Comprehensive Management of Atrial Fibrillation: Treating the Patient and not just the Rhythm!

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Disclosures:

Medtronic: Speaker Honorariums, Consultant
Atricure: Speaker Honorariums, Consultant
Outline: The 3 Pillars of Management

- Anticoagulation: understanding the CHADS-VASc score
- Symptom Relief:
  - Rate or rhythm control?
    - Options for rate control
    - Options for rhythm control and patient follow up
- Lifestyle Modification
  - HTN
  - Sleep Apnea
  - Alcohol reduction
  - Weight management
Global AF Epidemic right now!

• The prevalence of AF in the United States is rising markedly, with 2.7 million of affected individuals in 2010 and 5.6 million expected in 2050.

• Approximately 17% of hospital admissions have some type of arrhythmia.

• AF leads to bad outcomes:
  • 5x risk of CVA
  • 3x risk of CHF
  • Increased risk of dementia
  • Increased mortality

• AF detected and treated earlier leads to significantly better outcomes.

• Full attention with value-based care.

Circulation: Cardiovascular Quality and Outcomes. 2012;5:A206
ACC Guidelines1 Definition

- **Paroxysmal AF**: If the arrhythmia terminates spontaneously, and lasts less than 7 d, usually less than 24 hours.

- **Persistent**: More than 7 days
  - Termination with pharmacological therapy or DC cardioversion does not change the designation – although often used that way.

- **Permanent AF**: Often arbitrary but refers to AF where cardioversion has failed or deemed inappropriate/not attempted.

- **Recurrent AF**: 2 or more episodes.

- **“Lone AF”**: Young individuals (under 60 y of age) without clinical or echocardiographic evidence of cardiopulmonary disease.

1. Fuster et al. JACC Vol. 48, No. 4, 2006
PILLAR NUMBER 1

• ANTICOAGULATION
CHA$_2$DS$_2$-VASc Score

- C: Congestive Heart Failure ($EF \leq 40\%$) 1 Point
- H: HTN 1 Point
- A$_2$: Age $> 75$ 2 Points
- D: Diabetes 1 Point
- S$_2$: Stroke 2 Points
- V: Vascular (PVD/CAD) 1 Point
- A: Age 65-74 1 Point
- Sc: Female Sex 1 Point
**CHA\textsubscript{2}DS\textsubscript{2}-VASc Score**

- **Score = 0**  Low Risk  \hspace{1cm} Aspirin versus NOTHING

- **Score = 1**  Intermediate Risk  \hspace{1cm} Aspirin versus Anticoagulant

- **Score \geq 2**  High Risk  \hspace{1cm} Anticoagulant

**Exceptions:** Female Sex with true lone Afib <65 years old even though is a score of 1 fits into the low risk group

- **Mitral Stenosis** and **Hypertrophic cardiomyopathy** also exceptions as they are high risk group
A 59 yo old male with atrial fibrillation. DM, CKD, CAD, HTN. What do you recommend?

(1) No changes
(2) Aspirin 81mg daily
(3) Aspirin 325mg daily
(4) Aspirin 81mg + plavix 75mg daily
(5) Warfarin
(6) Novel anticoagulant
Anticoagulation Reduces Stroke and Death

Anticoagulation Reduces Stroke *and* Death

**Death**

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage</th>
<th>RRR</th>
<th>ARR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>143/1450 (9.9%)</td>
<td>26%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Warfarin</td>
<td>110/1450 (7.6%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NNT 43**

**Stroke**

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage</th>
<th>RRR</th>
<th>ARR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>133/1450 (9.2%)</td>
<td>62%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Warfarin</td>
<td>53/1450 (3.6%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NNT 18**
Non-valvular atrial fibrillation:
AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthesis heart valve, or mitral valve repair
CHADS-VASc=1 ≠ CHADS-VASc=1

<table>
<thead>
<tr>
<th>Risk Factor Components of the CHA₂DS₂-VASc Score</th>
<th>No. of Events</th>
<th>Person-Years</th>
<th>Annual Stroke Rate % (95% CI)</th>
<th>Hazard Ratio* (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>181</td>
<td>8,151</td>
<td>2.22 (1.91-2.57)</td>
<td>1.984 (1.672-2.353)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>303</td>
<td>15,864</td>
<td>1.91 (1.70-2.14)</td>
<td>1.711 (1.481-1.976)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age 65-74 yrs</td>
<td>521</td>
<td>15,602</td>
<td>3.34 (3.06-3.64)</td>
<td>3.031 (2.678-3.431)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>110</td>
<td>3,823</td>
<td>2.88 (2.37-3.47)</td>
<td>2.655 (2.158-3.267)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>59</td>
<td>2,618</td>
<td>2.25 (1.72-2.91)</td>
<td>2.152 (1.641-2.823)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>1,174</td>
<td>46,058</td>
<td>2.55 (2.41-2.70)</td>
<td>2.251 (2.024-2.504)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
A 59 yo old male with atrial fibrillation. DM, CKD, CAD, HTN. What do you recommend?

(1) Aspirin 81mg daily
(2) Aspirin 325mg daily
(3) Aspirin 81mg + plavix 75mg daily
(4) Warfarin
(5) Novel anticoagulant
CVA Risk without OAC: 5.4%
(CHADS-VASc=3)

CVA Risk with OAC: ~1.4%
(apixaban)

Major Bleed Risk with OAC: 0.4%
(apixaban)

Sample Case: use Sparctool.com
A Knowledge Gap Remains Among Physicians

Physician treatment of hypothetical patient with CHA₂DS₂-VASc score 3

N=507

36% Antiplatelet agent(s)

64% Oral anticoagulant (guideline recommendation)

151 General practitioners
202 Cardiologists
101 Electrophysiologists
53 Neurologists
Left Atrial Appendage Occlusion is Non-Inferior to Warfarin
PILLAR NUMBER 2

• Symptom Relief: Rate vs Rhythm Control
Rhythm or Rate Control -- The Big Question – The old way of thinking:

Randomized clinical trials used to show NO SIGNIFICANT difference with respect to mortality, major bleeding, and thromboembolic events, at least on an intention-to-treat analysis.


