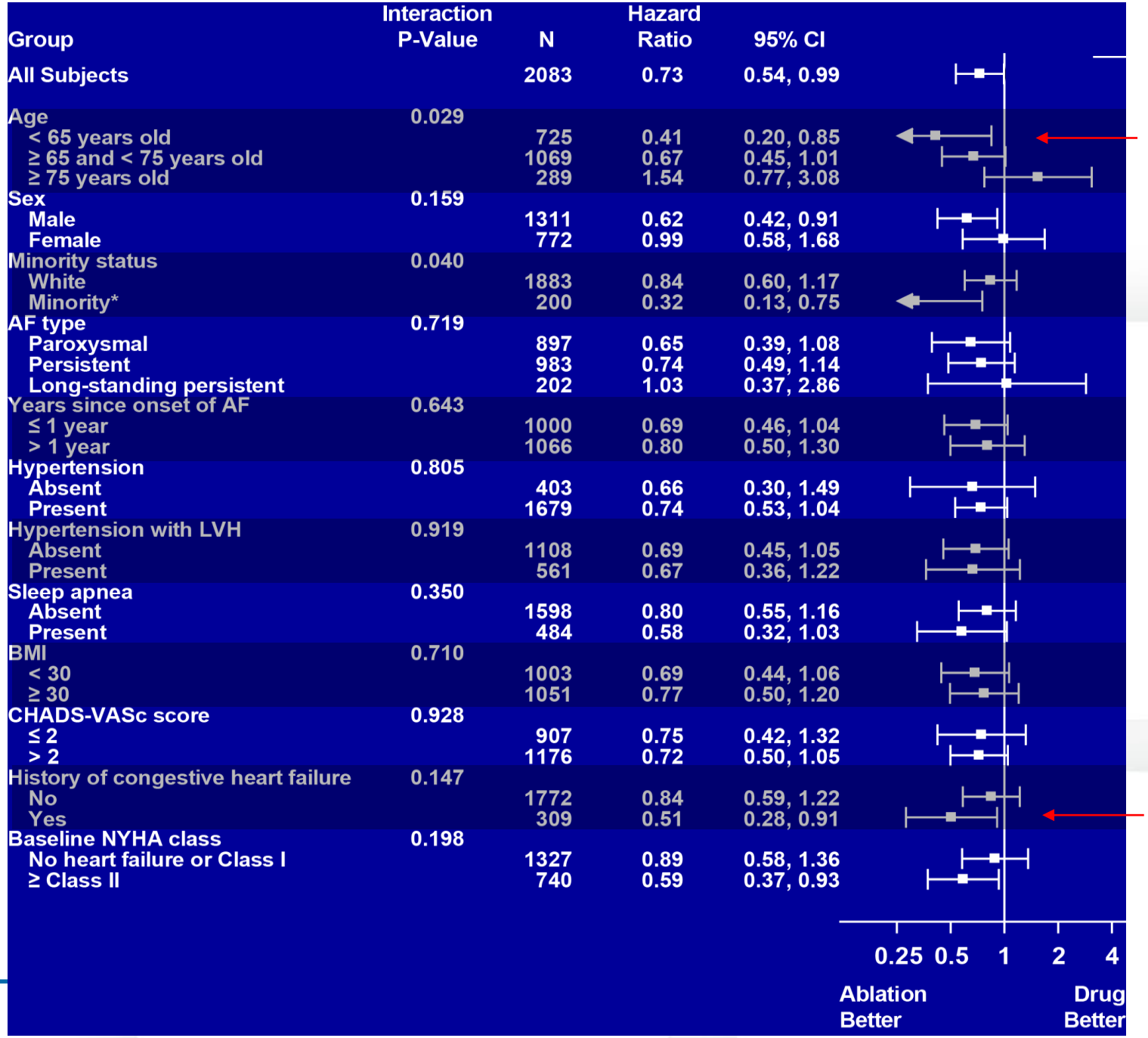
- No reduction in primary End point
- No reduction in all cause Mortality
- Reduced mortality or CV hospitalization (17%).
- Results affected by cross-overs in both directions.
- Reduced recurrent AF (47%): “Ablation actually works”
- On Treatment analysis (Treatment received) → Reduced Primary end point (33%)
  Reduced Total mortality (40%)
- Safety: Low adverse events

