Atrial Fibrillation in the ICU: Attempting to defend 4 controversial statements

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Conflict of Interest

• No financial, proprietary conflict with pharmaceutical industry

• No financial support for research from pharmaceutical industry
  • Heart and Stroke Foundation of Ontario
  • TOH Patient Safety Institute
  • The Ottawa Hospital

• All slides, opinions, most of the Data presented today are my own
4 Controversial Statements

1. Most of what we know (or think we know) about AF does not apply to new-onset AF in critically ill adults.

2. Goals of care should be determined by the presence/absence/risk of hemodynamic instability attributed to new onset AF.

3. The preferred agent for rate control for new onset AF in the ICU should be a beta blocker.

4. Amiodarone may be no better than placebo for rhythm conversion of new onset AF in the ICU.
Most of what we know (or think we know) about AF does not apply to new-onset AF in critically ill adults.

- Unlike in the community, new onset AF in the ICU is a transient phenomenon.

- The etiology of new onset AF in the ICU is different than in the community.

- The associated morbidity and mortality are different in critically ill patients.
New onset AF in the ICU is a transient phenomenon.

Estimated prevalence in critically ill patients
- Post cardiac surgery: 10-65%
- Post non-cardiac surgery: 10-30%
- Medical ICU patients: 5-20%
- Severe Sepsis: 5-15%

Less than 15% of patients with new-onset AF will leave the ICU in AF

New onset AF is often a reversible manifestation of critical illness

PMID: 11747385, 2245612, 2245612, 22081378
Most of what we know (or think we know) about AF does not apply to new-onset AF in critically ill adults.

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The etiology of new onset AF in the ICU is different than in the community.

Many risk factors have been identified:

- Major surgery
- Underlying cardiac disease
- High cardiac filling pressures
- Age
- Sepsis
- Cardiovascular failure
- Hypoxia
- Drugs (vasopressors, inotropes)
- Electrolyte abnormalities (Mg, K)
- Multi-organ dysfunction syndrome

In most cases these risk factors are potentially reversible (immediately or eventually)

PMID: 11747385, 14566263, 2245612, 22081378
The etiology of new onset AF in the ICU is different than in the community.

Fig. 1 Risk factors identified at the onset or immediately before the development of new-onset AF (n = 139).
The etiology of new onset AF in the ICU is different than in the community.

<table>
<thead>
<tr>
<th>Risk Factor (%)</th>
<th>New Onset AF (n=139)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of any risk factor</td>
<td>101 (73)</td>
</tr>
<tr>
<td>Presence of 2 or more risk factors</td>
<td>63 (45)</td>
</tr>
<tr>
<td>Presence of 3 or more risk factors</td>
<td>21 (15)</td>
</tr>
</tbody>
</table>

Modifiable risk factors are very common
The etiology of new onset AF in the ICU is different than in the community.

doi:10.1093/eurheartj/ehi645

Is atrial fibrillation an inflammatory disorder?

Christopher J. Boos¹, Richard A. Anderson², and Gregory Y.H. Lip¹*

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What is the Burden of Illness associated with AF in the critically ill?

- Morbidity associated with AF
  - More frequent ICU admissions
  - Longer ICU LOS, hospital LOS
  - More frequent pulmonary complications
  - Perioperative cardiac events
  - Congestive heart failure
  - Renal failure

- Mortality associated with AF
  - Post Cardiac Surgery: RR = 0 – 1.67
  - Post Non-Cardiac Surgery: RR = 4.0 - 5.0
  - Medical Intensive Care and Sepsis: RR = 1.07 - 1.63

Attributability in Question!
Perhaps AF is simply a marker of disease severity
Most of what we know (or think we know) about AF does not apply to new-onset AF in critically ill adults.

- New onset AF in the ICU is a transient phenomenon.

- The etiology of new onset AF in the ICU is different than in the community.

- The associated morbidity and mortality are different in critically ill patients.

*If the epidemiology, pathophysiology, etiology, associated morbidity and mortality are different then we need to re-evaluate our assumptions of AF in the ICU*
Goals of care should be determined by the presence/absence/risk of hemodynamic instability attributed to new onset AF.

What are the goals of care for patients with new-onset AF in the ICU?

• Rhythm Control
  • Electrical cardioversion
  • Pharmacological cardioversion
• Rate Control
  • Reduce the work of the heart, risk of ischemia
  • Counteract sympathetic drive, adrenergic state
  • Await spontaneous conversion (20-50%)
Goals of care should be determined by the presence/absence/risk of hemodynamic instability attributed to new onset AF.

Although not proven, it stands to reason that the population who would most benefit from return of their atrial kick would be those with hemodynamic instability.

