Heart failure and Atrial fibrillation: Chicken or Egg?

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Disclosures

- Online: TheCVC.ca

- I did not show up to the meeting where the talks were assigned
1. The following team will win the Stanley Cup
   a. Not the Flames, ever again
   b. Edmonton Oilers
   c. Edmonton Oilers
   d. Edmonton Oilers
Learning Objectives

1. Define the features common to both atrial fibrillation and heart failure.
2. Assess how beta blockade may affect heart failure differently in the setting of concurrent atrial fibrillation.
3. Contrast cases where heart failure is a complication of atrial fibrillation, as opposed to atrial fibrillation a complication of heart failure.
Lessons learned: debating Peter Liu
AF and HF:
- Lifetime risk: 1 in 5
- Prevalence: 2%
- Associated with increased age + other factors
- $ Costly
- Clinically:
  - When one develops the other, it amplifies the issues
2. Patients with atrial fibrillation develop heart failure at a rate of:
   a. <1% per year
   b. 2-5% per year
   c. 6-10% per year
   d. 11-20% per year
3. All 3 drugs (ACE-MRA-betablocker) prevent patients with heart failure from developing atrial fibrillation:

a. yes
b. no
Shared Epidemiology: a Syndemic?

Syndemic:

- A synergistic epidemic
- The hallmark of a syndemic is the **presence of two or more disease states** that **adversely interact with each other**, negatively affecting the mutual course of each disease **trajectory**, enhancing **vulnerability**, and which are made more deleterious by experienced inequities.

*Lancet, March 2017*
Figure: Models of epidemics co-occurring with HIV involving syndemic synergy and mutual causality

(A) In the syndemic model, the two epidemics are not mutually causal but show synergy: the dashed arrows indicate that epidemic A has a greater effect on the HIV epidemic in the presence of epidemic B, epidemic B has a greater effect on the HIV epidemic in the presence of epidemic A, and the combined effect of epidemics A and B on the HIV epidemic exceeds the sum of their independent effects were no synergy present. (B) In the model of mutual causality, the two epidemics do not show synergy but have reciprocal relationships with each other: epidemic A exacerbates epidemic B, which in turn worsens epidemic A, and both epidemics have similar bidirectional relationships with the HIV epidemic.
How are AF and HF related?

- ↑ LA size
- ↑ LA pressure
- Functional MR
- ↓ LA contraction

HF -> Fibrosis -> Neurohormonal activation -> AF

↓ effective cardiac output
↑ heart rate (tachy CM)

Adapted from Verma, *Circulation*, 2015
How are AF and HF related?

- Sympathetic tone
- TIMPs, MMPs, NPs (A/B)
- Aldosterone, AngII, cGMP
How are AF and HF related?

HF ➔ Reduce mortality ➔ Keep out of ED and hospital ➔ AF

HF ➔ Improve symptoms ➔ AF
Does AF beget HF (and VV)?

- HF \rightarrow AF: 5.4\% \text{/year}
- AF \rightarrow HF: 3.3\% \text{/year}
Incident AF/HF

1\textsuperscript{st} HF in patients with AF

1\textsuperscript{st} AF in patients with HF

Wang \textit{Circulation} 2003 (FHS)
Incident HF in patients with AF

Preserved EF
61%
P = 0.19

Reduced EF
39%
P = 0.93
### Incident HF in patients with AF

**Figure 1:** Cumulative Incidence of HF Events Over Time Among Patients With Atrial Fibrillation

**Table 3:** Significant Clinical Predictors of Incident HF Among AF Patients

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted HR (95% CI)*</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of AF (reference group: paroxysmal AF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First detected or new onset</td>
<td>1.01 (0.50-2.04)</td>
<td>0.99</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>0.98 (0.64-1.51)</td>
<td>0.94</td>
</tr>
<tr>
<td><strong>Permanent AF</strong></td>
<td><strong>1.60 (1.18-2.16)</strong></td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Age, yrs</td>
<td>1.17 (1.08-1.26)</td>
<td>0.0001</td>
</tr>
<tr>
<td>History of CAD</td>
<td>1.52 (1.16-1.99)</td>
<td>0.0025</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;80</td>
<td>1.16 (0.99-1.36)</td>
<td>0.066</td>
</tr>
<tr>
<td>≤80</td>
<td>0.89 (0.81-0.96)</td>
<td>0.0047</td>
</tr>
<tr>
<td>EGFR, mg/dl</td>
<td>0.95 (0.91-0.98)</td>
<td>0.0033</td>
</tr>
<tr>
<td>Significant valvular disease</td>
<td>1.50 (1.12-2.01)</td>
<td>0.0063</td>
</tr>
<tr>
<td><strong>Heart rate, beats/min</strong></td>
<td><strong>1.07 (1.02-1.13)</strong></td>
<td><strong>0.0048</strong></td>
</tr>
<tr>
<td>Sinus node dysfunction/sick sinus syndrome</td>
<td>1.37 (1.00-1.88)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Adjusted for covariates:
- Age
- Sex
- Diabetes mellitus
- Hypertension
- Chronic obstructive pulmonary disease
- Obesity
- History of CABG
- LV dysfunction
- Mitral valve disease
- Significant valvular disease
- Heart rate, beats/min
- Sinus node dysfunction/sick sinus syndrome

