Lessons Learned After CABANA

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Disclosures: Nothing relevant to disclose on this topic
Lessons Learned After CABANA

• Selective approach to AF ablation using shared decision-making
• Improving quality of life via a reduction of AF burden and curtailing drug intake
• Managing asymptomatic AF
• Managing AF in patients with failure
• Managing patients with AF who are not good candidates for ablation
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Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest: ITT)

Hazard ratio, 0.86 (95% CI, 0.65-1.15); Log-rank P = .30

CABANA was more than a “Negative” Trial

• CABANA tells us that either ablation or drug therapy is an acceptable treatment for AF.

• Even in higher risk patients, the rate of adverse events was low in both arms.

• That ablation reduced the secondary endpoints of mortality/CV hospitalization (17%) and recurrent AF (47%) has to be viewed in the context of the primary endpoint having been negative.
Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions on the basis of individual values, preferences, and associated conditions and comorbidities.
Why do we need drugs for AF?

• Both AAD therapy and ablation are acceptable 1\textsuperscript{st} and 2\textsuperscript{nd} tier alternatives
• Even after ablation, drugs often remain needed
• Considerations are the same for AADs and ablation:
  – Safety/adverse drug effects
  – Efficacy
Maximizing Safety: What Is a Structurally Normal Heart for the Purpose of Choosing an AAD?

- Normal history
- Normal cardiac physical exam
- Normal 12-lead ECG
- No significant ventricular abnormalities or dysfunction on echocardiogram
- Normal stress test in appropriate patients
AAD Therapy and All-cause Mortality after CA for AF: A Propensity-matched Analysis

3634 consecutive patients, 62% received an AAD
• Amiodarone 34%
• Propafenone 28%
• Flecainide 15%
• Sotalol 13%
• Dofetilide 9%
• Dronedarone 2%

Mean f/u 6.7±2.2 years
AAD use after CA not associated with increased mortality, p=0.02

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AF Adversely Affects QoL

AFFIRM: Rhythm Control Strategy Did Not Result in Improved QoL over Rate Control

Quality of Life Index Overall Scores

<table>
<thead>
<tr>
<th>Time</th>
<th>Rate</th>
<th>Rhythm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>354</td>
<td>360</td>
</tr>
<tr>
<td>2 months</td>
<td>326</td>
<td>322</td>
</tr>
<tr>
<td>1 year</td>
<td>303</td>
<td>314</td>
</tr>
<tr>
<td>2 years</td>
<td>269</td>
<td>280</td>
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<tr>
<td>3 years</td>
<td>198</td>
<td>217</td>
</tr>
<tr>
<td>4 years</td>
<td>114</td>
<td>116</td>
</tr>
</tbody>
</table>

Scale = 1-30; higher is better

* P < .01 compared to Baseline; no differences, rate versus rhythm

QoL Improvement With Restoration of SR
SAFE-T Study (amiodarone, sotalol, PLB): Symptomatic Patients


SR group: n=167; AF group: n=179
SCL=symptom checklist; SF-36=Short Form-36. aP=.05; bP=.01; cP=.001.
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Follow-up AF Detection Depends on Monitoring Strategy

Estimated correlation between follow-up technique and AF recurrence following catheter ablation

*During 3-month follow-up
†As the theoretical gold standard
Tele = transtelephonic

AHA SCIENTIFIC STATEMENT

Atrial Fibrillation Burden: Moving Beyond Atrial Fibrillation as a Binary Entity
A Scientific Statement From the American Heart Association

- AF Burden = amount of AF an individual has
  - Frequency (#episodes/unit time)
  - Percent (proportion of time in AF)
- Longest duration of AF

ASSERT: Incidence of Subclinical AF (SCAF)

N=2580 with HTN & PM/ICD

AF Burden and Stroke Risk


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**Graph Details:**
- **Y-axis:** HR for Thromboembolic Events (log)
- **X-axis:** SCAF Duration (log[minutes])
- **Points:**
  - **ASSERT (6 min):** 5.56
  - **MOST (5 min):** 2.79
  - **TRENDS (5.5 h):** 2.2
  - **SOS AF (5 min):** 1.51
  - **RATE (long):** 0.87
  - **RATE (short):** 1.76
  - **AT500 (24 h):** 5.6

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TRENDS: Most patients did not have AT/AF within 30 days of their stroke event.

Daoud EG. *HeartRhythm* 2011;8:1416-23.
### Recommendations for Device Detection of AF and Atrial Flutter

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>In patients with cardiac implantable electronic devices (pacemakers or implanted cardioverter-defibrillators), the presence of recorded atrial high-rate episodes (AHREs) should prompt further evaluation to document clinically relevant AF to guide treatment decisions.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients with cryptogenic stroke (i.e., stroke of unknown cause) in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize detection of silent AF.</td>
</tr>
</tbody>
</table>
**Apixaban for the Reduction of Thromboembolism in Patients with Device-Detected Sub-Clinical Atrial Fibrillation (ARTESIA)**

Patients with:
- SCAF (at least 1 episode ≥6 min but none >24 hrs)
- Increased risk of stroke