<table>
<thead>
<tr>
<th>Condition</th>
<th>New Onset AF (n=139)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamically unstable (any of the below)</td>
<td>60 (43)</td>
</tr>
<tr>
<td>Hypotension (MAP&lt;60 or SBP &lt;90 or 50% increase in vasopressors during first 2 hours of AF)</td>
<td>52 (37)</td>
</tr>
<tr>
<td>Myocardial Infarction/ Ischemia per enzymes or ECG diagnosis</td>
<td>9 (7)</td>
</tr>
<tr>
<td>New Pulmonary Edema per Confirmed on CXR per progress notes</td>
<td>6 (4)</td>
</tr>
</tbody>
</table>
New Onset Atrial Fibrillation

Hemodynamically Unstable
  (hypotension, rapid ventricular rate, worsening/new symptoms of heart failure)

Correct reversible causes
  (hypomagnesemia, hypokalemia, hypoxia)

Synchronized DCC

NSR

AF persists

Hemodynamically Stable

Correct reversible causes
  (hypomagnesemia, hypokalemia, hypoxia)

NSR

AF persists

Pharmacological Rate Control
Consider beta blockers for those with significant heart disease or calcium channel blockers for those without (See Table 1)

High risk for hemodynamic instability?
  (heart failure, severe coronary artery disease, septic shock)

Consider Pharmacological Rhythm Control (see table 2)

Low risk for hemodynamic instability?
  (no significant heart disease, age <60)

Continue pharmacological Rate Controlc
The preferred agent for rate control for new onset AF in the ICU should be a beta blocker.

- 55 Surgical ICU patients with new AF
  - randomized to Esmolol or Diltiazem infusions
  - Not blinded
  - Evaluated conversion rates within 12 hours

  - Esmolol: 79% Converted
  - Diltiazem: 62% Converted (p=0.116)

Hypothesis: The etiology of AF in the ICU is different from other settings. If rapid AF is caused by cardiac stimulation by excessive endogenous catecholamines (i.e. hyperadrenergic state) the it makes sense that a B-Blocker might blunt that response…
Amiodarone may be no better than placebo for rhythm conversion of new onset AF in the ICU.

Do the Drugs Work?

Treatment of new-onset atrial fibrillation in noncardiac intensive care unit patients: A systematic review of randomized controlled trials*

Salmaan Kanji, PharmD; Robert Stewart, MD; Dean A. Fergusson, MHA, PhD; Lauralyn McIntyre, MD, MSc, FRCPC; Alexis F. Turgeon, MD, MSc, FRCPC; Paul C. Hébert, MD, MSc, FRCPC


• Only 4 RCTs
  • None blinded
  • 143 patients evaluated (only 89 had AF)
  • Largest study: N=55
• Duration of study: 1-24h
• unstable patients excluded from all studies
• No study evaluated clinical impact of rhythm conversion
• Heterogeneous definition of successful cardioversion
• No study evaluated maintenance of conversion
Figure 2. Conversion rates (and 95% confidence intervals) for all drugs evaluated. Conversion rates reported as percent with 95% confidence intervals for reported conversion rates at 12 hours for each drug except flecainide and verapamil, which are presented as 1-hour conversion rates.
Atrial Fibrillation in the Intensive Care Unit: A Randomized Controlled Pilot Study (AFICU Pilot)

Feasibility Objectives:
• recruitment, randomization, blinding

Clinical Objectives:
• Does treatment with amiodarone in addition to rate control result in more frequent rhythm conversion than rate control alone?
• Does rhythm control result in faster resolution of AF when compared to rate control?
• Does rhythm conversion within 24 hours result in shorter ICU lengths of stay?
Clinical Outcomes: Rhythm Conversion

Spontaneous Conversion prior to Study Drug: 8/24 (33%)

<table>
<thead>
<tr>
<th>Efficacy Outcomes (%)</th>
<th>Amiodarone (n=8)</th>
<th>Placebo (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythm Conversion at any time</td>
<td>8 (100)</td>
<td>5 (63)</td>
</tr>
<tr>
<td>Relapse Rates</td>
<td>4/8 (50)</td>
<td>2/5 (40)</td>
</tr>
<tr>
<td>Need for urgent Open-Label cardioversion*</td>
<td>1/8 (13)</td>
<td>2/8 (25)</td>
</tr>
<tr>
<td>Was urgent open-label cardioversion successful?</td>
<td>0/1 (0)</td>
<td>0/2 (0)</td>
</tr>
<tr>
<td>Time to Conversion (median, range)</td>
<td>15.25 (0.5 – 36.5)</td>
<td>11.5 (4.5 – 26.5)</td>
</tr>
</tbody>
</table>

*Reason for open label cardioversion: uncontrolled tachycardia (2); uncontrolled tachycardia and new hypotension (1)
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