Catheter Ablation for Atrial Fibrillation with Heart Failure
-
The Implications of the CASTLE-AF Study

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Illustrative Case Study

66 yr old male with non-ischemic CM
LVEF 30%; Class II NYHA on optimum med Rx
Develops persistent Afib with heart rate $\approx$ 100-120 bpm

Questions:

• How often AF occurs in HF patients?

• Bidirectional relationship between AF and HF?
Epidemiology of AF and HF

- AF and HF, individually, affect 1-2% of the population: common problems

- Annual incidence of:
  - HF in AF patients: 3.3%
  - AF in HF patients: 5.8%

- Both share common etiologies
  - CAD, CM, valvular disease, HTN

- Bidirectional pathophysiologic relationship
  - AF prevalence increases with HF severity
  - HF prevalence increases with AF duration
Prevalence of AF in CHF Trials

AF (%)

Class I
SOLVD-P

Class II-III
SOLVD-T

Class II-III
US CARVD

Class III
ATLAS

Class IV
CONSENSUS
Interaction Between AF and HF

- Action potential duration heterogeneity includes spatial and temporal non-uniformities
- **This mechanistic hypothesis has fallen out of favor with recent evidence**

Trulock et al., JACC 2014; 64:710-721
With the onset of AF, patient more SOB and tired. Carvedilol uptitrated and heart rate better controlled. Started on NOAC. Feels better but echo showed ↓LVEF from 30% to 25%.

Questions:

• Does AF adversely affect outcome of HF patients?

• Should sinus rhythm be restored?
Time to All-Cause Mortality in CHARM Based Upon EF and AF at Baseline

7,599 patients
EF <40 in 4576 pts (60%)
AF in 1148 pts (15%)

Source: Olsson LG et al., Candesartan in Heart Failure-Assessment of Reduction in Mortality and Morbidity (CHARM) program. JACC 47:1997-2004, 2006
AF-CHF Trial

A. Death from Any Cause

Hazard ratio, 0.97 (95% CI, 0.80-1.17)  
P = 0.73

No. at Risk
Rhythm Control: 593, 514, 378, 228, 82
Rate Control: 604, 521, 381, 219, 69

B. Stroke

Hazard ratio, 0.74 (95% CI, 0.40-1.35)  
P = 0.32

No. at Risk
Rhythm Control: 589, 507, 367, 221, 79
Rate Control: 596, 512, 373, 216, 68

C. Worsening Heart Failure

Hazard ratio, 0.87 (95% CI, 0.72-1.06)  
P = 0.17

No. at Risk
Rhythm Control: 523, 436, 311, 174, 63
Rate Control: 509, 419, 289, 165, 54

D. Composite Outcome

Hazard ratio, 0.90 (95% CI, 0.77-1.06)  
P = 0.20

No. at Risk
Rhythm Control: 518, 432, 303, 169, 60
Rate Control: 502, 412, 281, 162, 53
Pharmacologic Rhythm Control of AF in HF Patients Consensus Statements

- Restore sinus rhythm in about 50-60%
- Efficacy declines over the ensuing years
- Offers no survival benefit and no impact on LVEF, stroke or CV hospitalizations
- Guidelines endorse AAD use only to improve persistent disabling symptoms despite adequate rate control

Do hazardous effects of AADs (proarrhythmia and LV ↓ function) neutralize the potential benefits of restoring sinus rhythm?
Patient loaded with amiodarone for 2 months and cardioverted to sinus with 150 J shock.

Felt better instantaneously.

Echo reveals improved LVEF back to 30%.

AF recurs 1 month later with return of symptoms.

