Ablation vs. Amiodarone for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure and an Implanted ICD/CRTD

(AATAC-AF in Heart Failure)

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ClinicalTrials.gov Identifier: NCT00729911/ P.I. Andrea Natale

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DISCLOSURES

I am a consultant for

- ✓Biosense Webster
- ✓St Jude Medical

I received speaker honoraria/travel expense from

- ✓Atricure
- ✓Biotronik
- ✓Medtronic
- ✓Boston Scientific
- ✓Epi EP

BACKGROUND

- Trans-catheter ablation represents a valid treatment option in patients with drug-refractory symptomatic atrial fibrillation (AF).

- The majority of catheter ablation trials have mainly enrolled patients with preserved left ventricular (LV) systolic function and paroxysmal AF.

- In these patients the ablative treatment has shown to be effective in reducing morbidity, improving the quality of life (QoL) and functional capacity.

- However, a significant number of patients with AF also have LV systolic dysfunction.

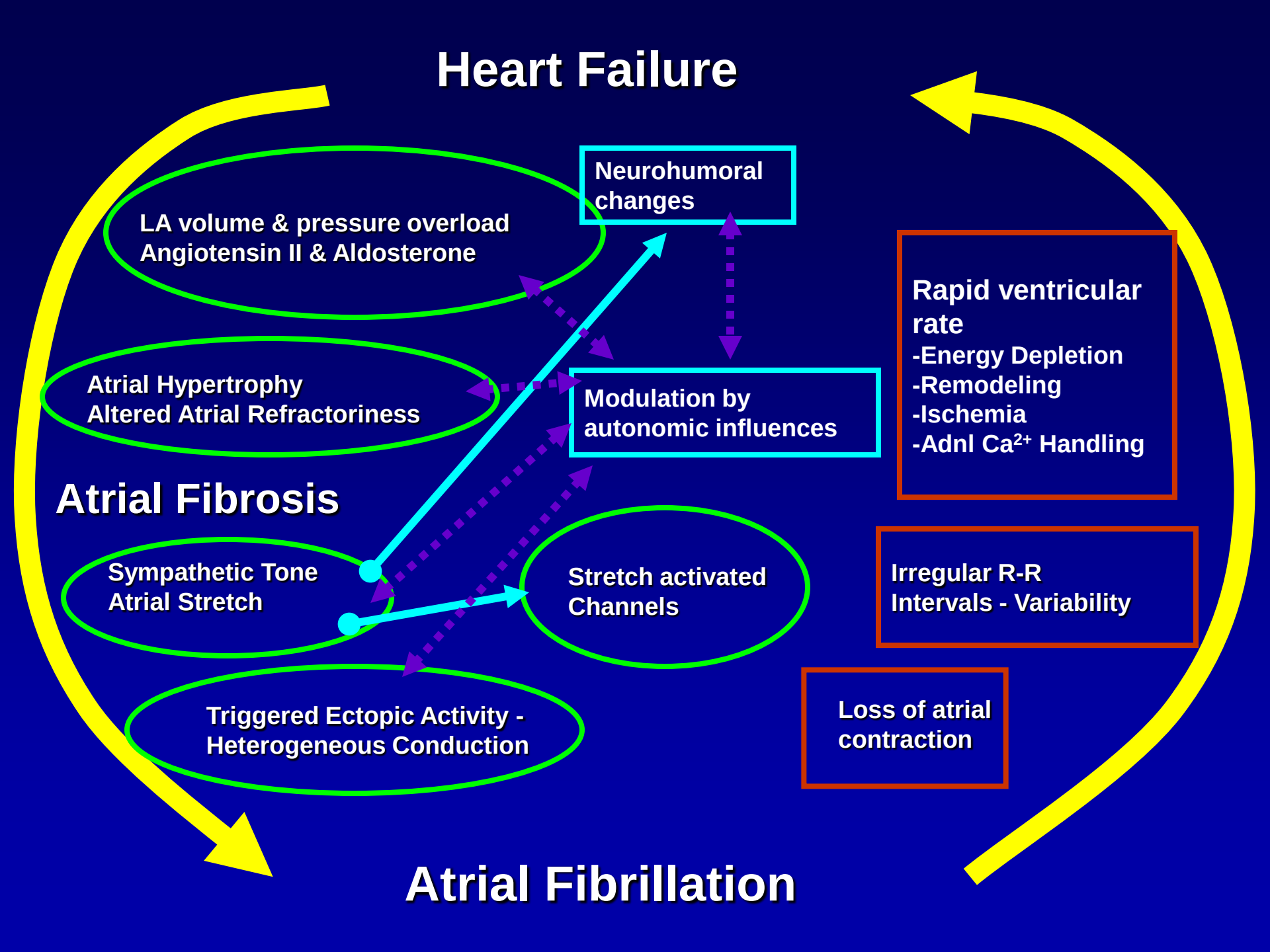
BACKGROUND

- AF and heart failure (HF) frequently coexist and are often associated with several common predisposing risk factors such as hypertension, coronary artery disease (CAD), structural heart disease (non-ischemic, valvular), diabetes mellitus, obesity and obstructive sleep apnea (OSA).

- Importantly, the prevalence of AF increases with HF severity, ranging from 5% in functional class I patients to approximately 50% in class IV patients.

- Also, the prevalence of HF in patients with AF has been estimated at 42%. The combination of HF and AF lead to deleterious hemodynamic and symptomatic consequences.

- Rhythm control with antiarrhythmic drugs (AADs) has not shown satisfactory results in randomized trials both in patients with or without HF.


Heart Failure
LA volume & pressure overload
Angiotensin II & Aldosterone
Neurohumoral changes
Rapid ventricular rate
-Energy Depletion
-Remodeling
-Ischemia
-Adnl Ca^{2+} Handling
Atrial Hypertrophy
Altered Atrial Refractoriness
Modulation by autonomic influences
Atrial Fibrosis
Sympathetic Tone
Atrial Stretch
Stretch activated Channels
Irregular R-R Intervals - Variability
Triggered Ectopic Activity - Heterogeneous Conduction
Loss of atrial contraction
Atrial Fibrillation