CABANA

- Primary Endpoint Sub-group Analysis

  All-Cause Mortality, Disabling Stroke, Serious Bleeding, Cardiac Arrest

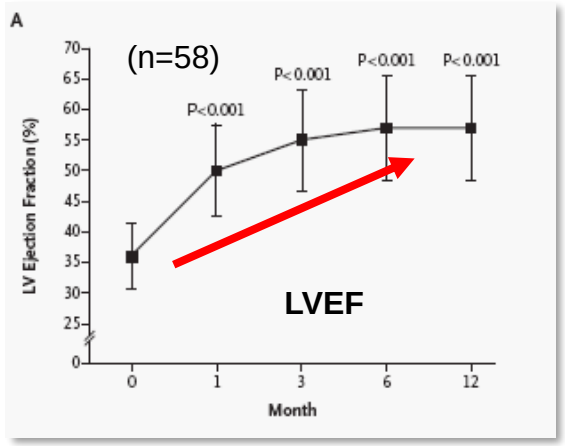
  (Per Protocol)

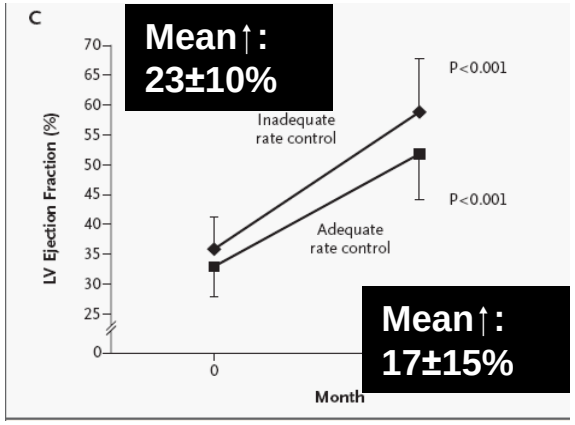


Patients with AF and LV dysfunction.

AF ablation in patients with LV dysfunction and CHF
Improvement in Left Ventricular Function and QoL

Hsu et al; NEJM 2004;351:2373

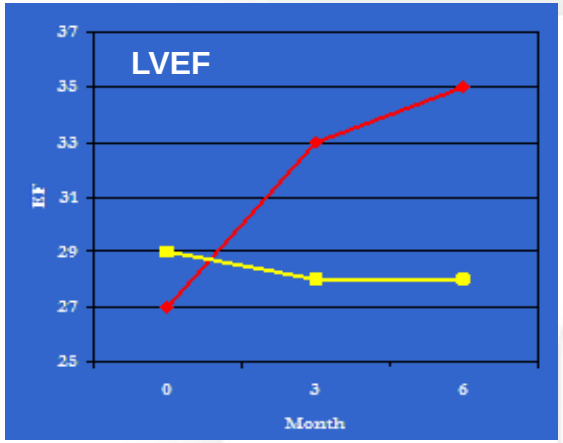


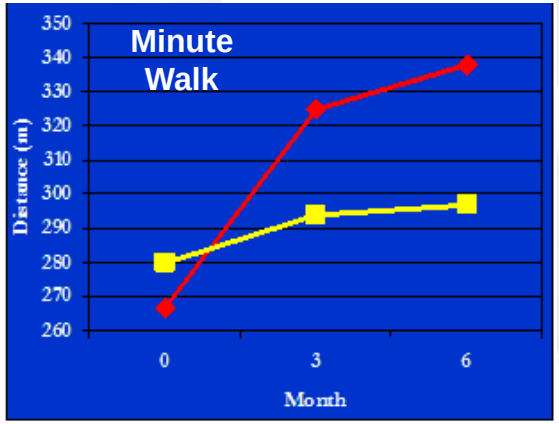


PABA-CHF

AF Ablation vs. AVN abl. + BiV

Khan et al. N EJM 2008;359:1778

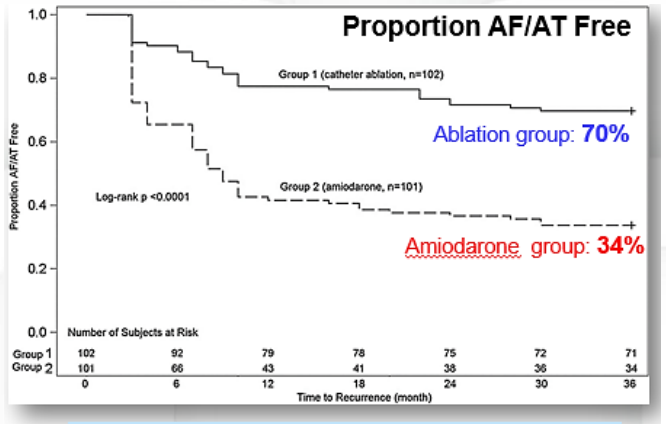




AATAC trial

AF Ablation vs. Amio

Di Biase et al. Circ. 2016;133:1637



In patients with HF (LVEF,40%) + persistent AF
Catheter Ablation is **superior** to AMIO