**ORBIT-AF registry**

N=6545

1-2%/year
Common issues: AF+HF

- How much do I slow this pts HR?
  - Rate control (RACE, RACEII)
- Do I cardiovert from AF-->SR?
  - Rhythm control (AF-CHF, AFFIRM)
- Do I anti-coagulate?
  - Stroke prevention
- Which drugs / devices do I use?
  - Therapeutic choices (device and drug)
- Which is causing the Sx?
  - Attribution of “cause” for symptoms
Heart rate has different risk for AF and SR

A: All-cause mortality: Atrial fibrillation

B: All-cause mortality: Sinus rhythm

AFFIRM, AF-CHF IPD

Andrade, Heart Rhythm 2016
Beta-blockers reduce new-onset AF

Newly Diagnosed Atrial Fibrillation

- Placebo
- Metoprolol CR/XL

Risk reduction 48%

p=0.0005

MERIT-HF; Van Veldhuisen *EJHF* 2006
Enalapril Decreases the Incidence of Atrial Fibrillation in Patients With Left Ventricular Dysfunction

Insight From the Studies Of Left Ventricular Dysfunction (SOLVD) Trials

Emmanuelle Vermes, MD; Jean-Claude Tardif, MD; Martial G. Bourassa, MD; Normand Racine, MD; Sylvie Levesque, MSc; Michel White, MD; Peter G. Guerra, MD; Anique Ducharme, MD, MSc

Vermes, Circulation 2003
MRA reduce new-onset AF

Karl Swedberg et al. JACC 2012;59:1598-1603
Beta-blockers in HF-REF and AF?

- IPD of 10 RCT of BB vs. placebo: 18k patients
- Are BB bad in HF-REF + AF?
### Beta-blockers in HF-REF and AF?

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Number of events/sample size</th>
<th>Sinus rhythm, β blockers versus placebo</th>
<th>Atrial fibrillation, β blockers versus placebo</th>
<th>p-value atrial fibrillation versus sinus rhythm</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality (including all reported deaths)</td>
<td>2870/17009</td>
<td>0.73 (0.67-0.80)</td>
<td>0.57 (0.42-0.77)</td>
<td>0.36</td>
</tr>
<tr>
<td>Cardiovascular deaths (including all reported deaths)</td>
<td>2297/17009</td>
<td>0.72 (0.65-0.79)</td>
<td>0.92 (0.77-1.10)</td>
<td>0.02</td>
</tr>
<tr>
<td>First cardiovascular hospital admission</td>
<td>4374/16644</td>
<td>0.78 (0.73-0.83)</td>
<td>0.69 (0.62-0.77)</td>
<td>0.05</td>
</tr>
<tr>
<td>Death or cardiovascular hospital admission</td>
<td>5670/16644</td>
<td>0.76 (0.72-0.81)</td>
<td>0.62 (0.57-0.67)</td>
<td>0.01</td>
</tr>
<tr>
<td>First heart failure-related hospital admission</td>
<td>2872/16644</td>
<td>0.71 (0.65-0.77)</td>
<td>0.66 (0.60-0.73)</td>
<td>0.005</td>
</tr>
<tr>
<td>Cardiovascular death (during study) or heart failure-related hospital admission</td>
<td>4151/16644</td>
<td>0.70 (0.65-0.75)</td>
<td>0.67 (0.61-0.73)</td>
<td>0.001</td>
</tr>
<tr>
<td>Non-fatal stroke</td>
<td>296/16644</td>
<td>1.02 (0.78-1.32)</td>
<td>1.04 (0.66-1.63)</td>
<td>0.81</td>
</tr>
</tbody>
</table>

#### Deaths in sinus rhythm (n=2237) vs Deaths in atrial fibrillation (n=633)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Deaths in sinus rhythm</th>
<th>Deaths in atrial fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myocardial infarction</td>
<td>126 (6%)</td>
<td>13 (2%)</td>
</tr>
<tr>
<td>Sudden death</td>
<td>927 (41%)</td>
<td>231 (36%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>539 (24%)</td>
<td>184 (29%)</td>
</tr>
<tr>
<td>Cardiac (not heart failure)</td>
<td>59 (3%)</td>
<td>11 (2%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>43 (2%)</td>
<td>27 (4%)</td>
</tr>
<tr>
<td>Vascular (not stroke)</td>
<td>99 (4%)</td>
<td>38 (6%)</td>
</tr>
<tr>
<td>Non-cardiovascular</td>
<td>180 (8%)</td>
<td>45 (7%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>264 (12%)</td>
<td>84 (13%)</td>
</tr>
</tbody>
</table>

Data are number (%), unless otherwise indicated. *including deaths reported after the closure or early termination of the study.

Hazard ratios, not p-values
Clinical meaning?

Kotecha *Lancet* 2014
Down with Digoxin

- Systematic review: 19 studies – RCT + cohort
- AF and HF: 326426 patients
- Digoxin ↑risk of death
- Summary: no role unless you are stuck

Vamos, EHJ 2015
ON THE JOB SAFETY BEGINS HERE! 345 DAYS WITHOUT A RECORDABLE INJURY ON THE JOB Thank you for WORKING SAFELY
AF and HF: stroke prevention

• *DOAC are preferred strategy
• Don’t forget to stop the ASA
Summary

• AF + HF are common/linked/amplified: A syndemic
• Outcomes remain poor if both AF + HF
• Rx should be studied + applied carefully