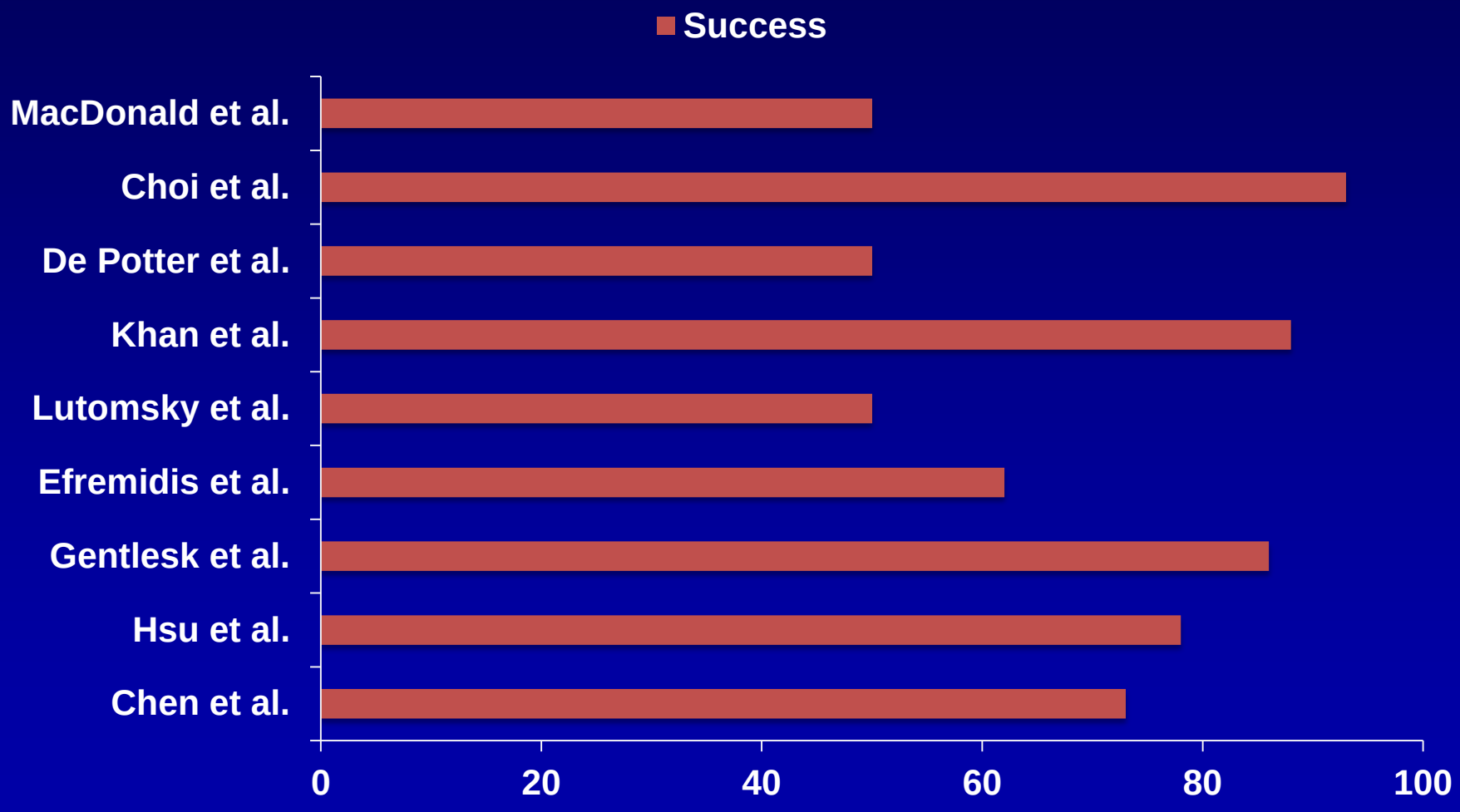
BACKGROUND

Outcomes in Heart Failure Patients With Catheter Ablation