- Freedom from AF
- Reducing Unplanned hospitalization
- Reducing mortality

CASTLE-AF

Catheter Ablation versus Standard conventional Treatment in patients with LVD and AF

- Symptomatic AF: Parox & Pers.
- Failure of AAD
- LVEF ≤ 35%
- NYHA class ≥ II
- ICD/CRTD

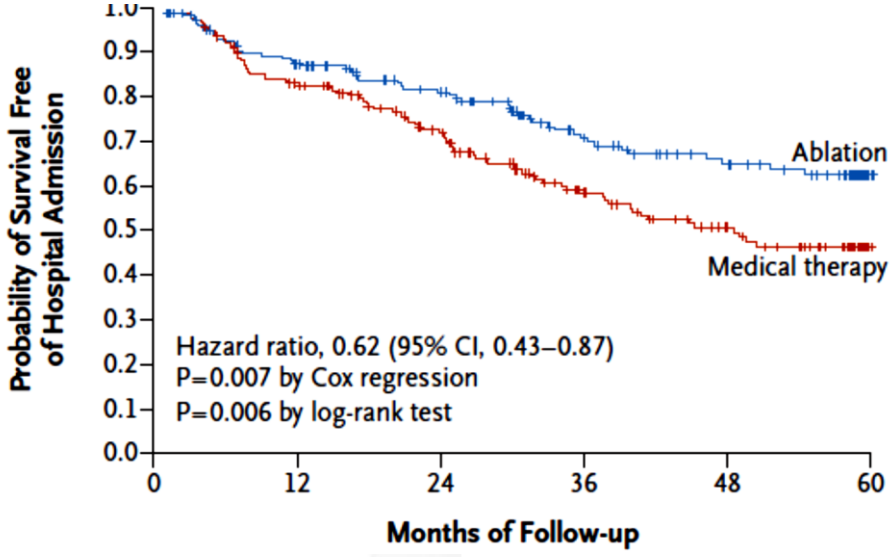
N=363

Primary Endpoint

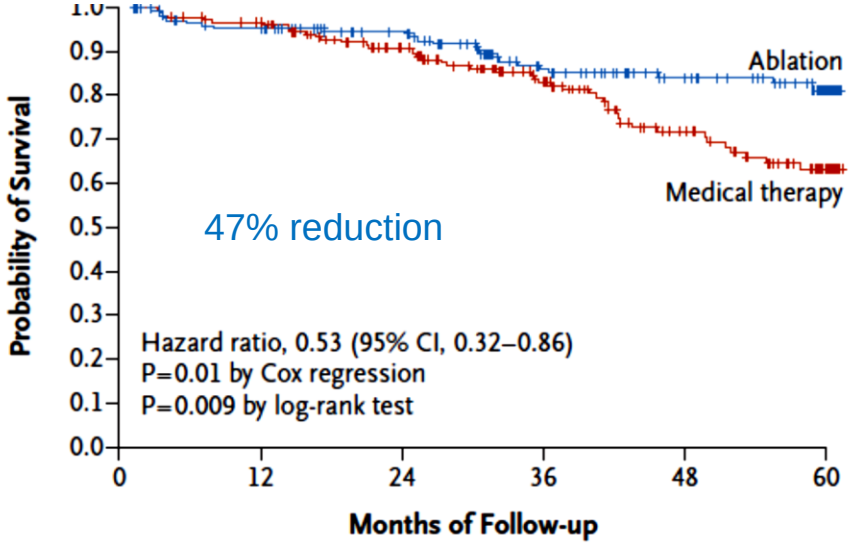
- All-cause mortality
- Hospitalization for Worsening HF

CA of AF improves primary endpoints of mortality and HF progression compared to conventional standard therapy

