HF with Systolic or Diastolic LV Dysfunction

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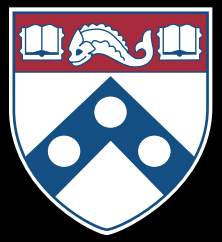

Penn
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Disclosures

- *Honoraria and consultant for Biosense Webster*
- *Honoraria from Boston Scientific*

AF in Diastolic HF

- 20%-40% prevalence of AF in patients with HF and preserved LVEF (>50%).
- AF may facilitate the development or progression of HF by causing rapid ventricular rates and short ventricular filling time
- LA function and structure is abnormal in patients with HFpEF

Owan et al. NEJM 2006
Bhatia et al. NEJM 2006
Olsson et al. JACC 2006
Zile et al. NEJM 2004
Melenovsky et al. JACC 2007

Catheter Ablation of AF in Diastolic HF

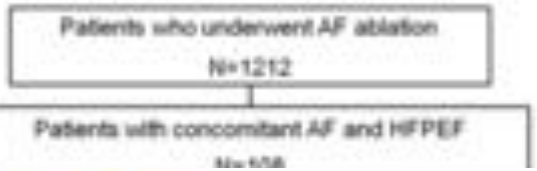


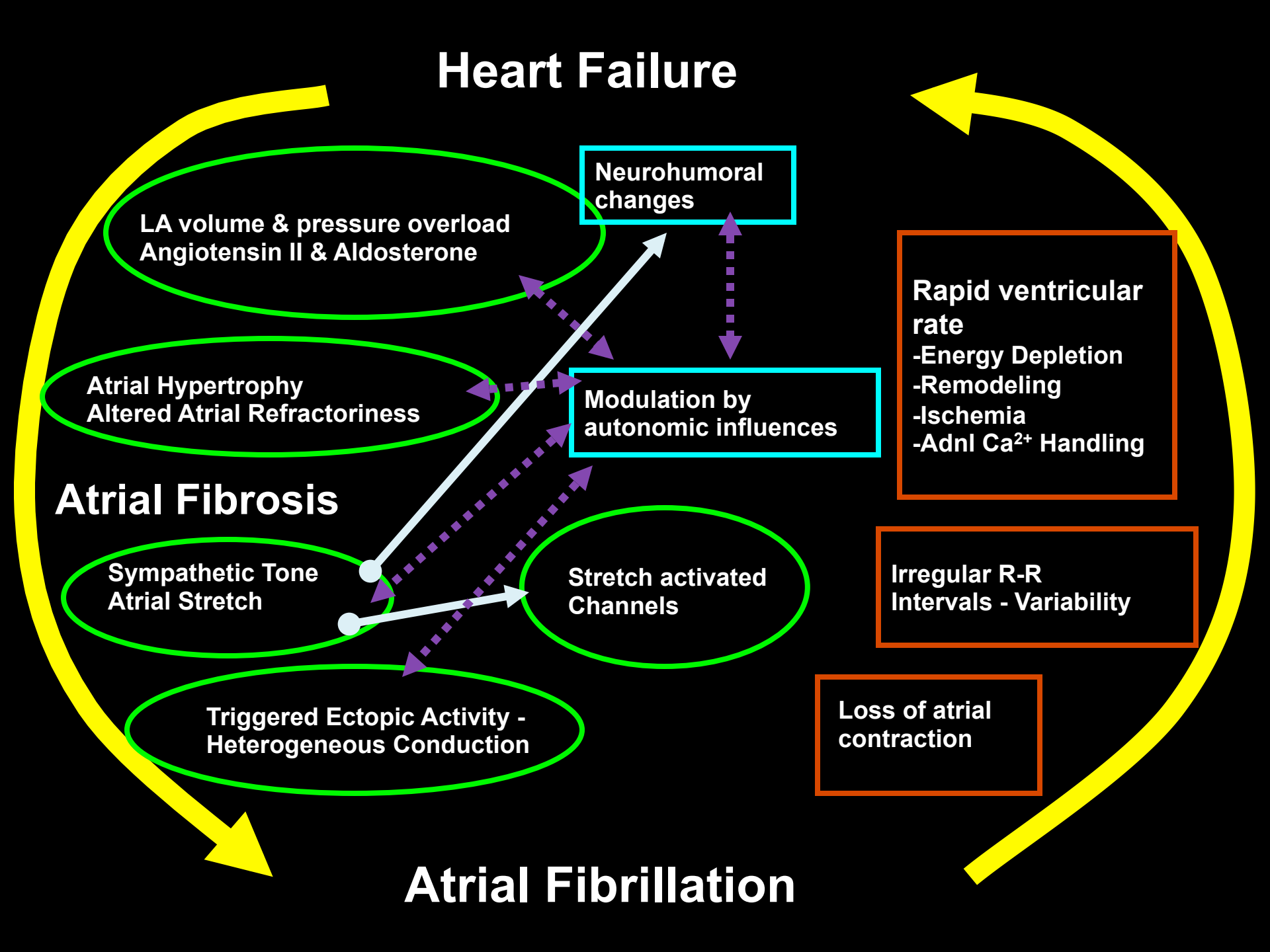
Table 4 Factors Related to Maintenance of SR After Ablation

	Univariate Analysis			Multivariate Analysis		
Variables	HR	95% CI	p Value	HR	95% CI	p Value
Age at enrollment, per 1-yr increase	0.99	0.96-1.03	0.69			
Duration of AF before CA, per 1-yr increase	0.95	0.90-1.00	0.048			
Type of AF*	1.87	1.07-3.27	0.03	1.81	1.03-3.17	0.04
Male	0.69	0.36-1.29	0.25			
Hypertension	0.50	0.25-0.99	0.046	0.49	0.24-0.96	0.04
Obstructive sleep apnea	1.28	0.71-2.32	0.42			
NT-proBNP†	0.76	0.58-0.99	0.04			
LA volume index†	0.89	0.64-1.24	0.48			
eGFR†	1.05	0.87-1.27	0.63			

