

Atrial Fibrillation in Heart Failure: *Is AFFIRM good enough?*

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Disclosures

- None

Objectives

- Review pitfalls of atrial fibrillation management in CHF
- Review literature
- Role of non pharmacologic treatment of atrial fibrillation in CHF
 - Subgroups who will benefit
- Case presentations

Atrial Fibrillation in Heart Failure

- Mechanisms of AF contributing to morbidity in CHF
 - Loss of atrial contractility
 - Excessive Ventricular Rates
 - Irregular Ventricular filling
- Prevalence of AF in CHF
 - 10% of NYHA I-II
 - 50% of NYHA III-IV
- Most Evidence suggest patients with AF and CHF
 - Worse prognosis
 - Independent Risk Factor?

Roy et al. *AI NEJM* 2008; 358(25): 2667-2676
Shrikumar K, Boyle N. *Current Heart Fail Rep* 2008; 5:11-15

Atrial Fibrillation in Heart Failure

- Data from several large trials not supporting benefit of rhythm control strategy
 - Important to document ventricular rate control
 - < 80bpm rest and < 110 bpm during 6 min walk
 - Minority of patients with CHF (23% AFFIRM)
 - CHF associated with worse outcomes
 - Warfarin associated with better outcomes
- Antiarrhythmic Therapy often complicated
 - Risk of proarrhythmia
 - Renal insufficiency
 - Amiodarone toxicity
 - Limited efficacy

AFFIRM Investigators. *NEJM* 2002;347:1825-33
Brignole M et al. *Eur Heart J* 2002; 23:892-900
Hohnloser SH et al. *Lancet* 2000;356:1789-94
Roy et al. *AI NEJM* 2008; 358(25): 2667-2676

Atrial Fibrillation in Heart Failure

- Can these results be extrapolated to patients in CHF ?
- Are there subgroups of patients who may benefit from rhythm control strategy?
- Are the results of non pharmacologic means of rhythm restoration similar to pharmacologic?

AF-CHF Trial

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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., Kenny L. Lee, Ph.D., Marial G. Bourassa, M.D., Malcolm Q. Arnold, M.D., Alfred E. Buxton, M.D., A. John Camm, M.D., Stuart J. Connolly, M.D., Marc Dubuc, M.D., Anliqun 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. *AI NEJM* 2008; 358(25): 2667-2676

AF-CHF

- Prospective Randomized Multicenter Trial
 - Hypothesis: rhythm control superior to rate control in CHF
- Most recent and complete trial comparing these two treatment strategies

Roy et al. *AI NEJM* 2008; 358(25): 2667-2676
Shikumar K, Boyle N. *Current Heart Fail Rep* 2008; 5:11-15

AF-CHF

Table 1. Baseline Characteristics of the Patients.*

Variable	Rhythm Control Group (N=662)	Rate Control Group (N=694)
Mean age (yr)	68.1	67.6
Body-mass index	27.8	28.3
Stroke class (n, %)	16 (2.4)	13 (1.9)
At baseline	36 (5.4)	31 (4.5)
During previous 6 mo	36 (5.4)	31 (4.5)
Medication used at baseline (%)		
Coronary artery disease	46	48
Valvular heart disease	3	3
Nonischemic cardiomyopathy	36	38
Congestive heart failure	1	1
Hypertensive heart disease	10	7
Coexisting conditions (%)		
Hypertension	49	46
Diabetes	22	20
Previous stroke or transient ischemic attack	11	9
Left ventricular ejection fraction (%)	27.6	27.4
Primary classification of atrial fibrillation (%)		
Paroxysmal	33	30
Persistent	33	30
All the time since first diagnosis of atrial fibrillation (%)	41	46
Atrial fibrillation on electrocardiography (%)	54	61

- Baseline Characteristics
 - Significant CHF
 - Older Patients
- Inclusion
 - LVEF <35%
 - AF episode > 6 hrs or requiring DCCV
 - AF episode > 10 min with prior DCCV
- Exclusion Criteria
 - reversible cause of CHF
 - Persistent AF for > 12 mo

Roy et al. *AI NEJM* 2008; 358(25): 2667-2676

AF-CHF Trial

- No reduction in death between rhythm and rate
 - No reduction in death from cardiovascular cause
 - No differences in subgroups
 - Death from any cause
 - Worsened CHF
 - Stroke

Roy et al. *AI NEJM* 2008; 358(25): 2667-2676

Relationships Between Sinus Rhythm, Treatment, and Survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study

The AFFIRM Investigators*

variables, and time-dependent variables. The following baseline variables were significantly associated with an increased risk of death: increasing age, coronary artery disease, congestive heart failure, diabetes, stroke or transient ischemic attack, smoking, left ventricular dysfunction, and mitral regurgitation. Among the time-dependent variables, the presence of sinus rhythm (SR) was associated with a lower risk of death, as was warfarin use. Antiarrhythmic drugs (AADs) were associated with increased mortality only after adjustment for the presence of SR. Consistent with the original intention-to-treat analysis, AADs were no longer associated with mortality when SR was removed from the model.