**Question:**

- Should he be referred for RF ablation for sinus restoration?
Consensus Statements (2018) Regarding RF Ablation of AF in HF Patients

- Superior to AADs for maintenance of sinus rhythm (60-80% vs 10-30%)

- Improve AF-related symptoms, exercise capacity and QOL better than AADs

- May improve LVEF but no meaningful survival benefit or reduction in CV hospitalization demonstrated

- Available data largely observational with small patient population and short follow up
Catheter Ablation versus Standard Conventional Treatment in Patients with Left Ventricular Dysfunction and Atrial Fibrillation

The CASTLE-AF Trial

Rationale and Objective

To study effectiveness of RF catheter ablation in HF patients in improving hard primary endpoints of mortality and heart failure progression when compared to standard Rx.
CASTLE-AF Trial
Inclusion Criteria

- HF patients with symptomatic paroxysmal or persistent AF
- Absence of response to, unacceptable side effects from, or unwillingness to take AADs
- LVEF ≤ 35%
- NYHA class ≥ II
- Already implanted ICD or CRT-D (Biotronik) with automatic daily remote-monitoring capabilities

Patients with candidacy for cardiac transplantation or other CV interventions excluded.
# CASTLE-AF Trial

## Primary Endpoints
- All-cause mortality
- Worsening heart failure admissions

## Secondary Endpoints
- All-cause mortality
- Worsening heart failure admissions
- Cerebrovascular accidents
- Cardiovascular mortality
- Unplanned hospitalization due to cardiovascular reason
- All-cause hospitalization
- Quality of Life: Minnesota Living with Heart Failure and EuroQoL EQ-5D
- Exercise tolerance (6 min walk test)
- Number of delivered ICD shocks, and ATPs (appropriate/inappropriate)
- LVEF
- Time to first ICD shock, and time to first ATP
- Number of device detected VT/VF
- AF burden: cumulative duration of AF episodes
- AF free interval: time to first AF recurrence after 3 months blanking period post ablation

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Marrouche et al., NEJM 2018;378:417-427
CASTLE-AF Trial
Study Design

- Investigator initiated, Prospective, Multicenter (31 sites, 9 countries), Randomized, Controlled

Marrouche et al., NEJM 2018;378:417-427
According to the ACC/AHA/ESC 2006 guidelines for treatment of AF in Heart Failure patients

Efforts to maintain sinus rhythm in this study arm were recommended

In case of rate control strategy:
- 60 and 80 bpm at rest
- 90 and 115 bpm during moderate exercise

Anticoagulation was initiated, if not already started, and maintained throughout the study. The INR was maintained between 2.0 and 3.0
CASTLE-AF Trial
Ablation Protocol

• Pulmonary Vein Isolation

• Additional lesions
  - at discretion of operator

• Repeat ablation after blanking

Marrouche et al., NEJM 2018;378:417-427
# CASTLE-AF Trial

## Baseline Characteristics - I

<table>
<thead>
<tr>
<th></th>
<th>Ablation group (79 patients)</th>
<th>Conventional group (184 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – years</td>
<td>64 (56-71)</td>
<td>64 (56-73.5)</td>
</tr>
<tr>
<td>New York Heart Association class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I (%)</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>II (%)</td>
<td>58</td>
<td>61</td>
</tr>
<tr>
<td>III (%)</td>
<td>29</td>
<td>27</td>
</tr>
<tr>
<td>IV (%)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Left ventricular ejection fraction - %</td>
<td>32.5 (25.0-38.0)</td>
<td>31.5 (27.0-37.0)</td>
</tr>
<tr>
<td>Current type of atrial fibrillation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal (%)</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Persistent (%)</td>
<td>70</td>
<td>65</td>
</tr>
<tr>
<td>CRT-D implanted (%)</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>ICD implanted (%)</td>
<td>73</td>
<td>72</td>
</tr>
</tbody>
</table>

*Marrouche et al., NEJM 2018;378:417-427*
# CASTLE-AF Trial

## Baseline Characteristics - II

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Ablation group (79 patients)</th>
<th>Conventional group (184 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-inhibitor or ARB – no. (%)</td>
<td>94</td>
<td>91</td>
</tr>
<tr>
<td>Beta-blocker – no. (%)</td>
<td>93</td>
<td>95</td>
</tr>
<tr>
<td>Diuretic – no. (%)</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>Digitalis – no. (%)</td>
<td>18</td>
<td>31</td>
</tr>
<tr>
<td>Oral anticoagulant – no. (%)</td>
<td>93</td>
<td>96</td>
</tr>
<tr>
<td>Antiarrhythmic drug – no. (%)</td>
<td>32</td>
<td>30</td>
</tr>
<tr>
<td>Amiodarone – no. (%)</td>
<td>97</td>
<td>85</td>
</tr>
</tbody>
</table>