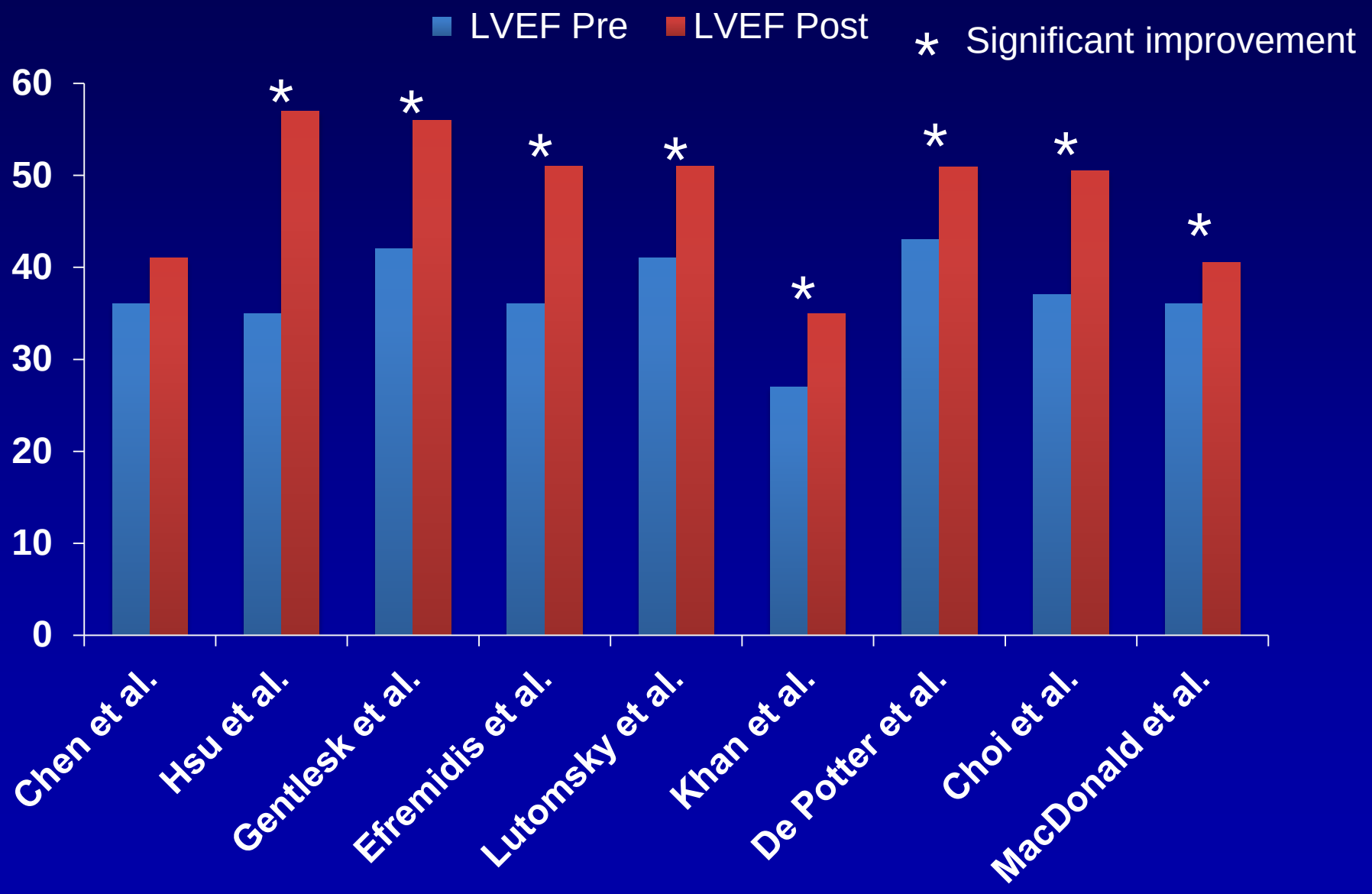
RFCA in Pts with Left Ventricular Dysfunction