Machino-Ohtsuka et al. JACC 2013;62:1857-65

AF in Congestive Heart Failure

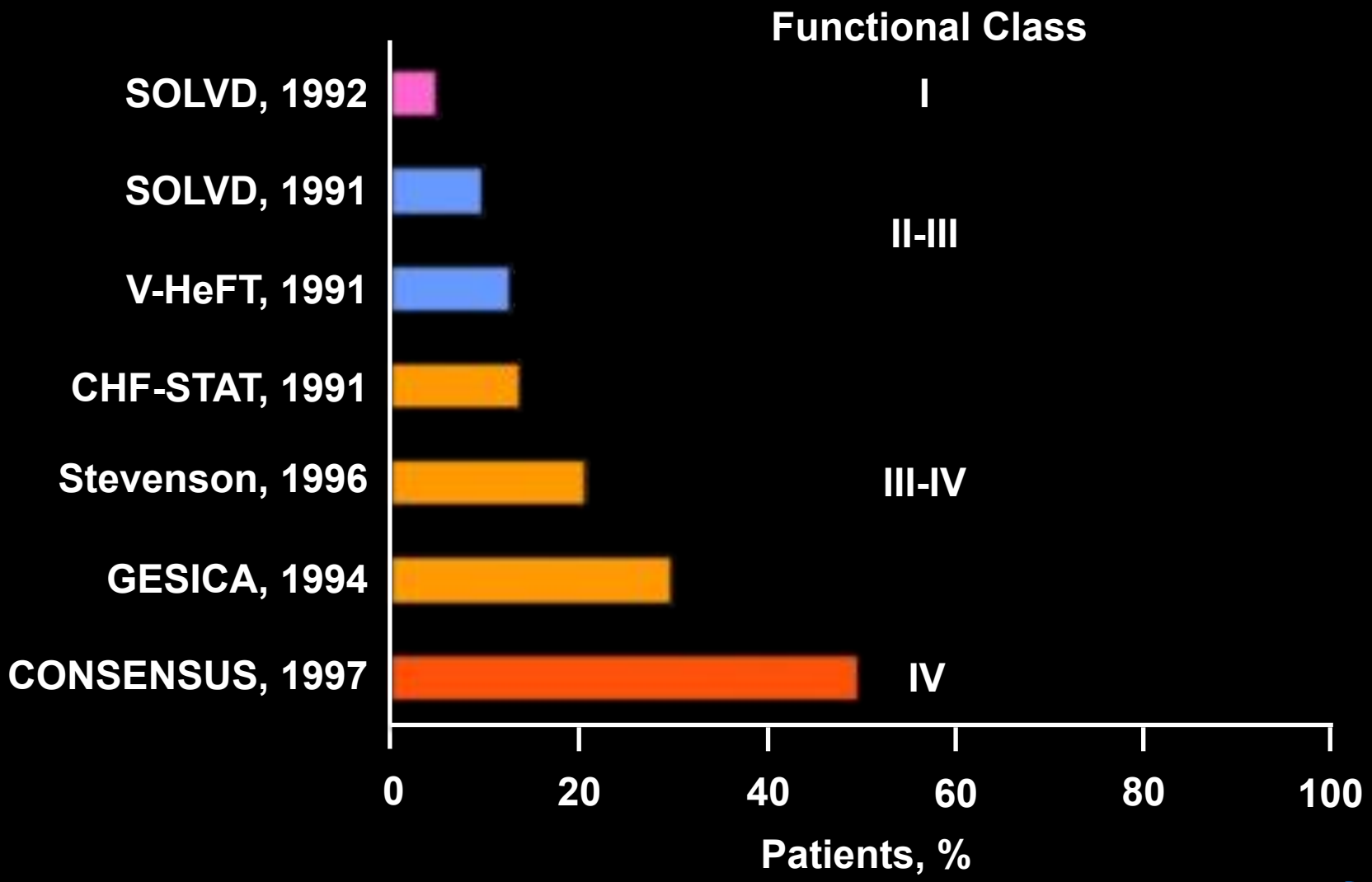
- AF and CHF often coexist and are associated with common predisposing factors such as HTN, DM, obesity, sleep apnea, and structural HD.
- The prevalence of AF increases with HF severity.
- Prevalence of HF in AF patients is up to 42%.
- Combination of AF and HF leads to hemodynamic and functional status deterioration.
- AF mainly persistent in HF patients.


Heart Failure
LA volume & pressure overload
Angiotensin II & Aldosterone
Neurohumoral changes
Atrial Hypertrophy
Altered Atrial Refractoriness
Modulation by autonomic influences
Rapid ventricular rate
-Energy Depletion
-Remodeling
-Ischemia
-Adnl Ca^{2+} Handling
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

Consequences of AF in CHF

- Loss of atrial mechanical activity.
- Impaired LV filling.
- Up to 30% cardiac output decrease.
- Worsening HF (tachycardia induced, dependent on rate irregularity)

Prevalence of AF in CHF

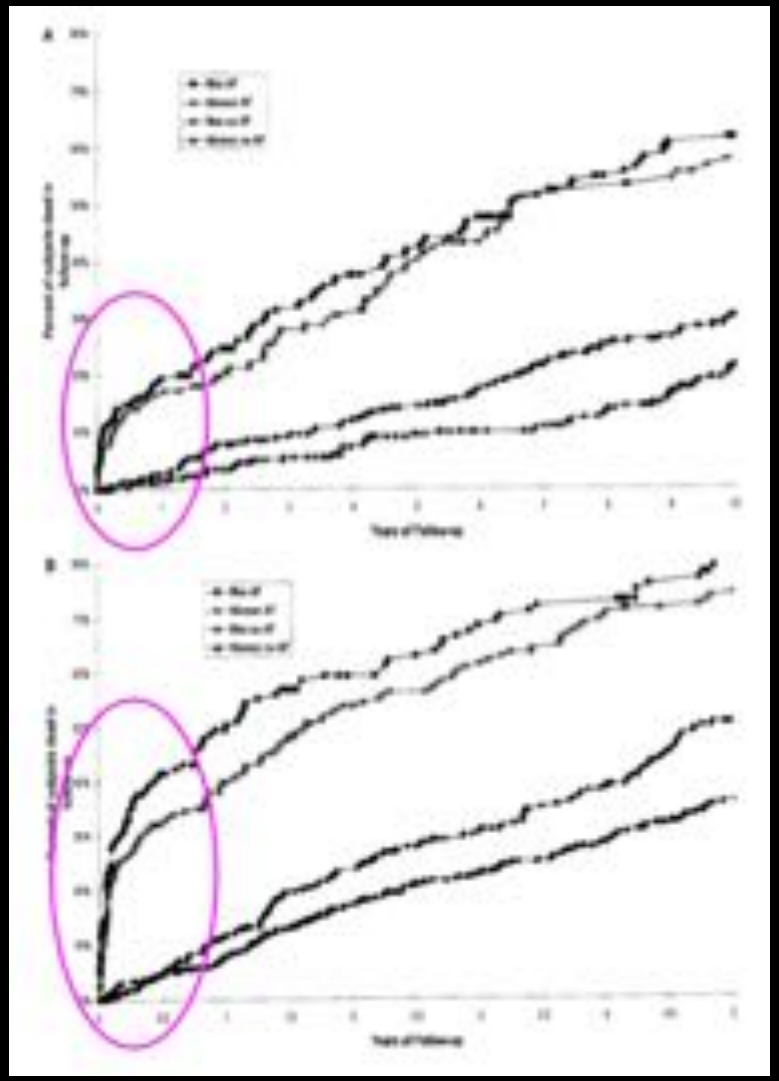


HF and AF mortality

- Development of AF in HF patients independently increases the risk of mortality (HR 1.7 in men and 2.7 in women – 4.2 year FU).
- Development of CHF in AF patients associated with increased risk of mortality (HR 2.7 in men and 3.1 in women – 5.6 year FU).