Marrouche et al., NEJM 2018;378:417-427
Outcome of CASTLE-AF

Marrouche et al., NEJM 2018;378:417-427
## CASTLE-AF Trial

### Primary and Secondary Endpoint Outcome

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Ablation (n=179)</th>
<th>Medical (n=184)</th>
<th>Hazard Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary – mortality and HF admissions</td>
<td>28%</td>
<td>45%</td>
<td>0.62</td>
<td>0.006</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>13%</td>
<td>25%</td>
<td>0.53</td>
<td>0.009</td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>21%</td>
<td>36%</td>
<td>0.56</td>
<td>0.004</td>
</tr>
<tr>
<td>CV death</td>
<td>11%</td>
<td>22%</td>
<td>0.49</td>
<td>0.008</td>
</tr>
<tr>
<td>CVA</td>
<td>3%</td>
<td>6%</td>
<td>0.46</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Marrouche et al., NEJM 2018;378:417-427
CASTLE-AF Trial
LVEF Δ from Baseline

Marrouche et al., NEJM 2018;378:417-427
CASTLE-AF Trial
AF Burden

- Derived from a Memory of Implanted Devices

Marrouche et al., NEJM 2018;378:417-427
CASTLE-AF
Procedural Complications of AF Ablation

- No deaths, strokes, or atrio-esophageal fistula
- Pericardial effusion in 3/151 patients (2%)
- Vascular complications in 3%
  - pseudoaneurysm
  - hematomas
- Asymptomatic PV stenosis in 1 patient
CASTLE-AF Trial
Conclusions

In patients with HF and AF, as compared to medical Rx, RF ablation of AF is associated with:

a) Lower rate of death from any cause
b) Lower rates of HF admissions
c) Long-term reduction in AF burden
d) Long-term improvement in LVEF
Should Catheter Ablation of AF in Heart Failure be First Line Therapy?

• Are the positive results of CASTLE-AF in concordance with previous trials?

• Effects of catheter ablation on LVEF, 6-min walk distance and peak oxygen consumption (VO₂ max)

• Can the positive CASTLE-AF results be extrapolated to all patients with HF?
Catheter Ablation of AF and LVEF in HF Trials

# Meta-Analysis of 6 RCIs of AF Catheter Ablation in HF

## All-Cause Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Controls</th>
<th>Studies</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAMTAF, 2014 (11)</td>
<td>0</td>
<td>26</td>
<td>1</td>
<td>24</td>
<td>6</td>
</tr>
<tr>
<td>ARC-HF, 2013 (9)</td>
<td>1</td>
<td>24</td>
<td>0</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>AATAC, 2016 (8)</td>
<td>8</td>
<td>102</td>
<td>18</td>
<td>101</td>
<td>24</td>
</tr>
<tr>
<td>CASTLE-AF, 2018 (14)</td>
<td>24</td>
<td>179</td>
<td>46</td>
<td>184</td>
<td>37.8</td>
</tr>
<tr>
<td>CAMERA-MRI, 2017 (10)</td>
<td>0</td>
<td>33</td>
<td>0</td>
<td>33</td>
<td>6</td>
</tr>
</tbody>
</table>

Random-effects model: 364 vs 368  
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = 0.67$  

## AF Hospitalization

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Controls</th>
<th>Studies</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacDonald et al, 2011 (12)</td>
<td>2</td>
<td>20</td>
<td>1</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>CAMERA-MRI, 2017 (10)</td>
<td>0</td>
<td>33</td>
<td>2</td>
<td>33</td>
<td>6</td>
</tr>
<tr>
<td>ARC-HF, 2014 (9)</td>
<td>3</td>
<td>24</td>
<td>3</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>CASTLE-AF, 2018 (14)</td>
<td>37</td>
<td>179</td>
<td>66</td>
<td>184</td>
<td>37.8</td>
</tr>
</tbody>
</table>

Random-effects model: 256 vs 261  
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = 0.57$  