Study Name	Year	Design	Pt. N	Mean Age	Mean LVEF	AF Type	FU (mos)
Chen et al.	2004	Cohort	94	57	36	All	6
Hsu et al.	2004	Case-Control	58	56	35	All	12
Gentlesk et al.	2007	Cohort	67	42	42	PAF, PerAF	3-6
Efremidis et al.	2007	Cohort	13	54	36	PAF, PerAF	9
Lutomsky et al.	2008	Cohort	18	56	41	PAF	6
Khan et al.	2008	RCT	41	60	27	All	6
De Potter et al.	2010	Case-Control	26	49	43	All	6
Choi et al.	2010	Case-control	15	56	37	PAF, PerAF	16
MacDonald et al.	2010	RCT	22	62	36	PerAF	10

Freedom from recurrent arrhythmia after RFCA of AF in pts with left ventricular dysfunction



LVEF Improvement after RFCA of AF



AIM OF THE STUDY

We sought to investigate whether catheter ablation is superior to Amiodarone for the treatment of persistent AF in patients with Heart Failure (HF) in a randomized trial.

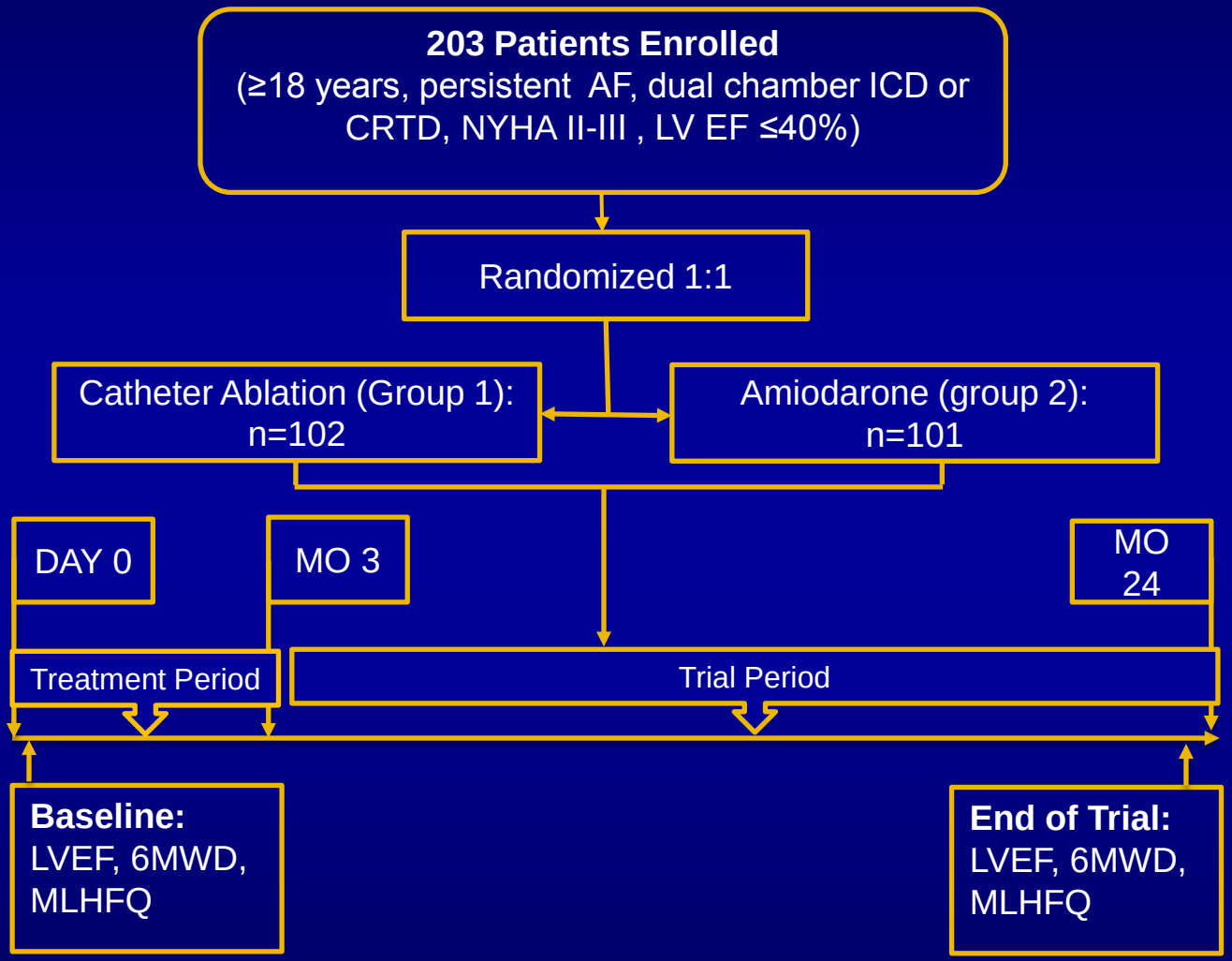
Methods

- AATAC was a randomized, parallel-group, multicenter study assessing whether catheter ablation is superior to amiodarone for the treatment of AF
- Power Calculation: 100 patients per group were required to detect at least 20% difference (30% to 50%) at 24 month follow-up with 5% alpha and 80% power, using log-rank test
- 203 patients were enrolled in the study and randomly assigned (1:1 ratio) to:
  - Undergo catheter ablation (Group I, n=102)
  - Or receive amiodarone, (group 2=101)
- Patients ≥18 years of age, with persistent AF, having dual chamber ICD or CRTD, NYHA II-III and LV EF ≤40% within the last 6 months were included in this trial

Methods

- Primary Endpoint: Long-term procedural-success
  - Procedural success was defined as freedom from AF, AFL, or AT of > 30 second duration off-AAD
  - In the ablation arm, a second ablation was allowed in the 3-month blanking period, and any AT after was considered as recurrence
- Secondary endpoints included:
  - All-cause mortality;
  - Cardiac related re-hospitalizations during post-ablation follow-up (AF/CHF related);
  - Change in LVEF;
  - 6-minute walk distance (6MWD);
  - Quality of Life measured by Minnesota Living with Heart Failure questionnaire (MLHFQ).

Methods



MO- month, 6MWD – 6 minute walk distance,
MLHFQ - Minnesota Living with Heart Failure questionnaire

Ablation

- The main goal of the ablation procedure was pulmonary vein antrum isolation.
- Additional linear lesions, ablation of complex fractionated electrograms and elimination of non PV triggers were advised but performed according to the preference of the center or the operator.