Death or Hospitalization for Worsening HF



Death from any cause

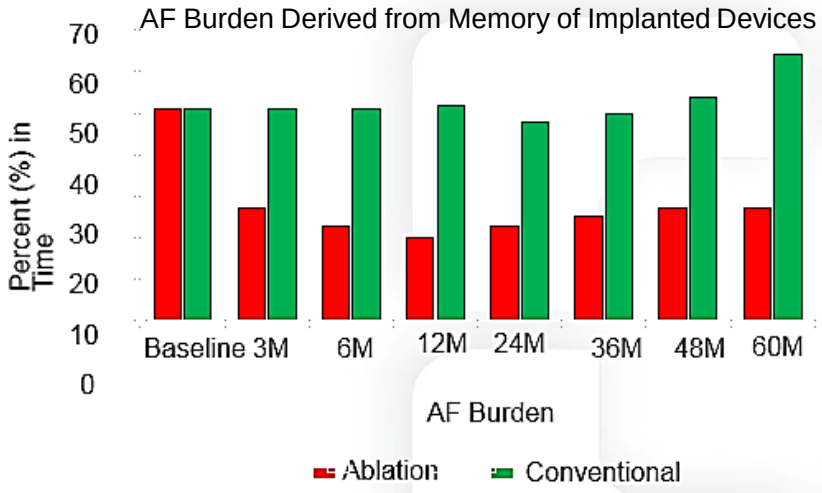


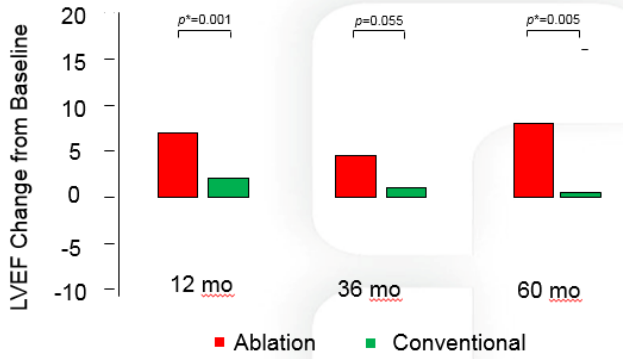
Marrouche et al, NEJM 2018; 378 (5)

CASTLE-AF

Catheter Ablation versus Standard conventional Treatment in patients with LVD and AF

AF burden is a major driver for primary outcome.





Reduction in AF burden but not Time to first recurrence
impacted both the composite endpoint and mortality in this high-risk population

CASTLE AF Conclusions

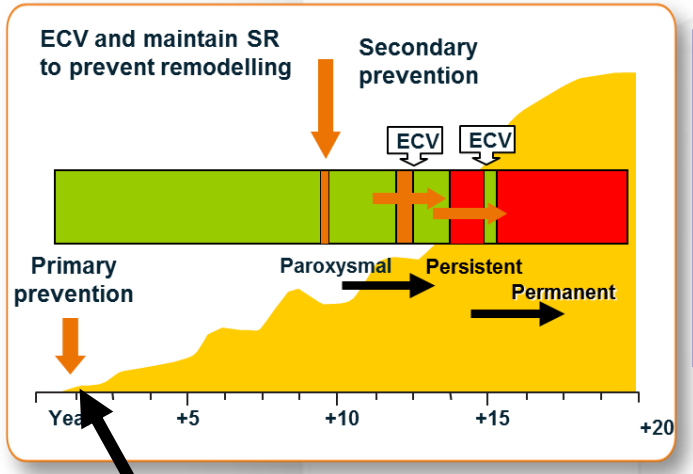
When compared to conventional standard therapy ***Catheter ablation*** of atrial fibrillation in patients with heart failure is associated with:

- **Improved all-cause mortality**
- **Fewer admissions for worsening heart failure**

AF Ablation: Why do we fail?