Mortality: the AFFIRM implication

• Substudy of the AFFIRM trial:
  • In the rhythm-control group, 129 patients (9%) died of a cardiac cause, versus 130 patients (10%) in the rate control group ($P=0.95$).
  • The numbers of vascular deaths were similar in the 2 groups: 35 (3%) in the rhythm-control group and 37 (3%) in the rate-control group ($P=0.82$).
  • There were no differences in the rates of ischemic stroke and central nervous system hemorrhage.
  • In the rhythm-control group, there were 169 noncardiovascular deaths (47.5% of the total number of deaths), whereas in the rate-control arm, there were 113 noncardiovascular deaths (36.5% of the total number of deaths) ($P=0.0008$).
    – Differences in noncardiovascular death rates were due to pulmonary and cancer-related deaths.

• Conclusions—"Management of atrial fibrillation with a rhythm-control strategy conferred no advantage over a rate-control strategy in cardiac or vascular mortality and may be associated with an increased noncardiovascular death rate."

More on Mortality

- Another substudy\(^1\) of AFFIRM based on “on-treatment” analysis showed that sinus rhythm was associated with a decreased mortality (HR = 0.53).

- Rhythm control drugs were associated with increased mortality after adjustment for covariates (HR = 1.49).

- Implication is that “if an effective method for maintaining SR with fewer adverse effects were available, it might be beneficial.”

Rate or Rhythm: Effect on CVA

- AFFIRM and RACE trials did not show a difference between the two strategies.
  - Majority of patients had 1 or more stroke risk factors.
  - Most strokes were diagnosed after discontinuation of anticoagulation or at sub-therapeutic INR.
  - Recurrent AF was detected in only about 1/3 of those in the rhythm-control groups who developed stroke at the time of the ischemic stroke.

- Important lesson: “Long-term oral anticoagulation therefore seems appropriate for most patients with AF who have risk factors for thromboembolism, regardless of treatment strategy and of whether AF is documented at any given time.”
Paradigm Shift

2012
• No benefit of rhythm control
• Wait to ablate until failing medical therapy

2022
• Rhythm control beneficial in many circumstance
• Ablation superior to rhythm medications
• Early ablation better than delayed ablation
Early Rhythm Control

- Rhythm control is often considered after the development of refractory symptoms, which may be too late to prevent AF progression
- Prevents irreversible atrial remodeling
- **Halts progression** and potentially saves patients from years of symptomatic AF
- Prevents AF-related death, heart failure and strokes
- AF registries suggest 75 – 85% patients are not treated with rhythm control therapy
Landmark trial of paradigm shift: EAST AF NET 4

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

Paulus Kirchhof, M.D., A. John Camm, M.D., Andreas Goette, M.D., Axel Brandes, M.D., Lars Eckardt, M.D., Arif Elvan, M.D., Thomas Fetsch, M.D., Isabelle C. van Gelder, M.D., Doreen Haase, Ph.D., Laurent M. Haegeli, M.D., Frank Hamann, M.D., Hein Heidbüchel, M.D., Ph.D., et al., for the EAST-AFNET 4 Trial Investigators.

### Table 3: Study Design and Outcomes of EAST-AFNET 4 and ATHENA Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>EAST-AFNET 4</th>
<th>ATHENA (ENRACI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>2,789</td>
<td>4,028</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Median 4.5 y</td>
<td>Mean 71 mm;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum 2.5 y.</td>
</tr>
<tr>
<td><strong>AF classification</strong></td>
<td>Recent-onset AF (≤10 mm) and at risk for stroke²</td>
<td>Paroxysmal or persistent AF or AFL and ≥1 further risk factor</td>
</tr>
<tr>
<td><strong>Rhythm control strategy</strong></td>
<td>Early rhythm control: AADs or ablation, as well as cardioversion for persistent AF. AADs: 87.0%, minitab: amiodarone (19.6%), dronedarone (17.3%), flecainide (32.3%), propafenone (7.0%), other AADs (14.0%).</td>
<td>Dronedarone</td>
</tr>
<tr>
<td><strong>Comparator arm</strong></td>
<td>Usual care, rate control supplemented by rhythm control only in symptomatic patients on adequate rate control therapy²</td>
<td>Mouse/hamster care</td>
</tr>
<tr>
<td><strong>Anticoagulation</strong></td>
<td>Standard care²</td>
<td>Rates of OAC were similar to those seen in community practice</td>
</tr>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>Composite of death from cardiovascular causes, stroke, or hospitalization with worsening heart failure or acute coronary syndrome.</td>
<td>First hospitalization due to cardiovascular cause or death from any cause.</td>
</tr>
<tr>
<td><strong>Primary endpoint result</strong></td>
<td>Occurs less often with early rhythm control than usual care (HR: 0.72; P = 0.005)</td>
<td>Dronedarone: 31.5% Placebo: 35.4% (HR: 0.76; P = 0.001)</td>
</tr>
<tr>
<td><strong>Patients in sinus rhythm</strong></td>
<td>Early rhythm control: 82.9% at 2 y</td>
<td>Dronedarone: 42.9% Placebo: 29.2%</td>
</tr>
</tbody>
</table>

*Age ≥ 75 years, previous Australia or ≥ 2 of the following criteria: age > 65 y, female, heart failure, hypertension, diabetes mellitus, severe coronary artery disease, chronic kidney disease, or left ventricular hypertrophy. **Percentages of patients receiving AADs: providers were asked to use the one that was most effective. **Percentages of patients receiving AADs or ablation: do not add up to 100%, as not all randomized patients received therapy. ***For exclusion on management of AF. **Although patients who did not have 45% response during the Aftrone trial of patients who had undergone prior ablation and were in AF at baseline.

ATHENA – A Placebo-Controlled Double-Blind Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg BID for the Prevention of Cardiovascular Hospitalization or Death from any Cause in Patients with Aftrone TIA – transient ischaemic attack, other abbreviations as in Tables 1 and 2.

(J Am Coll Cardiol 2022;79:1932–1948)
Catheter Ablation for Atrial Fibrillation with Heart Failure

Nadim F. Marrouche, M.D., Jehaneh Brahchmann, M.D., Dietrich Andristen, M.D., Jürgen Siebels, M.D.,
Vladimir Krikorian, M.D., terug, Jürgen Steiner, M.D., Bernd Wehler, M.D., Engy Peshkullaj, M.D.,
Paul W. Schaefer, M.D., Jochen Hoffe, M.D., Harald Schenkel, M.D., H. Egbert Christ, M.D.,
Jürgen Voigt, M.D., and Detmar Bärtsch, M.D. for the CASTLE-AF Investigators*

Table 1. Primary and Secondary Clinical End Points.

