Atrial Fibrillation Management post-CABANA Challenges and Unmet Need

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It is well known that in the late stages of mitral stenosis and in cases of general cardio-vascular degeneration, the pulse is frequently continuously and extremely irregular....the irregular pulse of mitral stenosis, etc....is due to fibrillation of the auricle.
Most common sustained cardiac arrhythmia observed in clinical practice

An estimated 2.7–6.1 million people in the US have AF.
  - With the aging of the population, this number is expected to increase worldwide.

Approximately 2% of people <65 have AF, while about 9% of people >65 years have AF.

Because AF cases increase with age and women generally live longer than men, more women than men experience AF.

Aging and World Population
2005-2025

% of population
60 years or older

- <5
- 5-12.4
- 12.5-20
- >20

By year 2030: >20% of the US population (~71.5 million) will be 65 years or older

Obesity (BMI ≥30 kg/m²)

- 1994
- 2000
- 2010

No Data <14.0% 14.0-17.9% 18.0-21.9% 22.0-25.9% >26.0%

Hypertension Diabetes Sleep Apnea

http://www.cdc.gov/diabetes/statistics
More than 750,000 hospitalizations occur each year because of AF.

The condition contributes to an estimated 130,000 deaths each year.

- The death rate from AF as the primary or a contributing cause of death has been rising for more than two decades.

AF costs the US about $6 billion each year.

Medical costs for people who have AF are about $8,705 higher per year than for people who do not have AF.
Lifecycle of AF Patients

- Diagnosis
- Stroke Prevention
- Treatment
  - Drugs
  - Devices
  - Ablation
- Risk Factor Modification
ECG Monitoring Tools

**Holter Monitoring (1-2 days)**
- Event Recorder
- Holter

**Mobile Telemetry Monitoring (Up to 30 days)**
- Spot Single-Lead ECG Check
- Smartphone (e.g., Alivecor)
- Smartwatch (e.g., Kardiaband)

**Holter Monitoring (1-2 weeks)**
- Patch Based (e.g., Zio, ePatch)

**Lead Based (1-Piece)**
- Lead Based (e.g., CardioKey)
- Scottcare – TeleSense, TeleSentry
- Spectacor – Pocket ECG
- TeleRhythmics – Heartrak TCAT

**Lead Based (2-Piece)**
- Lead Based (e.g., Zio)
- Lead Based (e.g., CardioKey)
- Applied Cardiac Systems – CORE
- Biomedys – TruVue
- Infobionic – MoMe Kardia
- Lifewatch – ACT Elite
- Medicomp – Duet

**Patch Based**
- Patch Based (e.g., SEEQ, Body Guardian)
- Garment Based (e.g., nECG)
- Biotelemetry – MCOT Patch
- Lifewatch – ECG mini
- Medicomp – TelePatch
- Medtronic – SEEQ
- Nuubo - nECG
- Preventice – Body Guardian

**Implantable Loop Recorder (Up to 3 years)**
- ECG Monitoring Tools

Mittal S et al. JACC 2011; 58: 1741-1749; Mittal S. CIR 2017; 25: 12-16; Lee RJ, Mittal S. Heart Rhythm 2018
AF and Stroke

- AF increases a person’s risk for stroke by four to five times compared with stroke risk for people who do not have AF.
- Strokes caused by complications from AF tend to be more severe than strokes with other underlying causes.
- AF causes 15%–20% of ischemic strokes.

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_atrial_fibrillation.htm
### Increasing AF Prevalence and Stroke with Age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>AF prevalence (%)</th>
<th>Strokes attributable to AF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–59</td>
<td>0.5</td>
<td>6.5</td>
</tr>
<tr>
<td>60–69</td>
<td>1.8</td>
<td>8.5</td>
</tr>
<tr>
<td>70–79</td>
<td>4.8</td>
<td>18.8</td>
</tr>
<tr>
<td>80–89</td>
<td>8.8</td>
<td>30.7</td>
</tr>
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</table>