Wang et al. The Framingham Heart Study. Circulation 2003

AF-Related Mortality



Pts > 55 years and <74 years

Early Increase in Mortality

Pts > 75 years

Benjamin et al. Circulation 1998

Rhythm-Control with AADs in CHF

The NEW ENGLAND JOURNAL of MEDICINE

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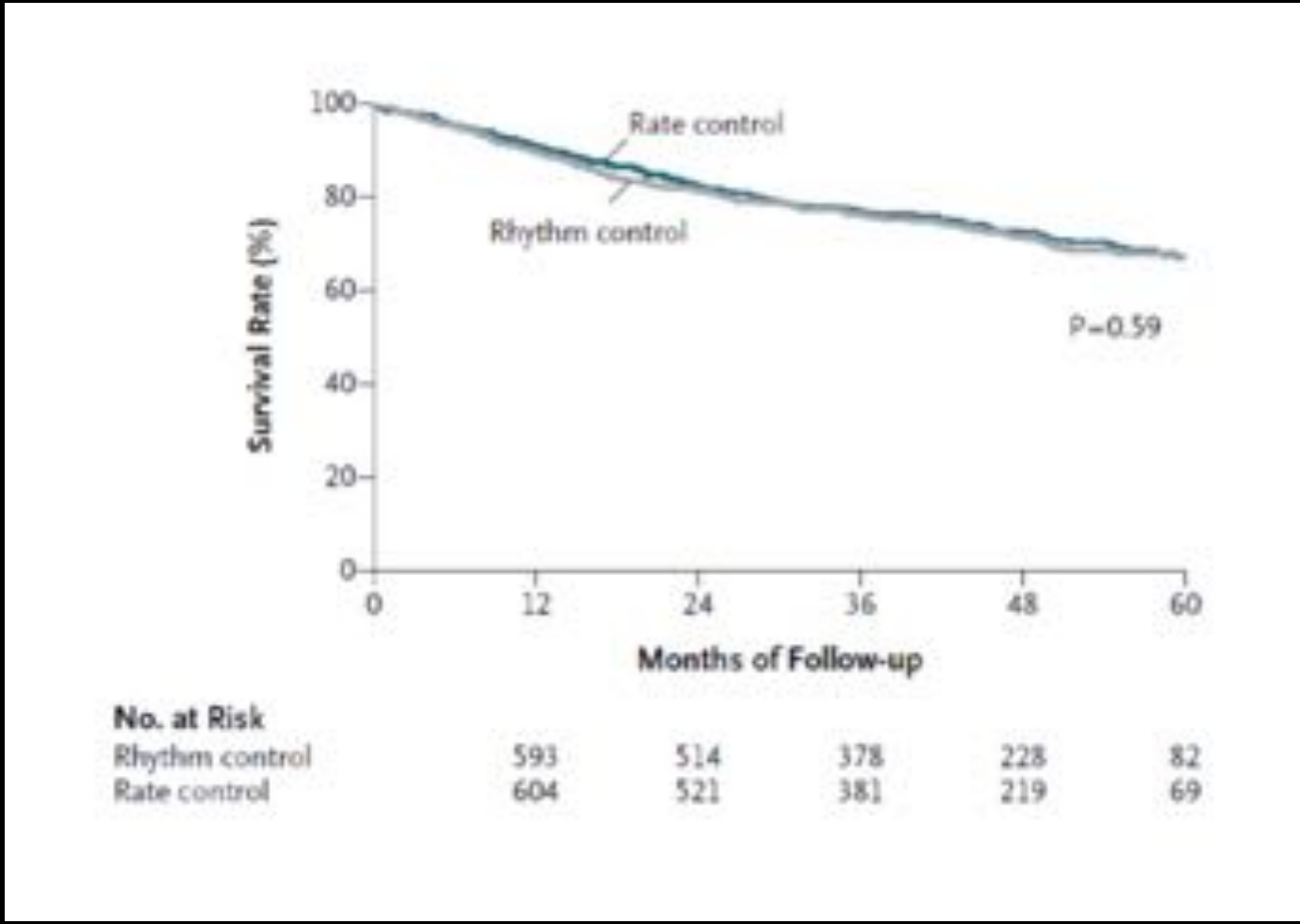
Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure

Denis Roy, M.D., Mario Talajic, M.D., Stanley Nattel, M.D., D. George Wyse, M.D., Ph.D., Paul Dorian, M.D., Kerry L. Lee, Ph.D., Martial G. Bourassa, M.D., J. Malcolm O. Arnold, M.D., Alfred E. Buxton, M.D., A. John Camm, M.D., Stuart J. Connolly, M.D., Marc Dubuc, M.D., Anique Ducharme, M.D., M.Sc., Peter G. Guerra, M.D., Stefan H. Hohnloser, M.D., Jean Lambert, Ph.D., Jean-Yves Le Heuzey, M.D., Gilles O'Hara, M.D., Ole Dyg Pedersen, M.D., Jean-Lucien Rouleau, M.D., Bramah N. Singh, M.D., D.Sc., Lynne Warner Stevenson, M.D., William G. Stevenson, M.D., Bernard Thibault, M.D., and Albert L. Waldo, M.D., for the Atrial Fibrillation and Congestive Heart Failure Investigators*

