Heart Failure and Atrial Fibrillation: a Deadly Combination

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Columbia University
New York, NY
Prevalence of AF in Heart Failure

From Maisel and Stevenson, AJC 2003
Prevalence of AF in Heart Failure

Annual Incidence ~ 5%

From Maisel and Stevenson, AJC 2003
Predictors of AF in Heart Failure

Prospective study of 344 patients in NSR followed for 19 mos; AF incidence = 5.2% and associated with clinical and hemodynamic deterioration and higher stroke and death rates.

- Development of chronic AF
  - No factor identified
    - Including LA dimensions, volume, pressure
    - Including HF status and parameters

- Development of late chronic AF
  - Prior history of reversible AF
  - Reduced LA contribution to filling (atrial myopathy)

Pozzoli et al, JACC 1998
Atrial Remodeling in Heart Failure

From Hanna et al, Cardiovasc Res 2004
Atrial Remodeling in Heart Failure

From Hanna et al, Cardiovasc Res 2004
Electrophysiologic Remodeling in Heart Failure

From Sanders et al, Circulation 20
Electrophysiologic Remodeling in Heart Failure

From Sanders et al, Circulation 2003
Pathology and Electrophysiology of AF in Heart Failure

• Pathology and Pathophysiology
  – White cell infiltration
  – Apoptosis
  – Increased collagen synthesis and fibrosis
  – Hypertrophy and chamber enlargement
  – Sympathetic and renin-angiotensin systems activation
  – Increased synthesis and activation of variety of maladaptive proteins and enzymes
  – Altered ion channel function

• Electrophysiology
  – Slow conduction
  – Abnormal sinus node function
  – Shortened and heterogenous atrial refractory periods
  – Increased automaticity and triggered activity

Heart Failure and AF: Vicious Cycle
## Interaction of AF and HF: Impact on Mortality

<table>
<thead>
<tr>
<th>TABLE 2. Cox Multivariable Proportional Hazards Models Examining the Impact of the Comorbid Condition on Mortality</th>
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From Wang et al, NEJM 2003
AF vs NSR in Heart Failure: SOLVD

Total Mortality

- Sinus Rhythm
- Atrial Fibrillation

P < 0.001

Follow-up time (days)

0 365 770 1095 1460

6,098 5,611 4,576 2,777 1,088 - Sinus
419 357 288 159 50 - Atrial Fib.

Pump Failure Mortality

- Sinus Rhythm
- Atrial Fibrillation

P < 0.001

Follow-up time (days)

0 365 770 1095 1460

6,098 5,611 4,576 2,777 1,088 - Sinus
419 357 288 159 50 - Atrial Fib.

Dries et al, JACC 1998
Possible Reasons for Adverse Effect of AF on Prognosis With HF

- Rapid and nonphysiologic ventricular rate
  - Diminished ventricular filling
  - Tachycardia-related cardiomyopathy
    - Pure/impure
  - Myocardial ischemia
    - Increased O₂ demand
    - Decreased coronary perfusion
  - Rate-related ventricular conduction delay
- Abnormal neurohormonal response
- Irregularly irregular pattern
  - Aggravation ventricular dysfunction and hemodynamic abnormalities
  - Increased ventricular electrical instability and VT/VF risk
- Loss of atrial kick
  - Decreased stroke volume
- Hypercoagulable state
  - Increased stroke risk
  - Possible increased thrombotic potential in other vascular territories
Failure of Beta Blocker Benefit

From Lechat et al, Circulation 2001
ICD Value in High Risk AF: Results from MADIT II

Zareba et al, AJC 2006
Therapeutic Objectives

- Symptom relief
- Stroke prevention
- Rhythm control
  - Medical therapy with AVN blockers
  - AVJ ablation and pacemaker (“Ablate + Pace”)


Subjective Benefits of Ablate + Pace

McMaster Health Index Questionnaire

Psychological General Well-Being Index

Kay et al, AJC 1988
Objective Benefits of Ablate + Pace

Left ventricular ejection fraction

Before: 43 ± 8
After: 54 ± 7
p < 0.001

Left ventricular end systolic diameter

Before: 40 ± 5
After: 34 ± 5
p < 0.003

Rodriguez et al, AJC 1993
Problem With Chronic RV Pacing

Steinberg et al, JCE 2005
Problem With Chronic RV Pacing

Steinberg et al, JCE 2005
PAVE: Results of 6-Minute Walk Relative to LVEF

LVEF ≤ 35%

LVEF > 35%

Δ = 59.0 m, p = 0.05

Δ = 4.3 m, p = 0.21
CRT in Heart Failure and AF: MUSTIC - AF

- N = 59
- Class III HF, LVEF < 35%
- Chronic AF and “slow” ventricular rate
- 6 month randomized crossover design: RVP vs BVP; 1o endpoint = 6 min walk
- Only 39 pts completed study
- No difference in 6 min walk: 341m vs 359m, respectively, and no difference in QoL
- More pts preferred BVP
Challenges to Achieving Consistent BV Capture in Patients With AF

- Higher intrinsic heart rate necessitates higher programmed pacing rate
- Frequent fusion beats
- Frequent pseudofusion beats
- Inaccurate assessment of BV capture by device counters

Steinberg, JACC 2006
Example of Problematic BV Pacing
# Definition of Pacing Complexes