**CONSENT and RANDOMIZE**

- Active aspirin 81 mg OD + Placebo apixaban bid
- Active apixaban 5 mg or 2.5 mg* bid + Placebo aspirin OD

Follow-up Visits at 1 month and every 6 months until 248 primary efficacy outcomes (est. avg 3 yrs)

**Primary Efficacy Outcomes:**
- Stroke (including TIA with imaging)
- Systemic Embolism

**Primary Safety:**
- Major Bleeding (ISTH)

* 2.5 mg if either of the following:
- At least 2 of 3 of:
  - Age ≥80
  - Weight ≤65 kg
  - Serum creatinine ≥133 µmol/L (1.5 mg/dL)
- Ongoing need for inhibitor of both CYP3A4 and P-glycoprotein

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**Recommendation for Catheter Ablation in HF**

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| IIb | B-R | 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.  
**NEW:** New evidence, including data on improved mortality rate, has been published for AF catheter ablation compared with medical therapy in patients with HF. |
DIAMOND: Dofetilide for AF in HF

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Efficacy and Safety of Quinidine Therapy for Maintenance of Sinus Rhythm After Cardioversion
A Meta-Analysis of Randomized Control Trials

Sharon E. Coplen, MD, Elliott M. Antman, MD, Jesse A. Berlin, ScD, Peg Hewitt, MS, and Thomas C. Chalmers, MD

Mortality Following Ventricular Arrhythmia Suppression by Encainide, Flecainide, and Moricizine After Myocardial Infarction
The Original Design Concept of the Cardiac Arrhythmia Suppression Trial (CAST)

Andrew E. Epstein, MD; Alfred F. Hjalmarson, PhD; William J. Rogers, MD; Philip R. Liebson, MD; A. Alan Seals, MD; Jeffery L. Anderson, MD; Jerome D. Cohen, MD; Robert J. Capone, MD; D. George Wyse, MD, PhD; for the CAST Investigators

Quinidine OR 2.98 for total mortality
Quinidine-treated 2.9%
Control 0.8%


JAMA 1993;270:2451-2455.
Drug Selection Considerations

• Adverse effects
  – Proarrhythmia, both bradycardia and tachycardia
    • Torsades de pointes VT (Class IA and III antiarrhythmic drugs)
    • Flutter with 1:1 conduction (Class IC antiarrhythmic drugs)
  – Heart failure

• Drug interactions
  – Amiodarone: warfarin, digitalis
  – Dofetilide: verapamil, inhibitors of cation transport (cimetidine, trimethoprim), megestrol, and QT-prolonging drugs
  – Digitalis: levels increase with amiodarone, propafenone, quinidine, verapamil

• Organ toxicity
  – Amiodarone: pulmonary, thyroid, skin, ocular
  – Procainamide: lupus, agranulocytosis
  – Quinidine: thrombocytopenia, lupus
Amiodarone: Not a Panacea

COMET

N = 3029
Amiodarone = 364
No amiodarone = 2665

Amiodarone: Not a Panacea
SCD-HeFT

# Out-Patient vs. In-Patient: Initiation of Antiarrhythmics for AF

<table>
<thead>
<tr>
<th></th>
<th>In AF</th>
<th>In NSR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospital</td>
<td>Out-Patient</td>
</tr>
<tr>
<td>IA</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>IC</td>
<td>(X)</td>
<td>X</td>
</tr>
<tr>
<td>Sotalol</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Dofetilide</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Dronedarone</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
ATHENA Primary Endpoint:
Reduction in CV Hospitalization or Death

Cumulative Incidence (%)

Patients at risk

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Placebo + standard therapy</th>
<th>DR 400 mg BID + standard therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>2327</td>
<td>2290</td>
<td>2250</td>
</tr>
<tr>
<td>DR 400 mg BID</td>
<td>2301</td>
<td>2274</td>
<td>2240</td>
</tr>
</tbody>
</table>

Mean follow-up 21 ± 5 months. DR=dronedarone.


HR = 0.76 (95% CI: 0.69-0.84), $P<0.001$
EURIDIS and ADONIS Primary Endpoint: First Recurrence of AF/AFI

Efficacy of AADs in AF Trials
Except for Amiodarone, 50% Efficacy is High

*At 6 months; †Mean follow-up 7 months.

CTAF = Canadian Trial of Atrial Fibrillation; SAFE-T = Sotalol Amiodarone Atrial Fibrillation Efficacy Trial; DAFNE = Dronedarone Atrial Fibrillation Study after Electrical Cardioversion; EURIDIS = European Trial in Atrial Fibrillation or Flutter Patients Receiving Dronedarone for the Maintenance of Sinus Rhythm; ADONIS = American-Australian-African Trial with Dronedarone in Atrial Fibrillation or Flutter for the Maintenance of Sinus Rhythm; DIONYSOS = Randomized, Double-blind Trial to Evaluate the Efficacy and Safety of Dronedarone vs Amiodarone for at Least 6 Months for the Maintenance of Sinus Rhythm in Patients with AF.

Antiarrhythmic Drug Versus Ablation Therapy

- Follow the guidelines
- Consider the pros and cons of each
- Talk to the patient