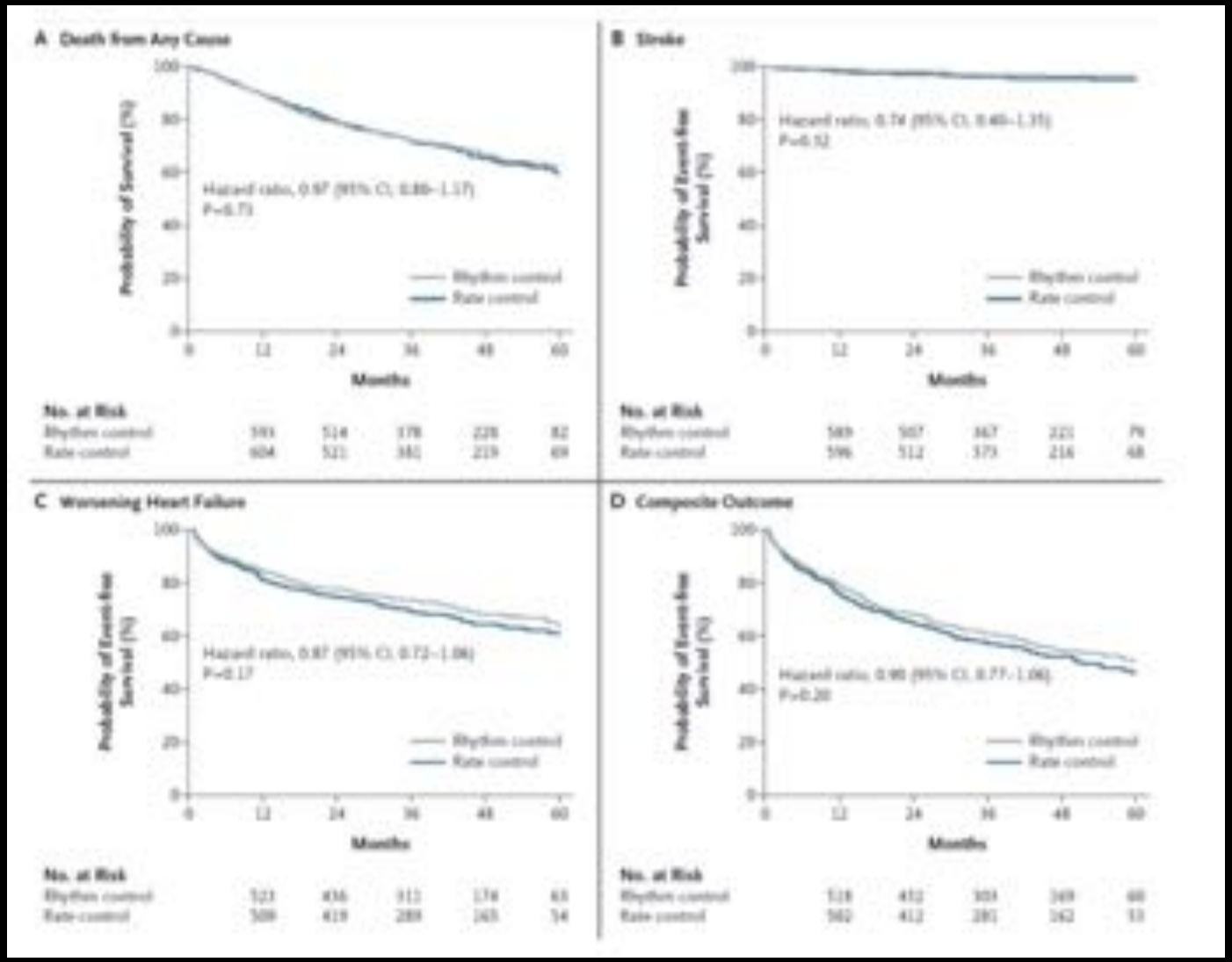
Roy et al. NEJM 2008;358:2667-77

Death from Cardiovascular Causes



Roy et al. NEJM 2008;358:2667-77

Secondary Outcomes



Roy et al. NEJM 2008;358:2667-77

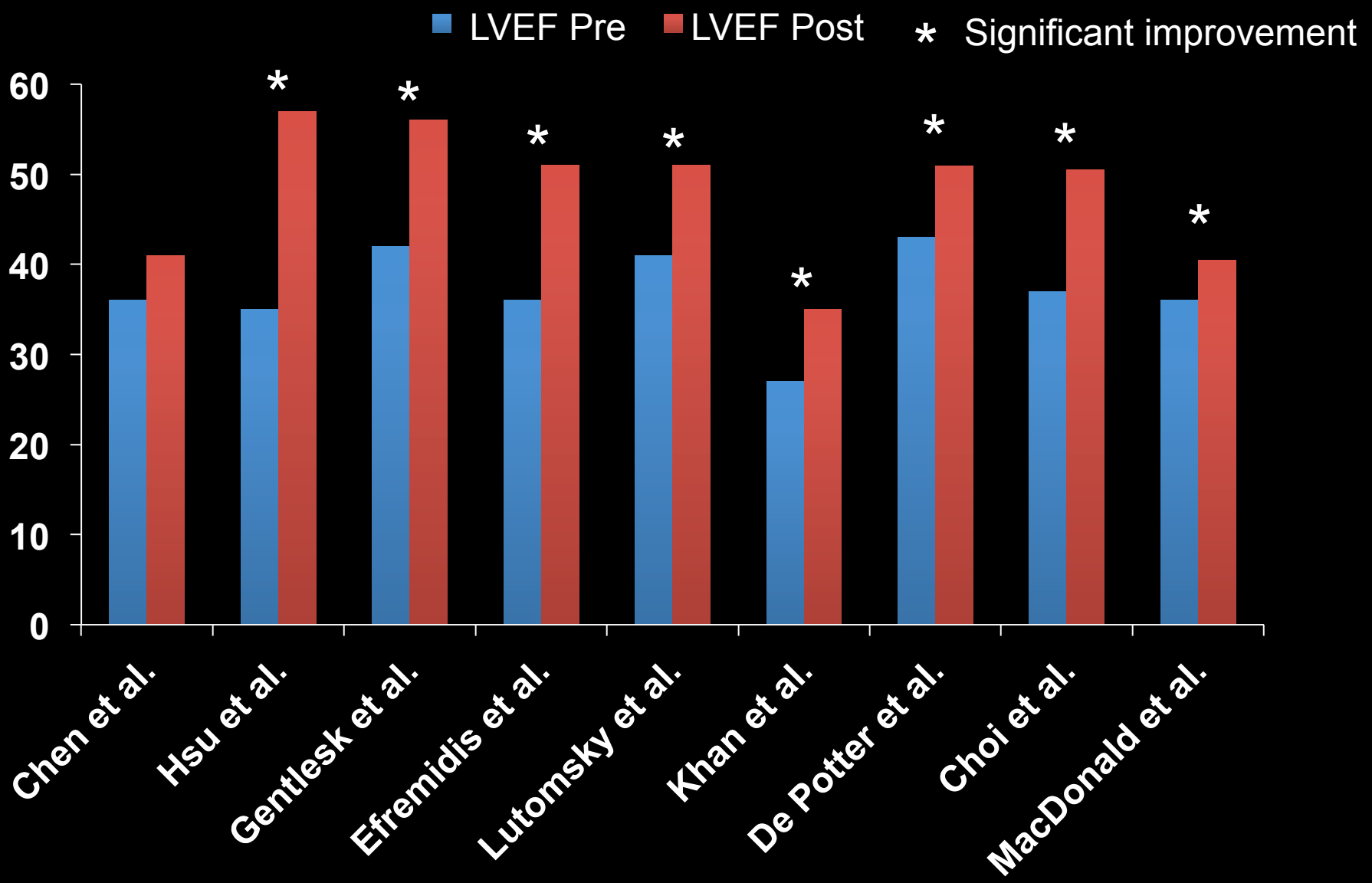
AF-CHF Trial Limitations

- Open-label trial
- 1376 patients randomized in 4 years by 123 centers: no information regarding the rate of patients selected but ineligible for randomization (and the related reasons)
- Sinus rhythm could be documented at repeated assessments in 75%-80% of patients in the rhythm-control group
- In the rate-control group, heart rate targets (<80 bpm at rest, <110 bpm during 6MWT) were achieved In 82% to 88% of patients during follow-up
  - However:
    - 58% of the patients of the rhythm control group had at least one recurrence of AF during follow-up
    - About 40% of the patients of the rate control group was not in AF during the trial