<table>
<thead>
<tr>
<th>End Point</th>
<th>Ablation (N=179)</th>
<th>Medical Therapy (N=184)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
<th>Cox Regression</th>
<th>Log Rank Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>21 (11.8)</td>
<td>16 (8.6)</td>
<td>0.53 (0.32-0.88)</td>
<td>0.01</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>Heart failure hospitalization</td>
<td>37 (20.7)</td>
<td>26 (14.1)</td>
<td>0.55 (0.27-0.83)</td>
<td>0.004</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>21 (11.8)</td>
<td>41 (22.2)</td>
<td>0.49 (0.22-0.88)</td>
<td>0.03</td>
<td>0.018</td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>61 (34.5)</td>
<td>80 (43.5)</td>
<td>0.72 (0.52-0.96)</td>
<td>0.04</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Hospitalization for any cause</td>
<td>124 (70.1)</td>
<td>157 (85.6)</td>
<td>0.39 (0.27-0.57)</td>
<td>0.007</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Cardiac-related death</td>
<td>7 (4.0)</td>
<td>8 (4.3)</td>
<td>1.0 (0.25-3.68)</td>
<td>0.97</td>
<td>0.016</td>
<td></td>
</tr>
</tbody>
</table>

*All numbers and percentages represent the total number of events and are event rates after a median follow-up of 28.8 months. Deaths and events occur in all-cause and were evaluated at baseline and 12 weeks after baseline for hospitalizations in the two groups after follow-up period. For Kaplan-Meier estimates at 12, 24, and 52 months, see Table S1 in the Supplementary Appendix.

The primary endpoint is a composite of death from any cause or hospitalization for worsening heart failure.
### Recommendation for Catheter Ablation in HF

Referenced studies that support the new recommendation are summarized in Online Data Supplement 7.

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIB</td>
<td>B-R</td>
<td>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. <strong>NEW</strong>: New evidence, including data on improved mortality rate, has been published for AF catheter ablation compared with medical therapy in patients with HF.</td>
</tr>
</tbody>
</table>
Options for Rate Control

Goal HR:
- Vary with patient age but usually target ventricular rates between 60 and 80 beats per minute at rest.\(^1\)
  - if mitral stenosis closer to 60 bpm at rest

No good data on target HR in exercise.

Can consider Holter monitoring and exercise testing to determine adequacy of rate control
- watch out for blunting the HR response too much during exercise.

1. Fuster et al. JACC Vol. 48, No. 4, 2006
### Table 9. Summary of Recommendations for Rate Control

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<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>
<td>267–269</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>
<td>270–273</td>
</tr>
<tr>
<td>For AF, assess heart rate control during exertion, adjusting pharmacological treatment as necessary</td>
<td>I</td>
<td>C</td>
<td>N/A</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>
<td>269, 274</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>
<td>275–277</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>
<td>278–280</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>
<td>274</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>
<td>N/A</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>
<td>N/A</td>
</tr>
<tr>
<td>Nondihydropyridine calcium channel antagonists should not be used in decompensated HF</td>
<td>III: Harm</td>
<td>C</td>
<td>N/A</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>
<td>281</td>
</tr>
<tr>
<td>Dronedarone should not be used to control ventricular rate with permanent AF</td>
<td>III: Harm</td>
<td>B</td>
<td>282, 283</td>
</tr>
</tbody>
</table>
Class IIa
- A strict heart rate control (resting heart rate <80bpm) strategy is reasonable for symptomatic management of AF
(Level of Evidence: B)

Class IIb
- A lenient rate-control strategy (resting heart rate <110bpm) may be reasonable as long as patients remain asymptomatic and LV systolic function is preserved
(Level of Evidence: B)
HR Targets

Strict <80bpm
Lenient <110bpm

78% patients in lenient arm had resting HRs <100bpm
Class III
- AV node ablation should not be performed without a pharmacologic trial to achieve ventricular rate control. (*Level of Evidence: C*)
Choice of rate controlling agents should be based on underlying conditions:

- None or hypertension:
  - β blocker
  - Diltiazem
  - Verapamil
  - Combination treatment
  - Digitalis

- CAD*:
  - β blocker
  - Diltiazem
  - Verapamil

- Heart failure:
  - β blocker
  - Digitalis

- COPD:
  - Diltiazem
  - Verapamil
  - Digitalis
  - β1-selective blocker
Clinical Pearls: Acute Setting

- Hemodynamically Unstable:
  - DC cardioversion

- Hemodynamically Stable:
  - IV Beta blockers or calcium channel blockers
    - Do not use verapamil in patient with LV dysfunction due to its potent negative inotropic effect -- drug of choice for patients with HCM and normal LV function
    - Prefer Beta blockers as first line, especially if hyperadrenergic state is the etiology of AF (i.e. post-operative, thyrotoxicosis, infection)
      - In AFFIRM, beta blockers were the most effective drug class for rate control, achieving the specified heart rate endpoints in 70% of patients compared with 54% with use of calcium channel blockers
    - Avoid in bronchospastic disorders
    - Careful in patients with LV dysfunction in acute setting although in the chronic setting they are the drugs of choice due to mortality benefits of BB in CHF.
Clinical Pearls: Acute Setting

- Use Digoxin IV or amiodarone if borderline BP or CHF
  - Watch for patients with renal failure and hypo/hyperkalemia when using digoxin
  - Digoxin can take several hours to have effect and usually ineffective in hyperadrenergic states
  - Can also consider esmolol due to short acting properties.
  - Do not use amiodarone in thyrotoxicosis due to iodine load.
Rhythm Control: Medical Options
Options for Rhythm Control:

- Within the first 24 h, up to 50% of patients with new onset of atrial fibrillation convert back to sinus rhythm.\textsuperscript{1}

- If the patient does not convert spontaneously, pharmacological or electrical cardioversion should be attempted if the rhythm control strategy has been chosen.

- Generally, in patients with non-valvular atrial fibrillation lasting less than 48 h, cardioversion can be safely done if sure of onset of AF.
  - WOULD STILL GIVE NOAC/ANTICOAG 2 hours before cardioversion if CHADSVASC=>2

- Due to the fact that AF is asymptomatic in many patients, different centers have different policies regarding cardioversion without a TEE first even if within 48 hours of onset.

- If unsure about timing of AF, then can anti-coagulate for 3 weeks then cardiovert and anticoagulate for an additional 4 more weeks; or perform a TEE guided cardioversion and anticoagulate for at least 4 more weeks.