Conclusions—Warfarin use improves survival. SR is either an important determinant of survival or a marker for other factors associated with survival that were not recorded, determined, or included in the survival model. Currently available AADs are not associated with improved survival, which suggests that any beneficial antiarrhythmic effects of AADs are offset by their adverse effects. If an effective method for maintaining SR with fewer adverse effects were available, it might be beneficial. (*Circulation*. 2004;109:1509-1513.)

Atrial Fibrillation in Heart Failure

- Can these results be extrapolated to patients in CHF ?
- Are there subgroups of patients who may benefit from rhythm control strategy?
- Are the results of non pharmacologic means of rhythm restoration similar to pharmacologic?
 - Risk of complications

Catheter Ablation for Atrial Fibrillation in CHF Hsu et al, NEJM 2004

- 58 patients with AF, CHF
- 58 age matched controls with no CHF
- PV isolation + linear ablation
- LV EF <0.45
- LV EF and dimensions, symptoms score, exercise capacity, quality of life at 0, 1, 3, 6 and 12 months.

Baseline Characteristics:

Variable	CHF (n=58)	No CHF (n=58)	P Value
Age — yr	64±9	64±9	0.98
Male — no. (%)	51 (88)	51 (88)	1.00
Duration of atrial fibrillation — mo	41±24	41±24	1.00
NYHA functional class	2.3±0.5	2.3±0.5	1.00
Left ventricular ejection fraction — %	33±7	66±7	<0.001
Left ventricular fractional shortening — %	20±5	35±4	<0.001
Left ventricular dimensions — mm			
End-diastolic	60±8	53±5	<0.001
End-systolic	46±9	33±5	<0.001
Left atrial parasternal dimension — mm	50±7	46±6	0.004

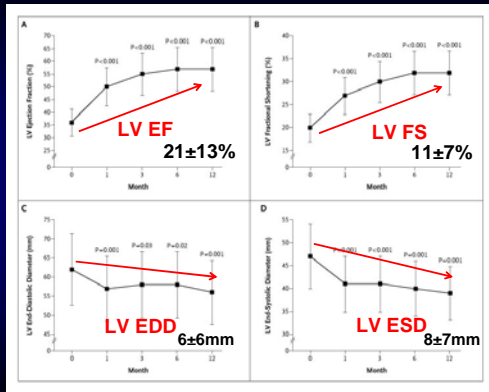
• Persistent/permanent AF 90%

Baseline Characteristics of the Patients with and without Congestive Heart Failure

Associated heart disease	CHF	No CHF	P Value
Dilated cardiomyopathy alone — no. (%)	32 (55)	2 (3)	<0.001
Concurrent structural heart disease — no. (%)	26 (45)	10 (17)	0.001
Coronary artery disease	12 (21)	5 (9)	0.07
Valvular disease	9 (16)	3 (5)	0.13
Congenital heart disease	2 (3)	0	0.50
Hypertrophic cardiomyopathy	4 (7)	2 (3)	0.68
NYHA functional class	2.3±0.5	1.3±0.5	<0.001
Left ventricular ejection fraction — %	33±7	66±7	<0.001
Left ventricular fractional shortening — %	20±5	35±4	<0.001
Left ventricular dimensions — mm			
End-diastolic	60±8	53±5	<0.001
End-systolic	46±9	33±5	<0.001
Left atrial parasternal dimension — mm	50±7	46±6	0.004

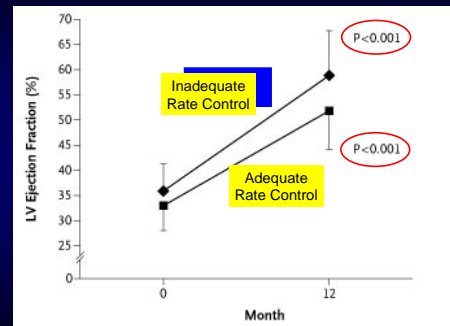
Hsu et al. NEJM 2004

Improvement after Ablation in Patients with Congestive Heart Failure



Hsu et al. NEJM 2004

Effect of Rate Control before Ablation on Left Ventricular (LV) Function after Ablation among Patients with Congestive Heart Failure



Hsu et al. NEJM 2004

Results:

- Mean follow-up 12±7 months
- 69% of CHF and 71% of no CHF groups were in SR without antiarrhythmic drugs.
- There was a significant improvement in LV EF/FS/EDd/ESd, exercise capacity, symptoms and QOL.
- Beneficial effects were observed in patients
 - With and without structural heart disease
 - With and without adequate rate control
- Repeat ablation in ~50%.