Stroke Prevention

Shared Decision Making
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
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<tbody>
<tr>
<td>Control ventricular rate using a beta blocker or nondihydropyridine calcium channel antagonist for paroxysmal, persistent, or permanent AF</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>IV beta blocker or nondihydropyridine calcium channel blocker is recommended to slow ventricular heart rate in the acute setting in patients without pre-excitation. In hemodynamically unstable patients, electrical cardioversion is indicated</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>For AF, assess heart rate control during exertion, adjusting pharmacological treatment as necessary</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>A heart rate control (resting heart rate &lt;80 bpm) strategy is reasonable for symptomatic management of AF</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>IV amiodarone can be useful for rate control in critically ill patients without pre-excitation</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>AV nodal ablation with permanent ventricular pacing is reasonable when pharmacological therapy is inadequate and rhythm control is not achievable</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>A lenient rate-control strategy (resting heart rate &lt;110 bpm) may be reasonable when patients remain asymptomatic and LV systolic function is preserved</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Oral amiodarone may be useful for ventricular rate control when other measures are unsuccessful or contraindicated</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>AV nodal ablation should not be performed without prior attempts to achieve rate control with medications</td>
<td>III: Harm</td>
<td>C</td>
</tr>
<tr>
<td>Nondihydropyridine calcium channel antagonists should not be used in decompensated HF</td>
<td>III: Harm</td>
<td>C</td>
</tr>
<tr>
<td>With pre-excitation and AF, digoxin, nondihydropyridine calcium channel antagonists, or amiodarone should not be administered</td>
<td>III: Harm</td>
<td>B</td>
</tr>
<tr>
<td>Dronedarone should not be used to control ventricular rate with permanent AF</td>
<td>III: Harm</td>
<td>B</td>
</tr>
</tbody>
</table>
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation - Recommendations for Rhythm Control

6.2.1. Antiarrhythmic Drugs to Maintain Sinus Rhythm: Recommendations

CLASS I
1. Before initiating antiarrhythmic drug therapy, treatment of precipitating or reversible causes of AF is recommended. (Level of Evidence: C)
2. The following antiarrhythmic drugs are recommended in patients with AF to maintain sinus rhythm, depending on underlying heart disease and comorbidities (Level of Evidence: A):
   a) Amiodarone
   b) Dofetilide
   c) Dronedarone
   d) Flecainide
   e) Propafenone
   f) Sotalol
3. The risks of the antiarrhythmic drug, including proarrhythmia, should be considered before initiating therapy with each drug. (Level of Evidence: C)
4. Because of its potential toxicities, amiodarone should only be used after consideration of risks and when other agents have failed or are contraindicated. (Level of Evidence: C)

CLASS IIa
1. A rhythm-control strategy with pharmacological therapy can be useful in patients with AF for the treatment of tachycardia-induced cardiomyopathy. (Level of Evidence: C)

CLASS IIb
1. It may be reasonable to continue current antiarrhythmic drug therapy in the setting of infrequent, well-tolerated recurrences of AF when the drug has reduced the frequency or symptoms of AF. (Level of Evidence: C)

CLASS III: HARM
1. Antiarrhythmic drugs for rhythm control should not be continued when AF becomes permanent (Level of Evidence: C), including dronedarone. (Level of Evidence: B)
2. Dronedarone should not be used for treatment of AF in patients with New York Heart Association (NYHA) class III and IV HF or patients who have had an episode of decompensated HF in the past 4 weeks. (Level of Evidence: B)
Asymptomatic Paroxysmal or Persistent AF

Class IIb

“A decision to perform AF ablation in an asymptomatic patient requires additional discussion with the patient because the potential benefits of the procedure for the patient without symptoms are uncertain.

Catheter Ablation of AF

J Am Coll Cardiol. 2014;64:10.1016/j.jacc.2014.03.022.
The Intermountain Health Study (n=4535)

Catheter ablation should be considered early in the AF disease process.

Catheter Ablation of AF

Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation
The CABANA Randomized Clinical Trial

Douglas L. Packer, MD; Daniel B. Mark, MD, MPH; Richard A. Robb, PhD; Kristi H. Monahan, RN; Tristram D. Bahnson, MD; Jeanne E. Poole, MD; Peter A. Noseworthy, MD; Yves D. Rosenberg, MD, MPH; Neal Jeffries, PhD; L. Brent Mitchell, MD; Greg C. Flaker, MD; Evgeny Pokushalov, MD; Alexander Romanov, MD; T. Jared Bunch, MD; Georg Noelker, MD; Andrey Ardashev, MD; Amiran Revishvili, MD; David J. Wilber, MD; Riccardo Cappato, MD; Karl-Heinz Kuck, MD; Gerhard Hindricks, MD; D. Wyn Davies, MD; Peter R. Kowey, MD; Gerald V. Naccarelli, MD; James A. Reiffel, MD; Jonathan P. Piccini, MD, MHS; Adam P. Silverstein, MS; Hussein R. Al-Khalidi, PhD; Kerry L. Lee, PhD; for the CABANA Investigators