1. Naccarelli GV, et al. \textit{Am J Cardiol} 2003; \textbf{91}: 15–26D.
Antiarrhythmics:

- Patients after electrical or pharmacological cardioversion may need to be placed on chronic antiarrhythmics or PRN “pill in the pocket”.
  - Decision is often multifactorial and patient specific, and is typically made in conjunction with cardiology consultation.
AFIB COREWELL ER PROTOCOL

- WE HAVE DEVELOPED AN ENTIRE AFIB PROTOCOL FOR ER.
- It details Pill in pocket and rate control.
Class I
- The following drugs are recommended for rhythm control of atrial fibrillation (Level of Evidence: A):
  - flecainide
  - propafenone
  - sotalol
  - dofetilide
  - dronedarone
  - amiodarone

Sodium Channel Blockers

Complex mechanism of action that involves blockade of multiple channels including sodium, potassium, and calcium
Amiodarone is the Most Effective Antiarrhythmic Drug

- 43% paroxysmal
- 57% persistent
Dofetilide Provides Reasonable Maintenance of NSR

- 58% in 500mcg group dosage adjustment (48%)
- 40% in 250mcg bid
- 37% in 125mcg bid
- 25% in Placebo

325 patients randomized
37/77 in 500mcg group dosage adjustment (~1%)
3/325 torsade
d1/325 sudden death
Efficacy: 30 trials, 6629 patients randomized

- Dronedarone: 1131 patients, efficacy 0.53 (0.40, 0.72, P=0.0002)
- Propafenone: 1228 patients, efficacy 0.36 (0.28, 0.48, P<0.0001)
- Amiodarone: 978 patients, efficacy 0.22 (0.16, 0.29, P<0.0001)
- Sotalol: 1404 patients, efficacy 0.40 (0.31, 0.52, P<0.0001)
- Flecaïnide: 305 patients, efficacy 0.31 (0.19, 0.49, P<0.0001)
Withdrawal due to AE: 29 trials, 11,763 patients randomized

<table>
<thead>
<tr>
<th>Antiarrhythmic Drug</th>
<th>Randomized Patients</th>
<th>Withdrawal Rate (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dronedarone</td>
<td>3,667</td>
<td>1.70 (1.30, 2.23)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Propafenone</td>
<td>1,261</td>
<td></td>
<td>0.078</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>716</td>
<td>2.91 (1.66, 5.11)</td>
<td>0.001</td>
</tr>
<tr>
<td>Sotalol</td>
<td>1,624</td>
<td>1.69 (1.14, 2.52)</td>
<td>0.011</td>
</tr>
<tr>
<td>Flecainide</td>
<td>224</td>
<td>1.65 (0.51, 5.37)</td>
<td>0.392</td>
</tr>
</tbody>
</table>

1363/11763 (11.6%) withdrawal rate due to severe adverse effects

Europace 2011;13:329-345
Antiarrhythmic Overview:

**Class 1C: Flecainide and Propafenone**
- Generally well tolerated
- Make sure patients stay on AV nodal blocking agents as these 1C drugs can increase conduction in AV node and therefore increase HR during AF.
- If patients develop CAD or LV dysfunction, find alternative drugs if possible.

**Sotalol:**
- monitor QTc at return visits as well as creatinine.
- In-hospital initiation for 72 hour observation for most patients – unless have an ICD or use IV sotalol (24 hour stay)
- AVOID ALL QT PROLONGING DRUGS
• **DOFETILIDE:**
  – Approved in patients with LV dysfunction
  – Monitor Qtc (<440 msec; <500 msec if bundle branch block) and creatinine.
  – In-hospital initiation for 72 hour observation.

• Avoid electrolyte disturbances (K and Mag) in all patients on antiarrhythmics due to pro-arrhythmias.

• **AVOID ALL QT PROLONGING DRUGS**
AMIODARONE:

- The most effective antiarrhythmic but also with the most side effects
- Monitor potential side effects of antiarrhythmic drugs. It can affect almost any organ:
  - Pulmonary toxicity: yearly CXR
  - Skin discoloration: avoid sun exposure
  - Hypothyroidism/hyperthyroidism: Thyroid studies at initiation and 3-6 months
  - Corneal deposits/optic neuropathy: yearly ophthalmologic exam.
  - Liver toxicity: LFT’s baseline and 3-6 months
  - Warfarin interaction: monitor INR closely when initiating therapy
  - Neurological effects

These adverse reactions are typically with chronic long term use so avoid maintaining patients on amiodarone who are young and have not tried other antiarrhythmics.

Also, there is no point in maintaining patients on amiodarone if it is not successful at reducing episodes of AF.

AV nodal blockers are better agents for rate control with less side effects.
RHYTHM CONTROL: AF ABLATION

**Class I**
- Catheter ablation is useful for symptomatic paroxysmal atrial fibrillation refractory to at least one antiarrhythmic medication (*Level of Evidence: A*)

**Class IIa**
- In patients with recurrent symptomatic paroxysmal atrial fibrillation, catheter ablation is a reasonable initial strategy before antiarrhythmic drug therapy (*Level of Evidence: B*)

**Class IIb**
- Catheter ablation may be considered prior to initiation of antiarrhythmic drug therapy with a class I or III antiarrhythmic medication for symptomatic persistent AF (*Level of Evidence: C*)
Current Indications for AF Ablation

• SYMPTOMATIC AF
• REFRACTORY or INTOLERANT to ≥ 1 antiarrhythmic drug (for EITHER PAF OR PERSISTENT)
• PAF symptomatic: even before failure of Antiarrhythmic (2a)
• Persistent Afib: should fail one antiarrhythmic but patient can be given choice especially if young and no significant remodeling of atrium
Ablation Outcomes

• PAROXYSMAL
  – 60-85% success with single procedure
  – 20-30% require > 1 procedure within the year
  – 20% require antiarrhythmics to be AF free

• PERSISTENT
  – 50-70% with single procedure
  – 30-40% require > 1 procedure within the year

Cappato et al. Circ 2005
Pappone JACC 2006
PVI vs. AAD for Initial Treatment of PAF

• 3 recent studies showed Superiority of PVI over AAD

**Cryo-FIRST**

7-day Holters every 3 months

**STOP AF First**

TTMs weekly and when symptomatic, 24-hour ambulatory monitoring at 6 and 12 months