<table>
<thead>
<tr>
<th></th>
<th>I-III</th>
<th>avR-F</th>
<th>V1-V3</th>
<th>V4-V6</th>
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</thead>
<tbody>
<tr>
<td><strong>Intrinsic beats</strong></td>
<td><img src="image1" alt="Intrinsic beats" /></td>
<td><img src="image2" alt="Intrinsic beats" /></td>
<td><img src="image3" alt="Intrinsic beats" /></td>
<td><img src="image4" alt="Intrinsic beats" /></td>
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<tr>
<td><strong>Paced beats</strong></td>
<td><img src="image5" alt="Paced beats" /></td>
<td><img src="image6" alt="Paced beats" /></td>
<td><img src="image7" alt="Paced beats" /></td>
<td><img src="image8" alt="Paced beats" /></td>
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<tr>
<td><strong>Fusion</strong></td>
<td><img src="image9" alt="Fusion" /></td>
<td><img src="image10" alt="Fusion" /></td>
<td><img src="image11" alt="Fusion" /></td>
<td><img src="image12" alt="Fusion" /></td>
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<tr>
<td><strong>pseudofusion</strong></td>
<td><img src="image13" alt="pseudofusion" /></td>
<td><img src="image14" alt="pseudofusion" /></td>
<td><img src="image15" alt="pseudofusion" /></td>
<td><img src="image16" alt="pseudofusion" /></td>
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Proportion of Effective vs. Ineffective Pacing

- Ineffective pacing (N=5) - 62.5%
- Effective pacing (N=3) - 37.5%

Cotiga et al, Circulation 2006
Holter Data

Cotiga et al, Circulation 2006
CRT Employed in AF: Outcomes From Observational Study

Courtesy of Gasparini et al
Inhibition of the R-A-A-S

From Healy et al, JACC 2005
Inhibition of the R-A-A-S

- Direct antiarrhythmic effect
- Indirect improvement in hemodynamics and wall stress
- Prevention of atrial fibrosis

From Healy et al, JACC 2005
Rhythm Control Strategy

• DIAMOND-CHF
  – Substudy - 506 pts with EF<0.35 in atrial flutter or AF at baseline showed that sinus rhythm at 1 yr was associated with improved survival whether on dofetilide or placebo

• CHF-Stat
  – Conversion to sinus rhythm on amiodarone led to improved survival
Primary Endpoint: All-Cause Mortality

Time (Years)

Mortality (%)

Rhythm N: 2033 1932 1807 1316 780 255
Rate N: 2027 1925 1825 1328 774 236

p = 0.058
Secondary Endpoint- Death, Disabling Stroke or Anoxic Encephalopathy, Major Bleed, or Cardiac Arrest

Rhythm Rate

\[ p = 0.283 \]

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<th>Time (Years)</th>
<th>Rhythm N:</th>
<th>Rate N:</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>2033</td>
<td>2027</td>
</tr>
<tr>
<td>1</td>
<td>1895</td>
<td>1889</td>
</tr>
<tr>
<td>2</td>
<td>1746</td>
<td>1760</td>
</tr>
<tr>
<td>3</td>
<td>1259</td>
<td>1264</td>
</tr>
<tr>
<td>4</td>
<td>719</td>
<td>722</td>
</tr>
<tr>
<td>5</td>
<td>231</td>
<td>208</td>
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**AFFIRM: Non-Cardiovascular Death**

**Graph:***
- **Y-axis:** Mortality (%)
- **X-axis:** Time (Years)
- **Legend:**
  - Rhythm
  - Rate
  - $p = 0.0008$

**Table:**

<table>
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<tr>
<th>Time (Years)</th>
<th>Numbers of Deaths</th>
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<tr>
<td>0</td>
<td>0(0%)</td>
</tr>
<tr>
<td>1</td>
<td>33(2%)</td>
</tr>
<tr>
<td>2</td>
<td>76(4%)</td>
</tr>
<tr>
<td>3</td>
<td>120(7%)</td>
</tr>
<tr>
<td>4</td>
<td>49(9%)</td>
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<tr>
<td>5</td>
<td>167(12%)</td>
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**Notes:**
- Steinberg et al, Circulation 2004
### Predictors of Mortality in AFFIRM

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AFFIRM Investigators, Circulation 2004
AFFIRM Subgroup Analyses

Age < 65 (N = 969)
Age > 65 (N = 3091)

No CAD (N = 2509)
CAD (N = 1551)

No hypertension (N = 1184)
Hypertension (N = 2876)

No CHF (N = 3121)
CHF (N = 939)

LVEF < 50% (N = 788)
LVEF ≥ 50% (N = 2244)

Female (N = 1594)
Male (N = 2466)

Overall (N = 4060)

Curtis et al, 2004
Ablation Strategy

- Target the LA-PV connections at orifice
- Aim to completely isolate each and every PV
- Technically feasible in all patients
Longitudinal Follow-Up After Ablation

Clinical improvement
Freedom from AF

Herweg et al, AJC 2005
Outcome Relative to Type of AF

Herweg et al, AJC 2005
Ablation Outcomes in Heart Failure

From Hsu et al, NEJM 2004
Linking AF Mechanism to Therapy

- Triggers
- Substrate
Linking AF Mechanism to Therapy
Linking AF Mechanism to Therapy

- Substrate
- Triggers
- PV Isolation
Linking AF Mechanism to Therapy

- Triggers
- Substrate
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- Substrate
- Triggers
- PV Isolation
- AADs
Linking AF Mechanism to Therapy

- Triggers
- Substrate

- PV Isolation
- AADs
Linking AF Mechanism to Therapy

- **PV Isolation**
- **AADs**
- **LA Modification**
Linking AF Mechanism to Therapy

- Triggers
- Substrate

PV Isolation
AADs
LA Modification
CHF-AF Treatment Algorithm

CHF

AF

Chronic Warfarin

Surgery Planned?

Yes: CABG/MVR/MVA + MAZE

No

Permanent AF?

Yes: BB/Amio

Severe symptoms?

Yes: Rate control?

Yes: Chronic Medication

No: Ablate + Pace

No

BB

Rate control?

BB

PVI

Amio or Dofetilide

LA RFA

Yes

No