Turagam et al., Ann Int Med 2019;170:41-50
Meta-Analysis of 6 RCIs of AF Catheter Ablation in HF

LVEF Improvement

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>8.2</th>
<th>12.0</th>
<th>18</th>
<th>1.4</th>
<th>5.9</th>
<th>Ablation vs. rate control</th>
<th>Low risk</th>
<th>6.80 (0.88 to 12.72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacDonald, 2011 (12)</td>
<td>20</td>
<td>8.2</td>
<td>12.0</td>
<td>18</td>
<td>1.4</td>
<td>5.9</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>6.80 (0.88 to 12.72)</td>
</tr>
<tr>
<td>ARC-HF, 2013 (9)</td>
<td>24</td>
<td>10.9</td>
<td>11.5</td>
<td>26</td>
<td>5.4</td>
<td>8.5</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>5.50 (0.14 to 11.14)</td>
</tr>
<tr>
<td>CAMTAF, 2014 (11)</td>
<td>26</td>
<td>8.1</td>
<td>12.5</td>
<td>24</td>
<td>5.4</td>
<td>8.5</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>5.50 (0.14 to 11.14)</td>
</tr>
<tr>
<td>AATAC, 2016 (8)</td>
<td>102</td>
<td>8.1</td>
<td>4.0</td>
<td>101</td>
<td>−3.6</td>
<td>9.7</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>11.70 (5.52 to 17.88)</td>
</tr>
<tr>
<td>CASTLE-AF, 2018 (14)</td>
<td>51</td>
<td>8.7</td>
<td>1.9</td>
<td>37</td>
<td>−1.0</td>
<td>3.1</td>
<td>Ablation vs. rate/rhythm control</td>
<td>Low risk</td>
<td>1.90 (0.65 to 3.15)</td>
</tr>
<tr>
<td>CAMERA-MRI, 2017 (10)</td>
<td>33</td>
<td>17.7</td>
<td>10.8</td>
<td>33</td>
<td>8.9</td>
<td>v28.2</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>9.70 (8.57 to 10.83)</td>
</tr>
</tbody>
</table>

Rando-effects model: 256, Heterogeneity: $I^2 = 94\%$; $t^2 = 12.1207; P < 0.01$

6-min Walk Distance

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>20.1</th>
<th>76.5</th>
<th>15</th>
<th>21.4</th>
<th>77.4</th>
<th>Ablation vs. rate control</th>
<th>Low risk</th>
<th>−1.30 (−54.75 to 52.15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacDonald, 2011 (12)</td>
<td>17</td>
<td>20.1</td>
<td>76.5</td>
<td>15</td>
<td>21.4</td>
<td>77.4</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>−1.30 (−54.75 to 52.15)</td>
</tr>
<tr>
<td>ARC-HF, 2013 (9)</td>
<td>26</td>
<td>21.0</td>
<td>103.7</td>
<td>26</td>
<td>21.4</td>
<td>77.4</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>−31.00 (−16.08 to 78.08)</td>
</tr>
<tr>
<td>AATAC, 2016 (8)</td>
<td>102</td>
<td>22.0</td>
<td>14.0</td>
<td>101</td>
<td>−10.0</td>
<td>65.2</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>−12.00 (1.26 to 22.74)</td>
</tr>
<tr>
<td>CASTLE-AF, 2018 (14)</td>
<td>50</td>
<td>−6.9</td>
<td>26.7</td>
<td>35</td>
<td>−38.5</td>
<td>31.3</td>
<td>Ablation vs. rate/rhythm control</td>
<td>Low risk</td>
<td>31.60 (18.86 to 44.34)</td>
</tr>
<tr>
<td>CAMERA-MRI, 2017 (10)</td>
<td>33</td>
<td>55.0</td>
<td>114.5</td>
<td>33</td>
<td>29.0</td>
<td>125.5</td>
<td>Ablation vs. rate control</td>
<td>Low risk</td>
<td>26.00 (−31.96 to 83.96)</td>
</tr>
</tbody>
</table>