**EARLY-AF**

Continuous monitoring with an ICM

Meta-Analysis of First Line AF ablation vs. AAD for Paroxysmal AF

PVI vs AAD in AAD Naive patients
- 5 RCT: PVI using RFA (3) and Cryo (2)
  - RAAFT, 2005 (Wazni)
  - MANTRA-PAF, 2012 (Nielsen)
  - RAAFT2 2014 (Morillo)
  - EARLY AF, 2021 (Andrade)
  - STOP AF First, 2021 (Wazni)
- 997 patients with Paroxysmal AF randomized
- Mean age 57.3 +/- 10.8
- 68.6% Male

Recurrences of AF with PVI vs AAD

Keheri, *Circ Arrhythm Electrophysiol* 2021
Early Ablation Strategy Superior to AAD for Paroxysmal AF

- 33% Reduction in Arrhythmia Recurrences with Ablation
- 45% Reduction in Symptomatic Recurrence with Ablation
- 67% Reduction in Hospitalizations
- NO Differences in Serious Side Effects (death, stroke/TIA)

Keheri, *Circ Arrhythm Electrophysiol* 2021
Safety Data of Ablation vs. ADD

CRYO-FIRST\(^1\)

THERE WAS NO DIFFERENCE IN TIME TO FIRST SAE

STOP AF FIRST\(^2\)

ESTIMATED 12-MONTH RATE OF PRIMARY SAFETY EVENTS:

- AAD:
  - 4%

- Cryoballoon:
  - 3%

EARLY-AF\(^3\)

SIMILAR RATE OF SAEs RELATED TO THE TRIAL REGIMEN:

- AAD: 4%
- Cryoballoon: 3%

AF burden markedly reduced PVI vs. AAD approach in Early AF Study

- All patients had Implantable Loop Recorders in place

Take home message:

• Increasing evidence for benefit of rhythm control
• Ablation is superior to rhythm medications
• Patients respond better to ablation when referred earlier
Additional Factors in Success of Treatment:

- Weight Loss: CRITICAL
- Sleep Apnea screening and treatment
- HTN treatment
- Alcohol cessation
Major Types of Ablations for AFIB

- **Radiofrequency**
  - Burning the tissue in the atrium

- **Cryo-balloon Ablation**
  - Freezing the tissue in the atrium
  - Newer of the two technologies

**COMING SOON!**
- Pulse Field: Very exciting
  - Electroporation
Pulmonary Vein Isolation is the Foundation of AF Ablation

69 Foci Triggering AF in 45 Patients
Radiofrequency Ablation:
Pulmonary Vein Isolation During AF

A

Pre-RF

B

Post-RF

Lasso

CS\textsubscript{d}

CS\textsubscript{p}

Stim

LA

L\textsubscript{A\textsubscript{uni}}
Typical Procedure:

- General Anesthesia
- Lasts 2-4 hours depending on how long patients had AFIB
- Same day discharge for >90% at our institution
- Minimally invasive
- Get back to usual life within a few days
- Need to be on anticoagulants post op at least two months after procedure.
The Safety Profile of Ablation Has Improved: FIRE AN ICE trial

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>RFA</th>
<th>CRYO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke or TIA</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Pericardial Effusion / Tamponade</td>
<td>1.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Atrioesophageal Fistula</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Groin-site Complication</td>
<td>4.3%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Phrenic Nerve Palsy</td>
<td>0%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Esophageal Ulcer</td>
<td>0%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Symptom status</td>
<td>Best candidate</td>
<td>Good candidate</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
<td>Very symptomatic</td>
<td>Symptomatic</td>
</tr>
<tr>
<td>Age</td>
<td>Younger</td>
<td>≤70 years</td>
</tr>
<tr>
<td>AF pattern</td>
<td>Paroxysmal</td>
<td>Paroxysmal or persistent</td>
</tr>
<tr>
<td>LA size</td>
<td>≤4.5 cm</td>
<td>≤5.0 cm</td>
</tr>
</tbody>
</table>
71yr old lady with paroxysmal AF refractory to dofetilide.
Specialty Programs: Convergent Procedure
Corewell Experience:

Kaji, Chalfoun et al presented 50 patient subset at Heart Rhythm 2023
<table>
<thead>
<tr>
<th>Drug</th>
<th>Baseline AAD N=170</th>
<th>1 year AAD N=166</th>
<th>2 year AAD N=137</th>
<th>3 year AAD N=75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>45.9%</td>
<td>5.4%</td>
<td>4.4%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>0.1%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>18.8%</td>
<td>4.2%</td>
<td>5.1%</td>
<td>12%</td>
</tr>
<tr>
<td>Dronaderone</td>
<td>5.9%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Flecaïnide</td>
<td>40%</td>
<td>6%</td>
<td>9.5%</td>
<td>9.3%</td>
</tr>
<tr>
<td>Propafenone</td>
<td>4.7%</td>
<td>0.6%</td>
<td>0%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Quinidine</td>
<td>0.1%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Sotalol</td>
<td>12.9%</td>
<td>1.8%</td>
<td>5.1%</td>
<td>2.7%</td>
</tr>
</tbody>
</table>
PILLAR NUMBER 3

• RISK FACTOR MODIFICATION
There is a High Prevalence of AF in the US

Prevalence of atrial fibrillation and flutter (per 100,000) by region, 2010

- 250 to 325
- 325 to 400
- 400 to 475
- 475 to 550
- 550 to 625
- 625 to 700
- 700 to 775
1. Genetics
2. Smoking
3. Hypertension
4. Alcohol
5. Stimulants
6. Sleep deprivation
7. Diabetes
8. Stress
9. Physical Activity
10. Obesity

56% increase in AF risk
HTN:

• Framingham study, hypertension increased risk of AF by 50% in men and 40% in women,

• Because of its higher prevalence hypertension accounts for more cases of AF than other risk factors.

• In patients with AF, HTN is present in 60% to 80% of individuals.

Huxley RR et al Circulation. 2011;123:1501–1508
Potential Mechanism of HTN causing AF

Intensive control of BP reduces AF:

HR 0.46

BP control reduces CVA in patients with AF (additive to anticoagulation)

• In a retrospective study from China, conducted in anticoagulated hypertensive patients with AF
  • those who achieved a target BP <130/80 mm Hg showed:
    – a lower incidence of ischemic stroke (0.9% versus 3.1% per year; \(P=0.01\))
    – similar risk of major bleeding (\(P=0.61\)) and intracranial bleeding (\(P=1.00\)) when compared with patients with higher BP values.