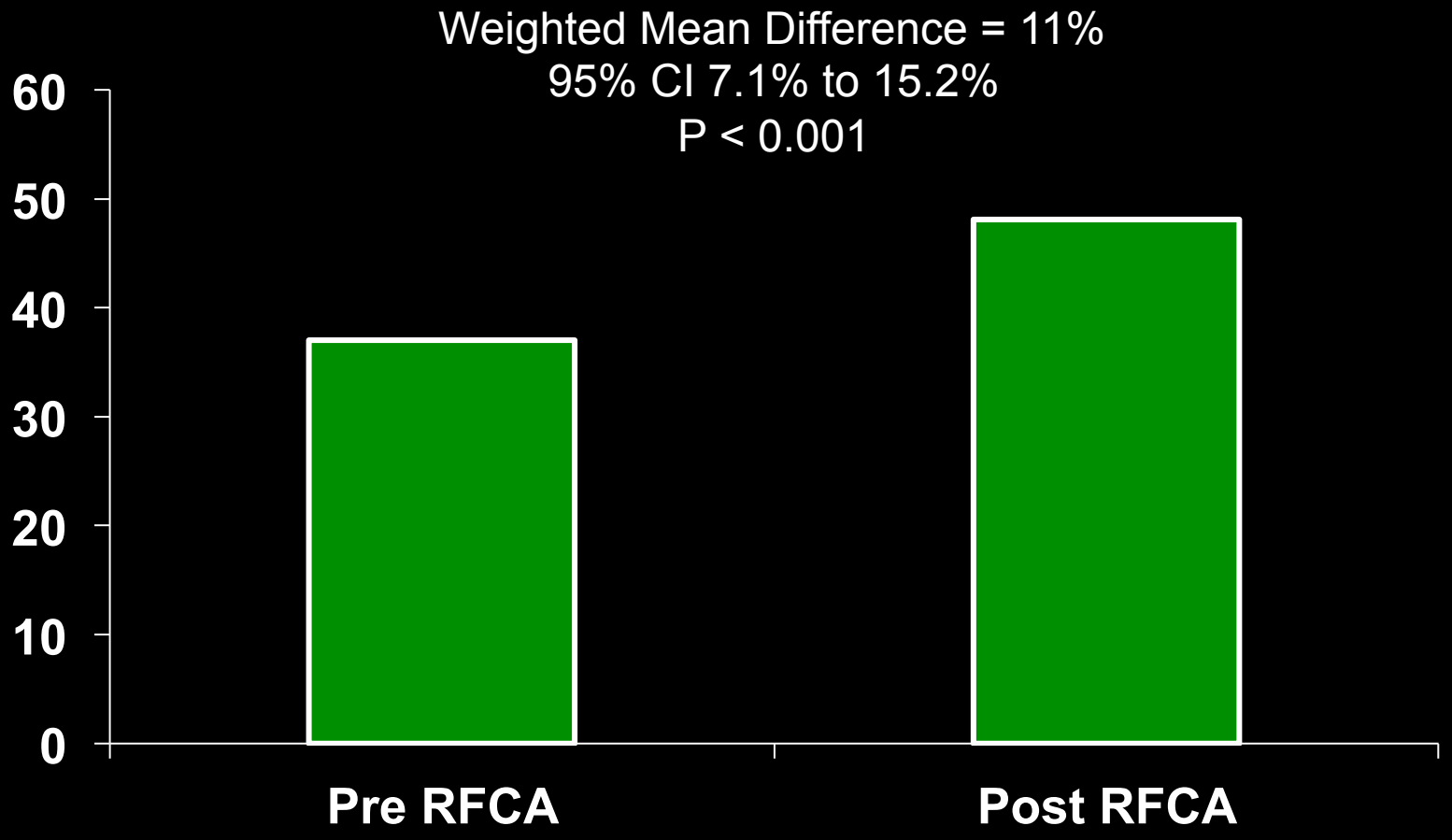
RFCA of AF in CHF

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

LVEF Improvement after RFCA of AF

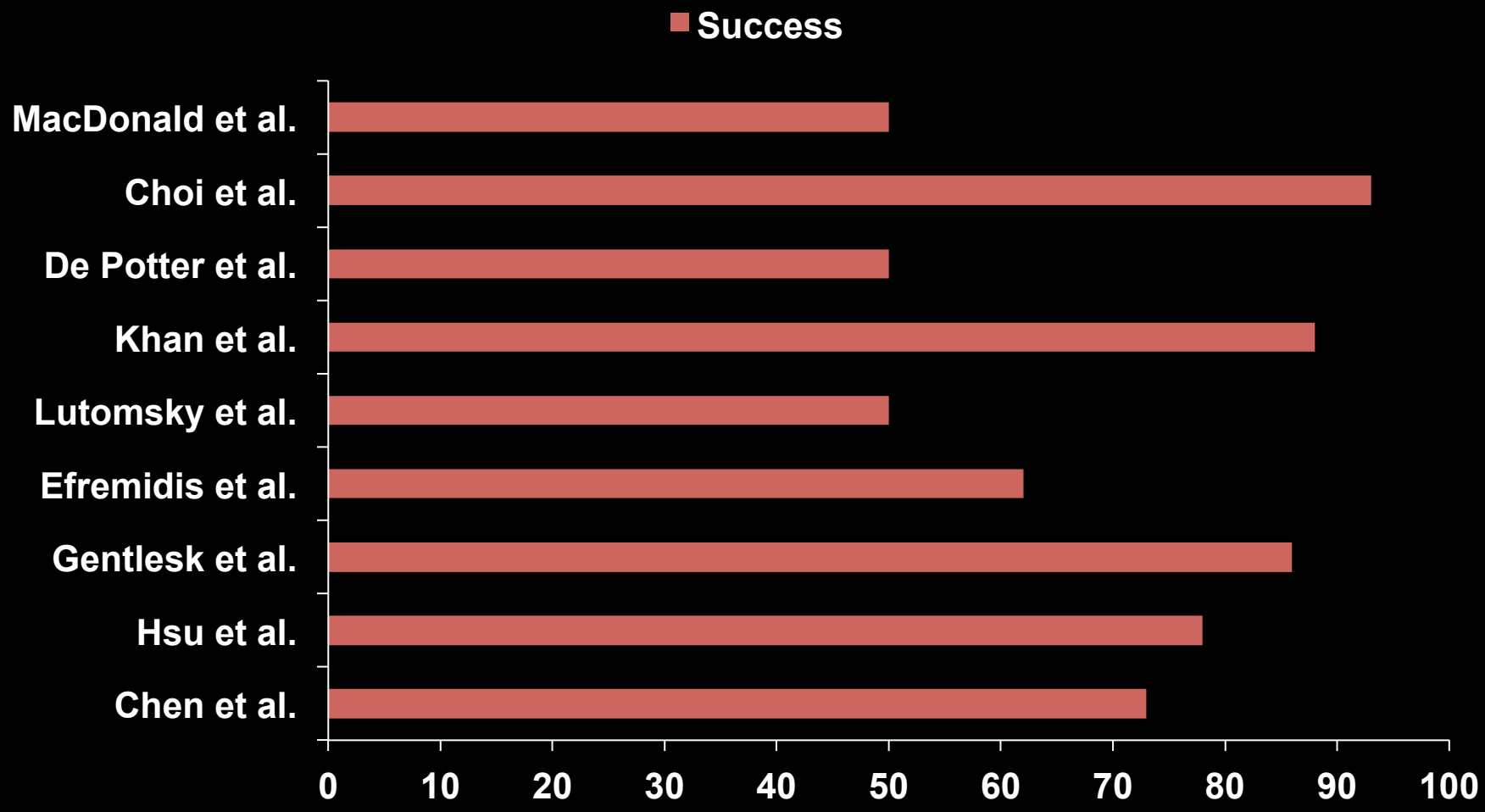


Pooled Analysis of LVEF Improvement

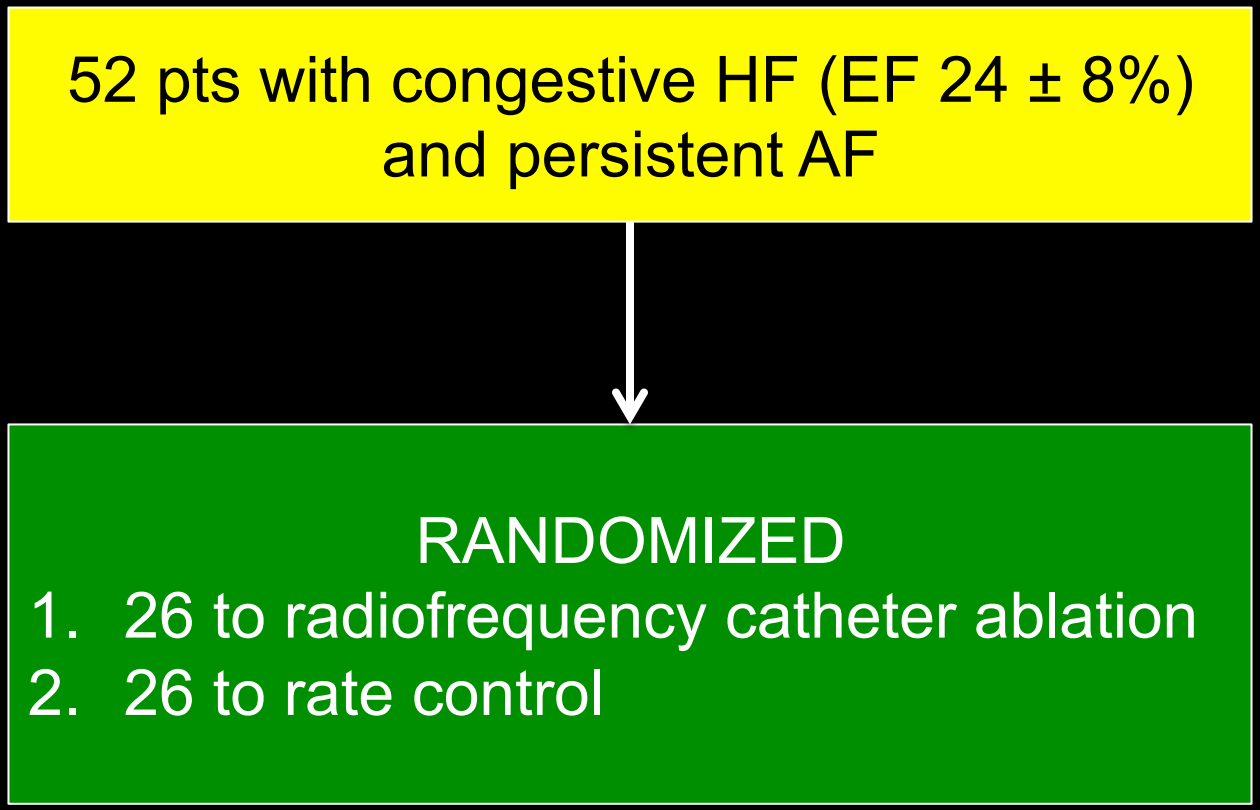


Santangeli et al. HRS 2012

Freedom from recurrent arrhythmia after RFCA of AF in pts with CHF



A Randomized Trial to Assess Catheter Ablation versus Rate Control in the Management of Persistent Atrial Fibrillation in Heart Failure (ARC-HF)