1. PV reconnection; Extrapulmonary Vein foci
2. Ignorance as to the mechanisms of AF

3. Progression of underlying disease

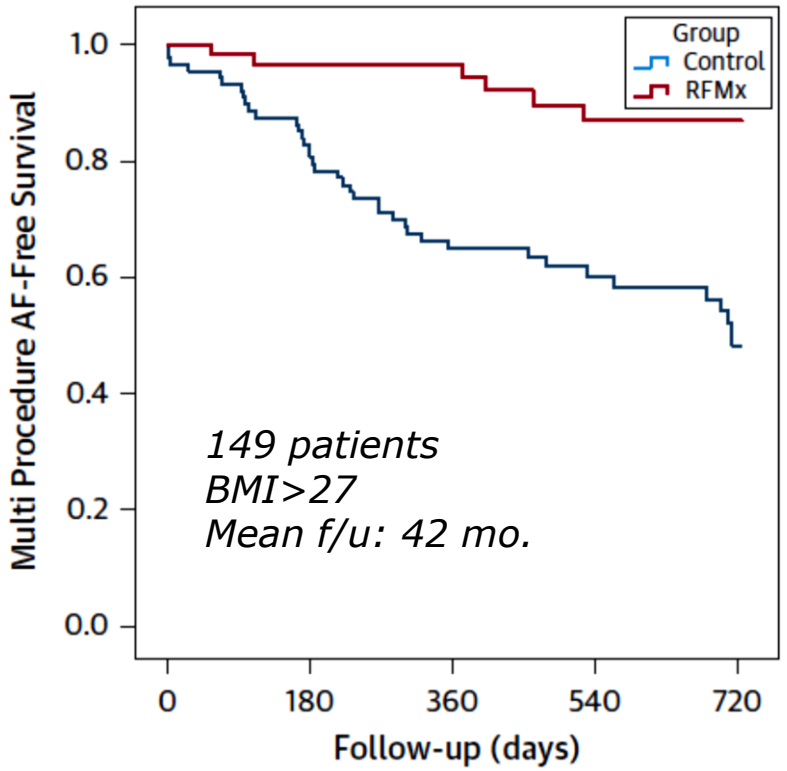


Risk Factors
Hypertension
Obesity
Sleep apnea
CHF
CAD
...

Primary prevention: Early and active management of associated conditions that precede AF

ARREST-AF

- Goal: Evaluate the impact of **Risk Factors** and **weight loss** on AF ablation outcomes



- Improved AF Burden
- Improved AF free survival

Concurrent risk factor treatment is an essential component of strategies for rhythm control

Pathak et al. JACC 2014 Dec 2;64(21):2222-31

REVERSE AF

PREVEntion and regReSsive Effect of weight-loss and risk factor modification on Atrial Fibrillation

- 1415 AF patients →355 with BMI≥ 27 kg/m2 included for analysis.
- 3 Weight loss groups

Weight Loss	Group 1 (<3%)	Group 2 (3–9%)	Group 3 (≥10%)
Paroxismal → Persistent	41%	32%	3%*
Persistent→Paroxismal or no AF	26%	49%	88%*
			* p< 0.001
Free from AF	39%	67%	86%*

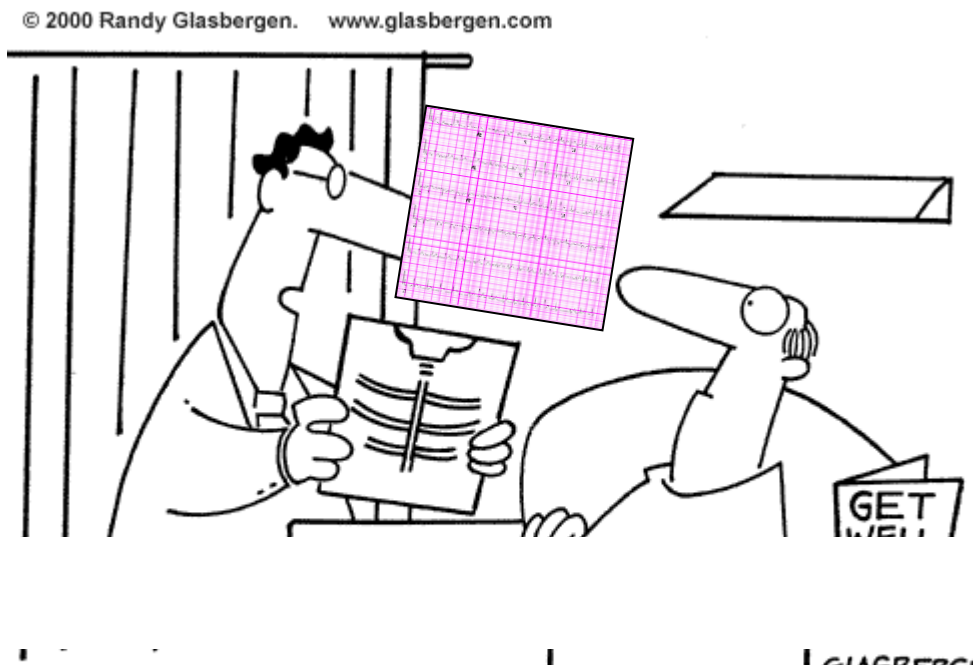
Weight-loss management and RFM reverses the type and natural progression of AF.

Middeldorp et al. EP Europace, June 2018

New Antiarrhythmic Drug for AF
No FDA Approval Required

A Pair of Sneakers

Treat the patient not just the disease



"Your EKG showed atrial fibrillation, but we fixed it with Photoshop"

Conclusion

- PVI: for symptoms
- Ablation in LVD
  - Mortality
- Upstream Therapy

Thank You