Are some antihypertensives preferred in AF over others?

• Use Beta Blockers/non-dihydropyridines for RATE control.
  – Start with them if need rate control but these do not reduce AF

• Add ACE/ARB: inhibition of RAAS system has been shown in multiple studies to reduce AF over other antihypertensive agents.
ACE/ARB reduce AF risk:

Table 2. Clinical Studies Investigating the Impact of Renin–Angiotensin–Aldosterone System Inhibition on the Risk of Atrial Fibrillation in Hypertensive Patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>No. of Patients</th>
<th>Antihypertensive Treatment</th>
<th>Mean Duration of Follow-Up, y</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Du et al139</td>
<td>Open-label RCT</td>
<td>149</td>
<td>Telmisartan vs nifedipine</td>
<td>2</td>
<td>Recurrence of AF not significantly different between telmisartan (56.7%) and nifedipine (56.4%). Persistent AF lower (P=0.036) with telmisartan (6.4%) than with nifedipine (10.0%)</td>
</tr>
<tr>
<td>Fogar et al111</td>
<td>Double-blind RCT</td>
<td>259</td>
<td>Losartan vsamlodipine</td>
<td>1</td>
<td>Non-onset AF lower (P=0.008) with valsartan (11.7%) than with amlo (35.1%)</td>
</tr>
<tr>
<td>Fogar et al111</td>
<td>Double-blind RCT</td>
<td>256</td>
<td>Valsartan+amlodipine vs atenol+amlodipine</td>
<td>1</td>
<td>Non-onset AF lower (P=0.010) with valsartan+amlodipine (16.9%) than with atenol+amlodipine (31.0%)</td>
</tr>
<tr>
<td>Hansson et al112</td>
<td>CAPPP</td>
<td>10 985</td>
<td>Captopril vs β-blockers or diuretics</td>
<td>5.5</td>
<td>Non-onset AF not significantly different between captopril (2.13%) and β-blockers or diuretics (2.45%)</td>
</tr>
<tr>
<td>Hansson et al112</td>
<td>STOP-2</td>
<td>6514</td>
<td>Enalapril (or lisinopril) vs various diuretics (or β-blockers) vs various calcium antagonists</td>
<td>5</td>
<td>Non-onset AF not significantly different between enalapril or lisinopril (19.0%) vs various diuretics or β-blockers (16.4%) vs various calcium antagonists (17.1%)</td>
</tr>
<tr>
<td>Hayward et al10</td>
<td>Post hoc analysis of ALLHAT</td>
<td>31 724</td>
<td>Lisinopril vs amlo vs chlorothiazide</td>
<td>4.9</td>
<td>Non-onset AF not significantly different between lisinopril, amlo, and chlorothiazide</td>
</tr>
<tr>
<td>Salomon et al112</td>
<td>Post hoc analysis of HOPE</td>
<td>6335</td>
<td>Ramipril vs placebo</td>
<td>4.5</td>
<td>Non-onset AF not significantly different between ramipril (2.1%) and placebo (2.0%)</td>
</tr>
<tr>
<td>Schar et al110</td>
<td>Nested case–control study</td>
<td>23 303</td>
<td>Various ACEis vs various ARBs vs various β-blockers vs various CCBs</td>
<td>&gt;1</td>
<td>Current exclusive long-term therapy with ACEis, ARBs, or β-blockers was associated with a lower risk for AF than current exclusive therapy with CCBs</td>
</tr>
<tr>
<td>Schroeter et al110</td>
<td>Post hoc analysis of VALUE study</td>
<td>15 245</td>
<td>Valsartan vs amlo</td>
<td>4.2</td>
<td>Non-onset AF lower (P=0.045) with valsartan (3.97%) than with amlo (4.34%) Persistent AF lower (P=0.0036) with valsartan (1.35%) than with amlo (1.92%)</td>
</tr>
<tr>
<td>Verdecchia et al111</td>
<td>Post hoc analysis of ORION/TRANSCEND study</td>
<td>30 424</td>
<td>Telmisartan+ramipril vs telmisartan vs ramipril</td>
<td>4.7</td>
<td>Non-onset AF not significantly lower with telmisartan+ramipril (6.0%) vs telmisartan (6.9%) vs ramipril (7.2%)</td>
</tr>
<tr>
<td>Vachtal et al110</td>
<td>Post hoc analysis of LIFE</td>
<td>5193</td>
<td>Losartan vs atenol</td>
<td>4.8</td>
<td>Non-onset AF lower (P=0.001) with losartan (6.1%) than with atenol (10.1%)</td>
</tr>
</tbody>
</table>

Verdecchia et al Circulation Research. 2018
1. Genetics
2. Smoking
3. Hypertension
4. Alcohol
5. Stimulants
6. Sleep deprivation
7. Diabetes
8. Stress
9. Physical Activity
10. Obesity

5-Fold AF risk with sleep apnea

Americans sleep average 2hrs less compared with 1960s
OSA and AF

- The estimated prevalence of OSA in the general population of North America ranges from 9% to 38%.
  - 2:1 male to female ratio
  - increases with age

- The prevalence of OSA in patients with AF is high, with estimates ranging from 21% to 74%. In the OSA population,

- Sleep Heart Health Study and the Multi Ethnic Study of Atherosclerosis found that patients with OSA had a twofold to fourfold increased risk of AF

- Most current American Heart Association guidelines recommend assessing OSA symptoms in all patients with AF and screening for OSA in recurrent patients with AF.

Senaratna CV, et al. Sleep Med Rev. 2017;34:70-81
• Tavares et al. Method Debakey
Cardio J 17 (1) 2021
OSA makes AF tougher to treat

• OSA makes treating AF more difficult.

• Patients with OSA had lower response rates to antiarrhythmic drugs,

• Less success with Rhythm control with cardioversion and catheter-based pulmonary vein isolation
  – meta-analysis shows patients with OSA had a 31% higher rate of AF recurrence after pulmonary vein isolation

• Unfortunately Prospective studies using CPAP to treat OSA have not demonstrated a reduced risk of adverse cardiovascular outcomes and AF.
  • Li L, et al. Europace. 2014;16[9]:1309-14
Why is treatment of OSA not effective in reducing AF?