Patient Characteristics

	Group 1 (Cather Ablation, n=102)	Group 2 (Amiodarone, n=101)	P
Age, yrs	62±10	60±11	0.18
Male, n (%)	77(75%)	74(73%)	0.72
AF Duration, month (median, IQR)	8.6±3.2	8.4±4.1	0.69
BMI, kg/m2	30±8	29±4	0.26
Hypertension, n (%)	46(45%)	48(48%)	0.73
Diabetes, n (%)	22(22%)	24(24%)	0.72
Coronary Artery Disease, n (%)	63(62%)	66(65%)	0.59
LA Diameter, mm	47±4.2	48±4.9	0.12
LV EF, %	29±5	30±8	0.32
OSA	46(45%)	48(48%)	0.73
6MWD (m)	348±111	350±130	0.89
MLHFQ Score	52±24	50±27	0.58

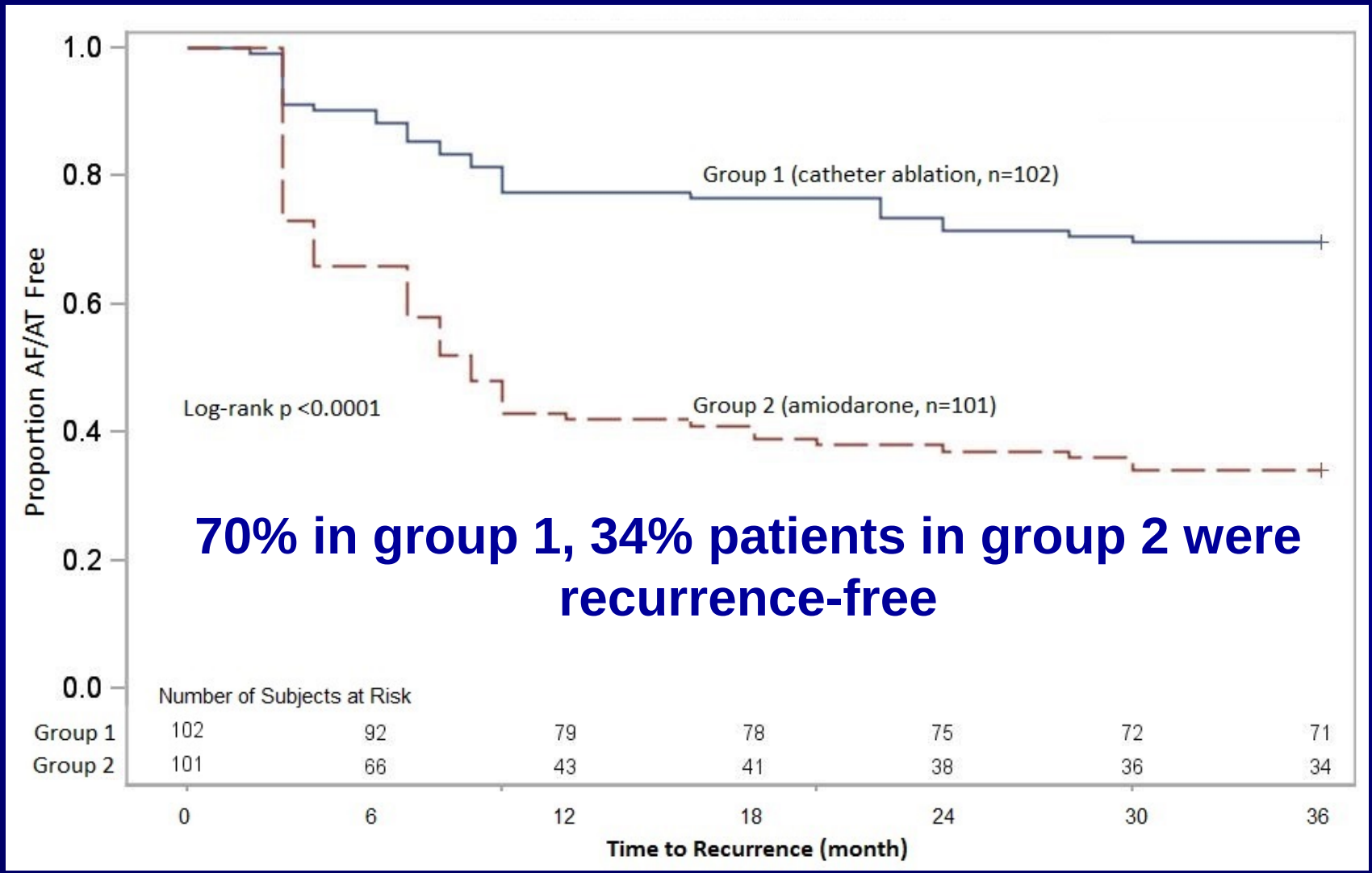
Results

- Group 1 and 2 did not differ in their baseline characteristics:
  - Left atrium size (47±4.2 mm, 48±4.9 mm, p=0.12)
  - median AF duration (8.6±3.2, 8.4±4.1 months, p=0.69)
  - LVEF (29±5%, 30±8%, p=0.32)

Results: Arrhythmia Recurrence

- Long-term Follow-up
  - No patient lost to follow-up; all patients had ≥6 month follow-up
- Freedom from recurrence at 26±8 month:
  - 71(70%) in group 1 (ablation arm)
  - 34(34%) patients in group 2 (log-rank p <0.001)
  - In Group 2 (AMIO) : 7 (10.4%) failed after amiodarone discontinuation due to adverse side effects
    - 4 had thyroid toxicity, 2 pulmonary toxicity, and 1 patient developed liver dysfunction

Kaplan–Meier curves comparing success rate



Results: Arrhythmia Recurrence

- In the 102 patients undergoing catheter ablation,
  - PVI plus posterior wall and non pv trigger ablation was done in 80 patients
  - PVI alone was performed in 22