Jones et al. JACC 2013

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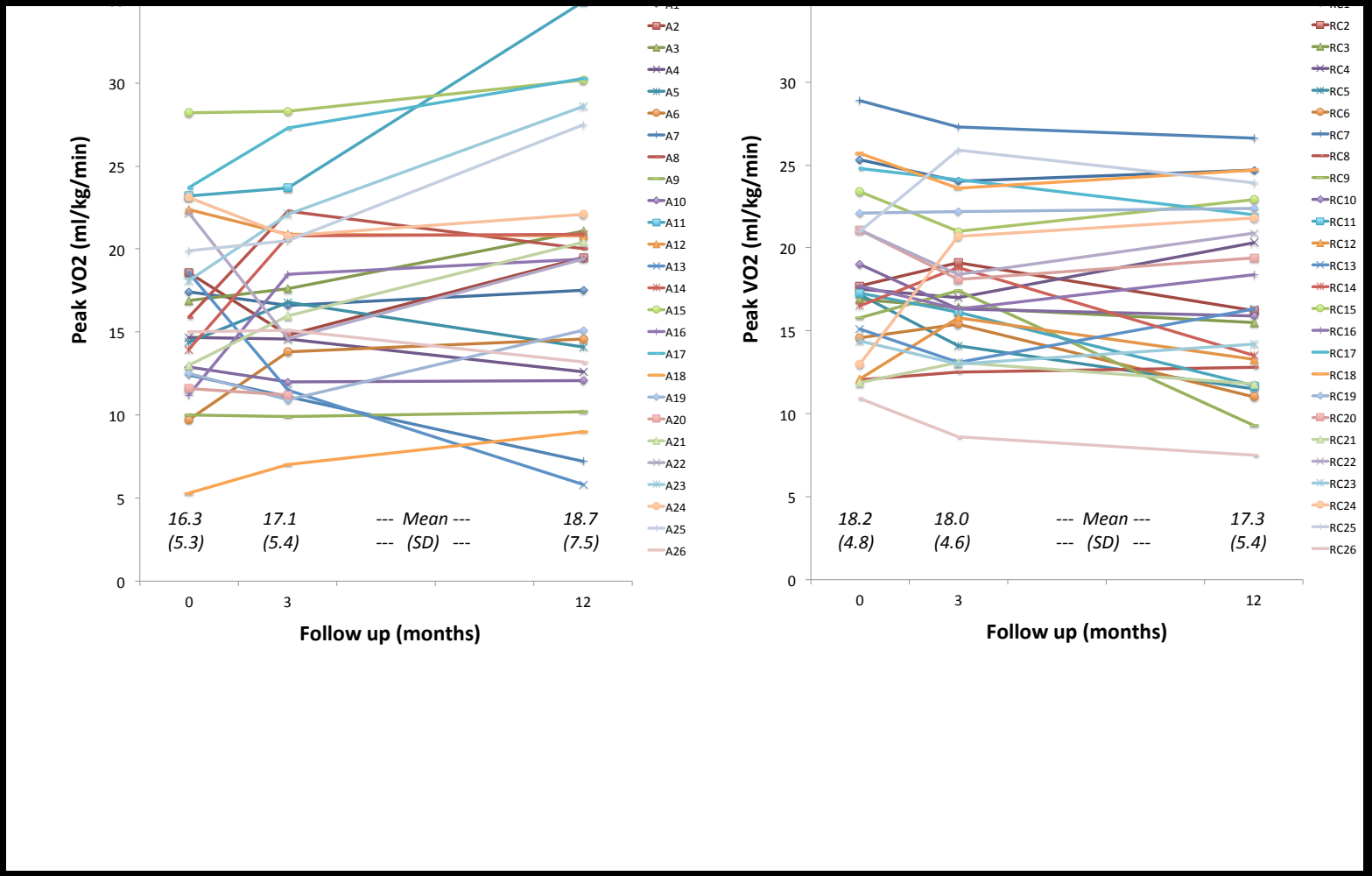

Jones et al. JACC 2013

A Randomized Trial to Assess Catheter Ablation versus Rate Control in the Management of Persistent Atrial Fibrillation in Heart Failure (ARC-HF)

Jones et al. JACC 2013

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

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

Luigi Di Biase, Prasant Mohanty, Sanghamitra Mohanty, Pasquale Santangeli, Chintan Trivedi, Dhanunjaya Lakkireddy, Madhu Reddy,Pierre Jais,
Sakis Themistoclakis, Antonio Dello Russo, Michela Casella, Gemma Pelargonio, Maria Lucia Narducci, Robert Schweikert, Petr Neuzil, Javier Sanchez,
Rodney Horton, Salwa Beheiry, Richard Hongo, Steven Hao, Antonio Rossillo, Giovanni Forleo, Claudio Tondo, J. David Burkhardt, Michel Haissaguerre, Andrea Natale

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- Cardiac Arrhythmia Research Centre, Centro Cardiologico Monzino IRCCS, Milan, Italy;
- Ospedale dell' Angelo, Mestre, Venice, Italy;
- Hôpital Cardiologique du Haut Lévêque, Université Victor-Segalen Bordeaux, France;
- Akron General Hospital, Akron, Ohio, USA;
- Department of Cardiology, Na Homolce Hospital, Roentgenova 2, Prague, Czech Republic

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

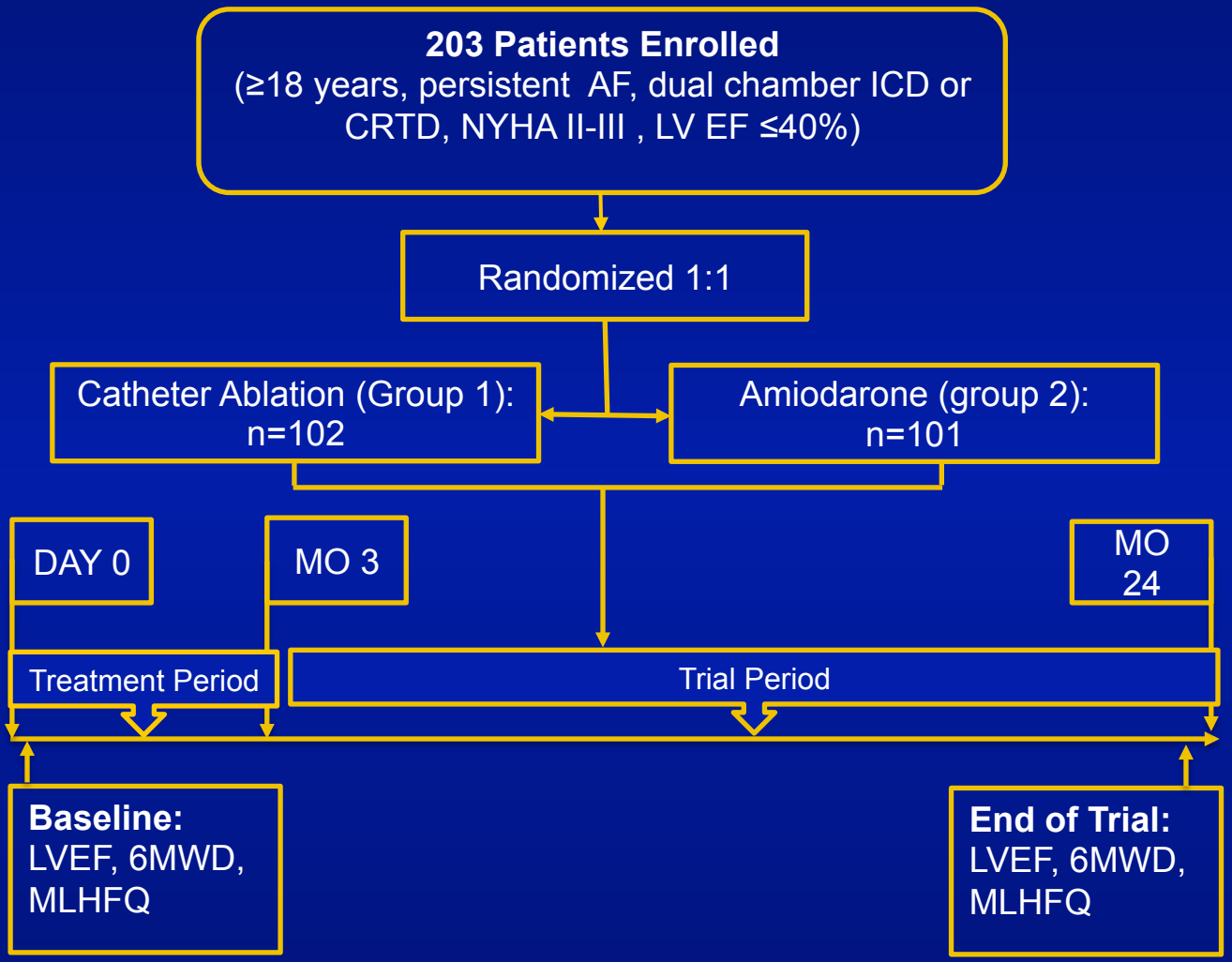
Courtesy of Dr. Di Biase, Natale et al ACC 2015