Rando-effects model: 228, Heterogeneity: $I^2 = 35\%$; $t^2 = 90.6227; P = 0.19$

Turagam et al., Ann Int Med 2019;170:41-50
Catheter ABlation vs ANtiarrhythmic Drug Therapy in Atrial Fibrillation (CABANA) Trial

Douglas L. Packer, MD, Kerry L. Lee, PhD
Daniel B. Mark, MD, MPH, Richard A. Robb, PhD
For the CABANA Investigators

Mayo Clinic Rochester
Duke Clinical Research Institute
National Heart Lung, and Blood Institute
All-Cause Mortality or Cardiovascular Hospitalization (ITT)

Ablation vs. Drug
Hazard ratio: 0.83 (95% CI, 0.74–0.93)
P=0.002
Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest) (ITT)

Ablation vs. Drug
Hazard ratio: 0.86 (95% CI, 0.65–1.15)
P=0.303

Packer, DL et al., CABANA Trial Slides-05092018
### Baseline History in CABANA

<table>
<thead>
<tr>
<th>Condition</th>
<th>Ablation</th>
<th>Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Apnea</td>
<td>23.6%</td>
<td>22.5%</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>8.9%</td>
<td>11.2%</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>15.7%</td>
<td>14.9%</td>
</tr>
<tr>
<td><strong>NYHA Class</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>13.9%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Class II/III</td>
<td>34.3%</td>
<td>36.7%</td>
</tr>
<tr>
<td>Prior CVA or TIA</td>
<td>10.6%</td>
<td>9.4%</td>
</tr>
</tbody>
</table>

Packer, DL et al., CABANA Trial Slides-05092018
All-Cause Mortality, Disabling Stroke, Serious Bleeding, Cardiac Arrest (ITT)

*Minority=Hispanic or Latino or non-white race

Packer, DL et al., CABANA Trial Slides-05092018
AF Catheter Ablation in HF: Generalization of CASTLE-AF to all HF Patients?

• Who are the ideal candidates?
  - Majority in CASTLE-AF had EF > 25%, HF Class II, and age < 65 yrs
  - Subgroup analysis showed limited benefit in Class III, LVEF < 25%, and age > 65 yrs
  - Limited data in HF PEF

• Are the results durable over years
  - Average F/U 37.8 months in CASTLE-AF
### Subgroup Analysis of Primary Endpoint in CASTLE-AF

Marrouche et al., NEJM 2018;378:417-427

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Ablation</th>
<th>Medical Therapy</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>18/96</td>
<td>34/99</td>
<td>0.48 (0.27–0.85)</td>
<td>0.17</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>33/83</td>
<td>48/85</td>
<td>0.79 (0.50–1.23)</td>
<td></td>
</tr>
<tr>
<td><strong>NYHA functional class</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>20/101</td>
<td>46/109</td>
<td>0.42 (0.25–0.72)</td>
<td>0.06</td>
</tr>
<tr>
<td>III</td>
<td>22/50</td>
<td>26/49</td>
<td>0.89 (0.51–1.58)</td>
<td></td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25%</td>
<td>20/34</td>
<td>15/27</td>
<td>1.36 (0.69–2.65)</td>
<td>0.01</td>
</tr>
<tr>
<td>≥25%</td>
<td>29/130</td>
<td>61/145</td>
<td>0.48 (0.31–0.74)</td>
<td></td>
</tr>
<tr>
<td><strong>Cause of heart failure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonischemic</td>
<td>26/107</td>
<td>29/88</td>
<td>0.74 (0.43–1.25)</td>
<td>0.56</td>
</tr>
<tr>
<td>Ischemic</td>
<td>25/72</td>
<td>53/96</td>
<td>0.60 (0.37–0.97)</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>32/136</td>
<td>48/117</td>
<td>0.52 (0.33–0.81)</td>
<td>0.06</td>
</tr>
<tr>
<td>Yes</td>
<td>19/43</td>
<td>34/67</td>
<td>1.01 (0.58–1.78)</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>12/50</td>
<td>19/48</td>
<td>0.59 (0.28–1.21)</td>
<td>0.88</td>
</tr>
<tr>
<td>Yes</td>
<td>39/129</td>
<td>61/136</td>
<td>0.63 (0.42–0.93)</td>
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<tr>
<td><strong>Amiodarone use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>37/122</td>
<td>61/133</td>
<td>0.65 (0.43–0.97)</td>
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<tr>
<td>Yes</td>
<td>13/55</td>
<td>18/46</td>
<td>0.55 (0.27–1.13)</td>
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<tr>
<td><strong>Digitalis use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>41/146</td>
<td>52/124</td>
<td>0.65 (0.43–0.98)</td>
<td>0.68</td>
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<tr>
<td>Yes</td>
<td>9/31</td>
<td>27/56</td>
<td>0.56 (0.26–1.19)</td>
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<tr>
<td><strong>Beta-blocker use</strong></td>
<td></td>
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<td></td>
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<tr>
<td>No</td>
<td>4/12</td>
<td>4/9</td>
<td>1.01 (0.25–4.05)</td>
<td>0.47</td>
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<tr>
<td>Yes</td>
<td>46/165</td>
<td>75/171</td>
<td>0.60 (0.42–0.87)</td>
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</tbody>
</table>
AF Catheter Ablation in HF
Unaddressed Questions