Hsu et al. NEJM 2004

Pulmonary Vein Isolation for the treatment of Atrial Fibrillation in Patients With Impaired Systolic Function

Chen et al. JACC 2004

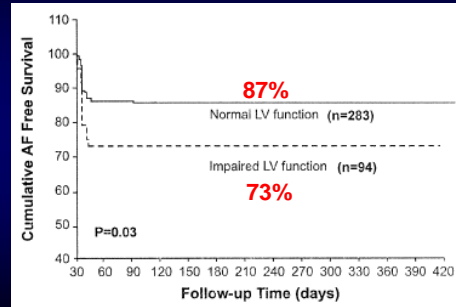
- Safety & efficacy of PVI in AF patients with impaired LV systolic function
- 377 consecutive pts
- Symptomatic AF refractory to AARx
- No indication for surgery
- 94 (25%) LVEF < 40%
- Retrospective case-series

PVI in Patients with Impaired Systolic Function

	Patients With Normal LV Function (n = 283)	Patients With Impaired LV Function (n = 94)	p Value
Women	22% (61)	20% (19)	0.1
Age (yrs)	55 ± 11	57 ± 8	0.9
LA size (cm)	4.5 ± 0.3	4.7 ± 0.8	0.06
Ischemic, hypertensive, or idiopathic heart disease*	22% (62)	91% (86)	0.02
Valvular heart disease*	13% (36)	16% (15)	0.1
Mean EF (%)	54 ± 3%	36 ± 8%	0.02
NYHA			
Class I	95% (268)	None	0.001
Class II	5% (15)	30% (28)	0.009
Class III	None	68% (64)	0.005
Class IV	None	2% (2)	0.01
Duration of AF (yrs)	5 ± 4	6 ± 2	0.7
Type of AF			
Paroxysmal	55% (155)	43% (39)	0.8
Persistent	12% (35)	13% (13)	0.9
Permanent	32% (93)	43% (42)	0.8
Number of anti-arrhythmic drugs tried before PVI	3 ± 1	2 ± 1	0.5

Chen et al, JACC 2004

Freedom from AF After PV Antral Isolation



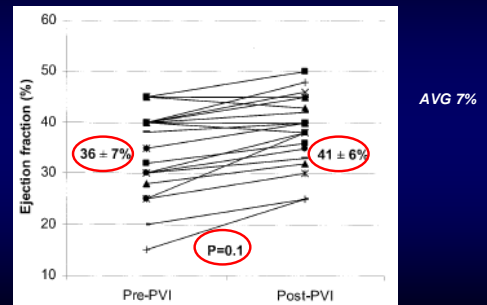
Chen et al, JACC 2004

Follow-up

	Patients With Normal LV Function (n = 283)	Patients With Impaired LV Function (n = 94)	p Value
Follow-up (months)	15 ± 8	14 ± 6	0.1
Recurrence	13% (36)	27% (25)	0.03
Controlled on AAD	6% (17)	3% (3)	0.1
Successful second PVI	7% (19)	22% (21)	0.05
Total cure of AAD (including second procedure)	94% (266)	96% (90)	0.2

Chen et al, JACC 2004

Improvement in LV EF After PVI



Chen et al, JACC 2004

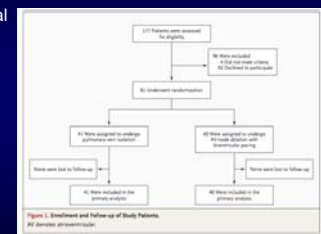
Complications:

	Patients With Normal LV Function (n = 283)	Patients With Impaired LV Function (n = 94)	p Value
CVA	1% (3)	2% (2)	0.7
Tamponade	<1% (2)	None	0.8
Pulmonary edema leading to procedure termination	None	1% (1)	0.8
Severe PV stenosis	1.7% (5)	1% (1)	0.08

Chen et al, JACC 2004

Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure

- Prospective multicenter trial comparing PVI with AV nodal ablation and BIV pacing
- LVEF < 40%
- 60% with Paroxysmal
- NYHA II-III
- Primary endpoint was composite of MLWHF scores, improvement in LVEF and 6 min walk test at 6 mo



Khan MN, et al. NEJM 2008;359: 1778-85.

Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure

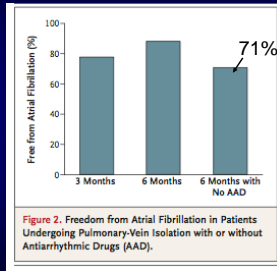
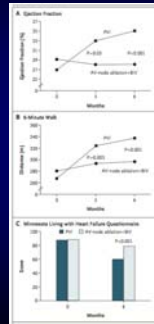


Figure 2. Freedom from Atrial Fibrillation in Patients Undergoing Pulmonary-Vein Isolation with or without Antiarrhythmic Drugs (AAD).

Khan MN, et al. NEJM 2008;359: 1778-85.



Left Ventricular Dysfunction in Atrial Fibrillation: Restoration of Sinus Rhythm by the Cox-Maze Procedure Significantly Improves Systolic Function and Functional Status

- 37 patients
- LV EF <0.55 and 65% with CHF
- Stand alone Cox-maze procedure
- No perioperative mortality / 3 PPM
- Median follow-up = 63 months
- 36/37 patients in sinus rhythm
- Significant improvement in LV EF

Stulak et al, Ann Thoracic Surgery 2006.

Clinical Characteristics

Male:female	34:3
Age (y)	35–74; median, 55
Chronic:paroxysmal AF	23:14
AF duration	3 months–19 years; median, 4 years
Severe (EF <0.35)	11
Moderate (EF 0.36–0.45)	8
Mild (EF 0.46–0.55)	18
Mean EF	0.439 ± 0.024

Stulak et al, Ann Thoracic Surgery 2006.

Case 1

- Pt. WC is 41 y/o Male with 4-5 week hx of palpitations
- AF Dx with mod-severe LV dysfunction
 - 2D echo LVEF 30%
 - Cardiac Cath: Normal Coronaries, LV EF 25-30%
- Initial attempts at rhythm control with DCCV failed
- Loaded with Amiodarone with therapeutic levels obtained and despite >3 attempts ERAF
- Rate Control moderate with rates at rest < 90 bpm
 - Multiple recorded events of rates 140-150
- Pt tolerating:
 - Lanoxin 0.25 mg QD, Lopressor 75 mg BID, Lisinopril 5mg QD, and Lasix 40 mg BID
 - Anticoagulated with ASA 81mg and Coumadin

Case 1

- Pt with persistent LV dysfunction and symptoms 2-3 mo post original diagnosis
 - Pt offered to options for treatment
 - AF ablation (quoted 65-70% success with likely 2 procedures)
 - AV nodal ablation with implantation of BiV/ICD

Case 1

- Pt underwent PV Antral Isolation
 - Confirmed isolation of all four PV
 - LA Roof line with confirmed block
 - Mitral Isthmus Line with confirmed block
- Maintaining SR without recurrence and off AAD
- LVEF repeated 4 weeks post
 - 40-45%
 - Reports no palpitations
 - Continues with NYHA II-III functional class symptoms

Case 2

- Pt RS is a 70 y/o male with past history:
 - Severe COPD, DM, Permanent AF and prior mild LV dysfunction, ASCHD medically managed
- Presented for outpatient referral for management of atrial fibrillation
 - Denied palpitations, c/o increasing SOB with NYHA class III symptoms
 - Documented AF >6 yrs
 - Prior management with rate control and anticoagulation with difficulties with rate control
 - Tachy-brady syndrome prior PPM
 - Relative hypotension SBP 90's
 - Moderate renal insufficiency GFR 42 mL/min/1.73 m²

Case 2

- AV node ablation
 - Decision was made to attempt AV nodal ablation
 - Immediate preoperative 2D Echo:
 - LVEF estimated 25-30% LA moderately dilated
 - Discussed with patient two mo waiting period to observe symptom improvement and repeat LVEF
- Within 6 wk period the patient presenting with decompensated CHF
 - One pre-syncopal event without documented VHR
 - No improvement in symptoms or LVEF despite good rate control
- Pt upgraded to BiV/ICD system

CASTLE-HF

- Randomized controlled trial to evaluate effectiveness of RF ablation in patients with AF and CHF vs conventional treatment
- Composite endpoint of all-cause mortality or worsening HF
- Patient enrollment started Jan 2008 expected completion Dec 2010
- Should define the value of AF ablation in patients with LV dysfunction

Conclusion

- No improvement in mortality for CHF patients treated with rhythm control strategy with AAD
 - Important to have diligent rate control
 - AAD often difficult to administer and efficacy limited
 - Proper anticoagulation imperative
- Suggestion of reduction of death for patients if SR can be maintained off AAD
- Atrial fibrillation ablation may offer potential for improvement of LVEF in a population with LV dysfunction
 - Especially in selected populations
- Risk of complications does not appear to be increased in CHF patients
- Large randomized controlled studies looking at rate control vs ablation and mortality reduction are on the way

Thank You.