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)

Courtesy of Dr. Di Biase, Natale et al ACC 2015

Methods



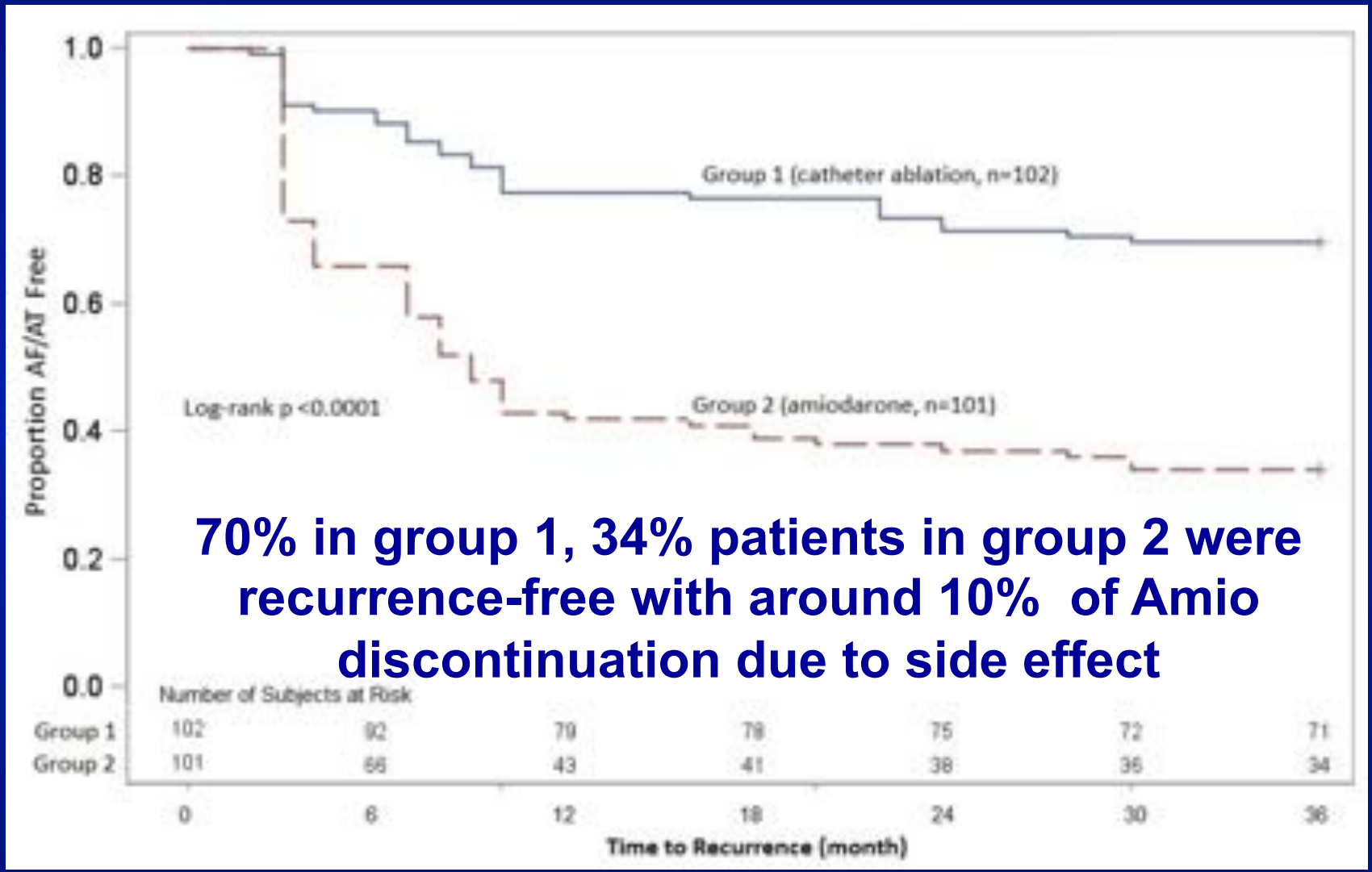
MO- month, 6MWD – 6 minute walk distance,
MLHFQ - Minnesota Living with Heart Failure questionnaire

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

Courtesy of Dr. Di Biase, Natale et al ACC 2015

Kaplan–Meier curves comparing success rate



70% in group 1, 34% patients in group 2 were recurrence-free with around 10% of Amio discontinuation due to side effect

Courtesy of Dr. Di Biase, Natale et al ACC 2015

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

Courtesy of Dr. Di Biase, Natale et al ACC 2015

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)

Courtesy of Dr. Di Biase, Natale et al ACC 2015

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

Di Biase, Natale et al ACC 2015

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);

Di Biase, Natale et al ACC 2015

RFCA of AF in HF: Conclusions

- AF and HF (systolic and diastolic) often coexist. Development of AF is associated with worse prognosis.
- Elimination of AF in these patients *may* improve prognosis. It has been associated with improved LV function and exercise capacity. No conclusive effect on mortality or other hard endpoints.
- RFCA is significantly more effective than AADs to achieve and maintain SR in HF patients.
- More extensive ablation beyond PV antrum appears to enhance arrhythmia-free survival in HF patients.