• How to select HF patients where AF is a contributing factor vs a bystander?
  - Detection of myocardial fibrosis by Gadolinium enhanced MRI?

• Cardioversion Trial to screen patients for AF ablation

• Optimum ablation strategy in long-standing persistent AF?
  - Paroxysmal and recent onset (< 1 yr) persistent AF better candidates
AF Ablation in HF
Recommended Algorithm

**AF + HF Population**

- Optimize HF/AF Rx

Symptoms/Recurrent Hosp/ ↓EF

- AAD + Cardioversion
- Continue Rx

**Yes**

- Symptoms↓
- LVEF↑

- Continue AAD

**No**

- Failed cardioversion

- Sinus but no improvement

- Continue Rate Control Strategy

**Symptoms**
- No improvement

**Side effects**
- Recurrence of AF

**Failed cardioversion**
- AF Ablation

**Continue Rx**

Age > 75 yrs, multiple comorbidities, EF < 25%, HF Class III/IV, LA > 60mm less desirable candidates
Illustrative Case Study (cont’d)

- RF Ablation performed and sinus restored.
  Amiodarone reduced to 100 mg/d

- Feels great. Exercise capacity improved

- LVEF back to 35%, three months later
### Trial Sample Size Study Group Primary Endpoint

<table>
<thead>
<tr>
<th>Trial</th>
<th>Sample Size</th>
<th>Study Group</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMICA</td>
<td>202</td>
<td>Persistent AF, EF $\leq 35%$ Any AF with ICD</td>
<td>EF and AF class improvements</td>
</tr>
<tr>
<td>RAFT-AF</td>
<td>600</td>
<td>Paroxysmal/Persistent AF HFrEF/HFpEF</td>
<td>All-cause mortality and HF hospitalization</td>
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<tr>
<td>CATCH-AF</td>
<td>220</td>
<td>Symptomatic AF EF 20-45%</td>
<td>HF hospitalization AF recurrence</td>
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<tr>
<td>AFRC-LVF</td>
<td>180</td>
<td>Persistent AF and EF $\leq 35%$</td>
<td>Composite of EF And HF class</td>
</tr>
</tbody>
</table>
AF Catheter Ablation in HF
Conclusions

• AF catheter ablation superior to Amiodarone for sinus maintenance

• Available data suggests improvement in total mortality, HF hospitalization, LVEF, HF functional class, exercise capacity and QOL?

• Benefits appear to be maintained over 3-5 years

• RF ablation complications relatively low, 1-2%

• Guidelines endorsed option

• Clinicians may consider a lower threshold for AF catheterization in HF
2019 AHA/ACC/HRS Focus Update of 2014 Guidelines for AF

### Recommendation for Catheter Ablation in HF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
</table>
| IIb | B-R | 1. AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF (S6.3.4-1, S6.3.4-2).  
**NEW:** New evidence, including data on improved mortality rate, has been published for AF catheter ablation compared with medical therapy in patients with HF. |