- Higher success rate in patients undergoing PVI plus ablation compared to PVI alone
  - PVI+PW: 63 (78.8%)
  - PVI alone: 8 (36.4%) , $p < 0.001$

Predictors of Recurrence: univariate model

Variables	Hazard Ratio (95% CI)	P
Amiodarone Treatment	**3.00 (1.96 to 4.61)**	**<.0001**
Sex	1.14 (0.92 - 1.41)	0.219
Age, years	0.99 (0.98 to 1.019)	0.940
BMI, kg/m2	0.99 (0.94 - 1.03)	0.587
LVEF, %	0.96 (0.93 - 0.99)	0.012
Hypertension	1.12 (0.93 - 1.36)	0.241
LA Size, cm	1.02 (0.99 - 1.05)	0.180
Cardiomyopathy	0.84 (0.56 - 1.3)	0.360
Diabetes Mellitus	**2.22 (1.31 - 3.75)**	**0.003**

Predictors of Recurrence

- Multivariate analysis was performed using Cox model
- After adjusting for age, gender, diabetes, and hypertension:
  - Patients on amiodarone therapy were **2.5 times** more likely to fail (HR 2.5 [95% CI 1.5 to 4.3], p <0.001)
  - Diabetes mellitus was associated with higher recurrence (HR 1.1 [95% CI 1.07 to 1.26], p=0.01)

Change in LVEF, 6MWD, and MLHFQ score by recurrence status

At baseline the LVEF, 6MWD, and MLHFQ scores were not different between catheter ablation and amiodarone groups.

At the end of follow-up, recurrence free patients (n=105) experienced significantly better improvement in all parameters compared to those who experienced recurrence (n=98).

- LVEF improved 9.6±7.4%, vs. 4.2±6.2% ($p<0.001$),
- 6MWD changed 27±38 vs. 8±42 ($p<0.001$),
- MLHFQ score reduced 14±18 vs. 2.9±15 ($p<0.001$) in recurrence-free versus patients with recurrence