• Are we treating too late in the course of OSA? Cardiac remodeling already occurred?

• Maybe AF is not causally related, but rather an association between two disease states that share common risk factors? (BMI HTN etc …)

• More research needed.
1. Genetics
2. Smoking
3. Hypertension
4. Alcohol
5. Stimulants
6. Sleep deprivation
7. Diabetes
8. Stress
9. Physical Activity
10. Obesity

There are many Modifiable AF Risk Factors
Alcohol and AF:

• Alcohol is the most common trigger of atrial fibrillation reported by 35% of patients

• associated with autonomic modulation with reduced heart rate variability, sympathetic effects, and vagal stimulation.

• Binge drinking has also been associated with acute cardiac inflammation.

• Observational studies link regular alcohol consumption (as compared with no alcohol consumption) with dose-related increases in left atrial size, impairments in atrial mechanical and reservoir function, and adverse electrical remodeling.

• Numerous studies have also reported higher rates of recurrence of atrial fibrillation after catheter ablation among regular drinkers than among nondrinkers.

• Voskoboinik et al. NEJM Jan 2020
Alcohol Abstinence reduces AF!

Alcohol Abstinence in Drinkers with Atrial Fibrillation


NEJM Jan 2, 2020
Alcohol AF (continued)

Time to Recurrence of Atrial Fibrillation.

The time to recurrence was longer in the abstinence group than in the control group (HR = 0.55; 95% CI, 0.36 to 0.84; P=0.005).

• Voskoboinik et al. NEJM Jan 2020
1. Genetics
2. Smoking
3. Hypertension
4. Alcohol
5. Stimulants
6. Sleep deprivation
7. Diabetes
8. Stress
9. Physical Activity
10. Obesity

Increasing physical activity in sedentary patients has been shown to lower AF by 50%

Conversely, extreme exercise (ultra-marathons) can increase AF risk by as much as 30%
1. Genetics
2. Smoking
3. Hypertension
4. Alcohol
5. Stimulants
6. Sleep deprivation
7. Diabetes
8. Stress
9. Physical Activity
10. Obesity

Up to 52% increased risk due to LA dilation changes

4% increased AF risk for every 1 point in BMI

Bariatric surgery leads to a decrease in AF burden
The Pandemic

• Obesity has now reached a pandemic state
  • 1.9 billion overweight worldwide
  • 655 million obese

• Obesity directly associated with:
  • Hypertension
  • Diabetes mellitus
  • Sleep-related breathing disorder
  • Ischemic heart disease

World Health Organization
Obesity is a growing national epidemic

- Currently affects ~40% of US adults
- Black adults have the highest rate of obesity in the US (49.9%) compared with Hispanics (45.6%), whites (41.4%), and Asians (16.1%)
- ~22% of 12-19yr olds have obesity in US
- Accounts for 4M deaths / year
- Obesity tripled risk of hospitalization from COVID-19
- Medical costs are 30-40% higher in patients with obesity in the US

Nearly half of Americans will have obesity by 2030

Forbes Health, Mar 2023
Hampl SE et al. Pediatrics 2023;151
Obesity and atrial fibrillation are tightly correlated

- Multiple studies have identified a strong association between AF and obesity:
  - Framingham Cohort Study
  - Danish Diet, Cancer, and Health Study
  - Women’s Health Study

- In the Framingham Heart Study, every unit increase in BMI correlated with a 4-5% increase in AF risk

- Association between obesity and AF mediated by LA enlargement

Eur Heart J 2016;37:1565-72
JAMA 2004;292:2471-2477
Mechanisms of increased AF risk in obesity

- Highly complex, incompletely understood

- Related to dysregulation in several domains
  - Hemodynamics: ↑ LA pressure, LA dilation/stretch
  - Neurohormonal: ↑ RAAS, ↑ IL,TNF,ROS, Mitochondrial dysfunction, Leptin resistance, Autonomic dysfunction
Obesity and link to AF

Figure 2. Mechanisms of atrial fibrillation in obesity.

European Heart Journal (2016) 37, 1565–1572
Obesity as risk factor

- Obesity 2\textsuperscript{nd} most predictive risk factor for AF after HTN

- Exponential increase in AF coinciding with rise of obesity

- First noted link seen in multiple studies with high BMI and post-op AF

- Together with overweight, accounts for 18\% of AF in Atherosclerosis Risk in Communities (ARIC) study

- Rise in BMI parallels rise in AF risk

JACC Clin Electrophysiol 2015;1:139–52
Circulation 2011;123:1501–8
JAMA 2004;292:2471–7
Obesity as risk factor

• For every 1 kg/m² increase in BMI > 4.7% increase in risk of AF (WHS)

• BMI independently correlated with increased AF risk regardless of gender (DDCHS, cohort study of 47,589)

• New onset AF independent of age, diabetes, hypertension and gender (US healthcare claims cohort study, 67,238)

J Am Coll Cardiol 2010;55:2319–27
Am J Cardiol 2018;121:1072–75
Obesity as risk factor

- BMI associated with progression of AF from paroxysmal to persistent
- Link between holds across geographic and racial boundaries
- 30% increased risk of AF in metabolically healthy obese

Eur Heart J 2008;29:2227–33
J Am Heart Assoc 2014;3:e000916
Obesity and its co-morbidities

• HTN
  • Stimulates the RAS system via adipocyte secreted aldosterone
  • Increases blood volume, cardiac output leading to eccentric or concentric hypertrophy
  • Induced hemodynamic changes:
    • Increases LV filling pressure
    • Induces diastolic dysfunction
    • Increases LA volume, LA pressure

Transl Res 2014;164:345–56
J Am Coll Cardiol 2017;70:2022–35
Obesity and its co-morbidities

- DM
  - Produces advanced glycation end products
  - Stimulates TGF-beta
  - Infiltrate the myocardium causing fibrosis and hypertrophy

References:
Rev Endocr Metab Disord 2010;11:31–9
Cardiovasc Diagn Ther 2015;5:364–73
Obesity and its co-morbidities

• Sleep-related breathing disorder
  • Repeated hypoxia, acidosis, sleep interruption alters autonomic tone
  • 4x increased risk of AF
  • 3x increased risk of VT
  • Bariatric study, ~90% with sleep-related breathing disorder

Am J Respir Crit Care Med 2006;173:910–6
Epicardial adipose tissue:

• Nearly 100% of obese patients with increased EAT

• EAT volume associated with increased risk of AF
  • OR 2.6 per each standard deviation increase in EAT volume
  • Associated with worse outcomes following RFA and post-op AF

Arch Intern Med 1933;52:911–31
J Am Coll Cardiol 2010;56:784–8
Circ Arrhythm Electrophysiol 2016;9:1–15
Epicardial adipose tissue

• Viscerally active tissue
  • Produces pro- and anti-inflammatory adipocytokines and growth factors including TNF-α, IL-1β, IL-6
  • Can diffuse directly into the myocardium due to shared vascular bed with coronary arteries
  • Leads to lympho- and monocyte infiltration in the myocardium resulting in fibrosis

Arch Intern Med 1933;52:911–31
J Am Coll Cardiol 2010;56:784–8
Circ Arrhythm Electrophysiol 2016;9:1–15
Difference in epicardial adipose tissue (EAT) on ICE imaging
What can be done?
Fitness and AF

• For every one MET achieved during treadmill testing, 7% lower risk of incident AF (HF-FIT Cohort Study, 64,561)
Fitness and AF

- For every two METs gained following tailored exercise program, nearly two-fold improvement in arrhythmia-free survival

- 12-week interval training program with paroxysmal AF reduced AF burden 50%

J Am Coll Cardiol 2015;66:985–96
Circulation 2016;133:466–73
Improvement in AF following weight loss

- Multiple studies demonstrating improvement in AF burden associated with weight reduction

- ARREST-AF
  - 149 obese patients, >1 cardiac RF
  - 88 patients control, 61 patients RFM
  - Arrhythmia-free survival 87% with RFM vs 17.8% for the control group after multiple ablation procedures

- LEGACY
  - 825 obese AF patients
  - AF burden most improved with >10% weight loss

- Weight loss of at least 10% was associated with a 6-fold greater probability of arrhythmia-free survival

Eur H Journal 2016;37:1565-1572
Improvement in AF following bariatric surgery

• 51 morbid obese (BMI>40) patients s/p bariatric surgery matched 2:1 manner with 102 nonobese and 102 morbidly obese patients

• All patients underwent ablation

• Recurrent arrhythmia observed in:
  - 20% in bariatric surgery group
  - 24.5% in non-obese group
  - 55% in morbidly obese group

• Morbidly obese patients should be considered for bariatric surgery before AF ablation
The association between obesity and AF from combination of evidence

Clinical evidence

1. Weight loss results in decreased AF duration and burden.\(^\text{43}\)
2. Weight loss is associated with cardiac remodelling.\(^\text{43, 45}\)
3. Long-term weight loss is associated with lower recurrent AF.\(^\text{15}\)
4. Weight loss is associated with improved AF-free survival after AF ablation.\(^\text{44}\)
5. Weight fluctuation is associated with AF recurrence.\(^\text{45}\)

Epidemiological evidence

1. Obesity is associated with higher rates of incident AF (increase per unit BMI).\(^\text{7, 19–22}\)
2. Weight increase is associated with increased AF risk.\(^\text{9}\)
3. Increased weight is associated with AF progression.\(^\text{53}\)

Mechanistic evidence

1. Obese patients have electrophysiologic and structural atrial changes.\(^\text{46}\)
2. Weight gain results in electrophysiologic, structural and histological change.\(^\text{96–98}\)
3. Pericardial fat is associated with incident AF, AF severity and freedom from AF.\(^\text{61, 65}\)
4. Both are AF and obesity associated with diastolic impairment.\(^\text{8, 77}\)
5. Weight loss is associated with freedom from AF and a concomitant decline in inflammatory markers.\(^\text{45, 87}\)
So…then patients just need to “lose weight” before ablation?

- Very poor overall outcomes with lifestyle changes and dietary modifications
- Many reasons for weight gain, however adverse hormonal effects of weight loss are the most detrimental
- Unfortunately even patients enrolled in our Metabolic Wellness clinic, while may experience initial positive results, often have rebound weight gain
- Many patients are unwilling to undergo bariatric surgery
The body and hypothalamus “fight back” against weight loss

• Humans are “wired” to eat all the time
• Hypothalamus is turned on continuously, favoring consumption
• The appetite drive is then suppressed after a meal by the release of a multitude of gut and pancreatic hormones and adipokines
GLP-1 agonists have been found to have a multitude of beneficial effects

- GLP-1 agonists are hormonal treatments that trick the body into satiety

Seminal trial of Semaglutide demonstrated impressive weight loss effects

- Semaglutide (Ozempic, Wegovy)
- Randomized, double-blind placebo-controlled trial at 129 sites in 16 countries
- Adults aged 18yrs+ with BMI ≥ 27 (with at least one weight-related co-morbidity) or BMI ≥ 30 enrolled
- Randomized 2:1 semaglutide vs placebo
- Titration to target dosage 2.4mg once weekly (target for diabetes: 1.0mg)

Seminal Trial of Semaglutide

• Mean body weight reduction (ITT) - 14.9% vs 2.4%

• On treatment body weight reduction - 16.9% vs 2.4%

• Discontinuation rate: - 7% semaglutide, 3% placebo

• GI side effects extremely common, mostly nausea/vomiting related to decreased gastric emptying

EP-Bariatric collaboration to improve outcomes

• Accelerated pathway criteria:
  - BMI > 40
  - Candidate for AF ablation
  - EP MD approval

• Limited to 10 patients / month

• Focused weight loss group and individual sessions

• Visits will include GLP-1 titration, nutrition & exercise counseling

• Coverage for GLP-1 agonists remains a barrier!!!
Conclusion in terms of AF and obesity:

• Obesity is a chronic long-term disease and a growing national epidemic

• Body weight/adiposity is highly correlated with AF burden and success of rhythm control therapies

• Hypothalamic body weight reset, amongst other factors, makes long-term weight loss extremely challenging

• GLP-1 agonists offer a compelling and exciting therapeutic option for obese and morbidly obese patients

• collaboration with PMD/endocrine/surgical bariatric teams for GLP1 inhibitors and bariatric surgery
Summary
TAKE HOME:

• Anticoagulation is often under-utilized and reduces stroke and mortality.

• The decision to anti-coagulate should be shared with the patient and based on risks and benefits.

• Catheter ablation is a reasonable and often preferred initial strategy for the management of patients with symptomatic PAROXYSMAL atrial fibrillation.

• Risk factor modification is crucial to the long-term success of AF management.
THANK YOU