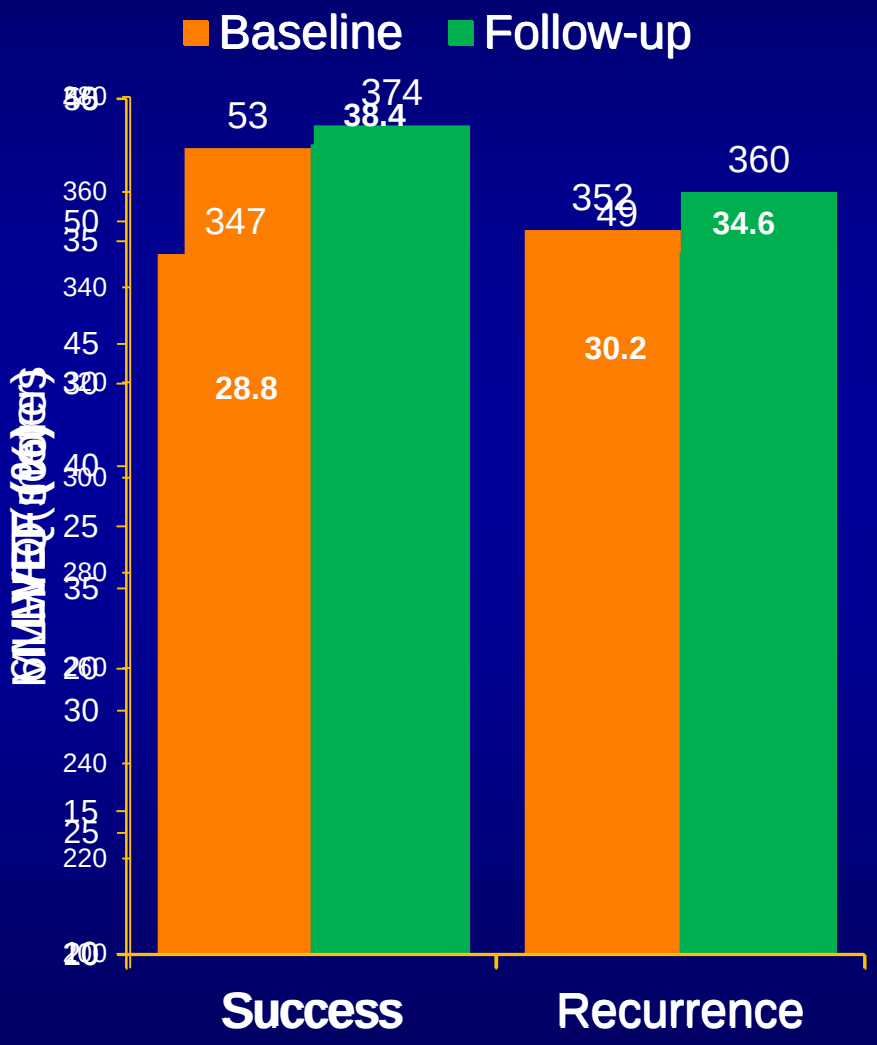
LVEF- left ventricular ejection fraction
6MWD – 6 minute walk distance
MLHFQ - Minnesota Living with Heart Failure questionnaire

Change in LVEF, 6MWD, and MLHFQ score by recurrence status

Measures	No Recurrence (n=105)		Recurrence (n=98)		P for **change** between groups
	Baseline	Change	Baseline	Change	
LVEF (%)	28.8±10	9.6±7.4	30.2±9	4.2±6.2	<0.001
6MWD (meter)	410±102	18±40	413±111	7±34	0.038
MLFHQ Score	53±24	-6±13	49±26	-1.4±12	0.013

LVEF- left ventricular ejection fraction
6MWD – 6 minute walk distance
MLHFQ - Minnesota Living with Heart Failure questionnaire
Data are summarized as mean ± standard deviation

Results:


Baseline
Follow-up
53
374
38.4
347
28.8
352
49
360
34.6
30.2
Success
Recurrence

Hospitalization and Mortality

- Over the 2 year follow-up:
  - Hospitalization rate substantially lower in Group 1 (32 [31%] vs. 58 [57%] in group 2, p <0.001)
  - All-cause Mortality in
  - Group 1 (8 [8%]) and 18 [18%] group 2, log-rank p=0.037);

CONCLUSIONS

- This multicenter randomized study shows that catheter ablation of Persistent AF is superior to Amiodarone in achieving freedom from AF at long term follow up and reducing hospitalization and mortality in patients with heart failure.

- The potential socio-economic repercussion of these results will require further investigation.

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