Perioperative management on the patient with postoperative atrial fibrillation and flutter

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French National Congress
SFAR 2016

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22 – 24 September 2016

Paris

www.sfar.org
Conflicts of interest

- Scientific Advisory Board Baxter SAS France
Epidemiology

• **A frequent complication**
  - 20 to 60% following cardiothoracic surgery *(Cochrane database 2013)*
  - More than 40% in severe sepsis and septic shock *(Crit Care 2010)*
  - 8 to 20% in ICU *(Crit Care 2010)*

• **A serious complication**
  - Increase in morbidity *(JTCVS 2011)*
  - Increase in short- and long-term mortality *(JTCVS 2011)*
  - Increase in LOS in ICU and in hospital
  - Increase in health costs
**Major clinical consequences**

- **Recurrence**: one (40%) or two times (20%)

- **Immediate hemodynamic consequences**: decrease in stroke volume related to the lost of atrial contraction (*age, underlying cardiac disease*)

- **Delayed hemodynamic consequences**: atrial and ventricular anatomical changes (*tachycardia-induced cardiomyopathy*)

- **Thromboembolism risk**: high (*stroke*)

- **POAF is transient**: 50% of patients have returned to sinus rhythm within 24h and almost 100% within 7 days
Pathophysiology of POAF is well known

Patient-related chronic factors
Age, history of AF, withdrawal of beta-blockers, hypertension, heart failure, atrial dilation, COPD

Surgery-related acute factors
- SIRS
- Hyperadrenergic state
- Oxidative stress
Pathophysiology: the threshold theory

B. Maesen et al. Europace 2012
**Prevention of AF**

**Settings with a high-incidence of AF (> 20%)**
- Cardiac surgery
- General thoracic surgery
- Severe sepsis/septic shock

*Risk/benefit and cost/benefit ratios in favor*

**Prevention strategy**
- Treatment of associated factors
- Optimization of perioperative beta-blocker therapy
- Magnesium 1.5-3 g/d during 1 to 4 days
Prevention of POAF

Treatment of associated factors (I-C)

- Hypovolemia
- Electrolytic disturbances (*hypokalemia ++*)
- Hypoxemia
- Anemia
- Avoid positive inotropic agents
- Pain relief
Prevention of AF

Settings with a high-incidence of AF (> 20%)
- Cardiac surgery
- General thoracic surgery
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Risk/benefit and cost/benefit ratios in favor

Prevention strategy
- Treatment of associated factors
- Optimization of perioperative beta-blocker therapy
- Magnesium 1.5-3 g/d during 1 to 4 days
Table 2. Multivariable Predictors of Postoperative Atrial Fibrillation Among Patients in the Derivation Cohort

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Incidence of Postoperative Atrial Fibrillation, No/Total (%)</th>
<th>Risk Score*</th>
<th>OR (95% CI)†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>0</td>
<td>6</td>
<td>1.75 (1.59-1.93)†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>30-39</td>
<td>2/36 (5.6)</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>19/229 (8.3)</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>160/795 (20.1)</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>378/1145 (33.0)</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-79</td>
<td>377/817 (46.1)</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥80</td>
<td>40/68 (58.8)</td>
<td>42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>142/268 (53.0)</td>
<td>7</td>
<td>2.11 (1.57-2.85) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>137/320 (42.8)</td>
<td>4</td>
<td>1.43 (1.09-1.87) .009</td>
<td></td>
</tr>
<tr>
<td>Concurrent valve surgery</td>
<td>154/286 (53.9)</td>
<td>6</td>
<td>1.74 (1.31-2.32) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>Withdrawal of treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>396/784 (50.5)</td>
<td>6</td>
<td>1.91 (1.52-2.40) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>320/692 (46.2)</td>
<td>5</td>
<td>1.69 (1.38-2.08) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>Preoperative and postoperative treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>228/1289 (17.7)</td>
<td>-7</td>
<td>0.49 (0.39-0.61) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>126/626 (20.1)</td>
<td>-5</td>
<td>0.62 (0.48-0.79) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>Postoperative β-blocker treatment</td>
<td>51/228 (17.7)</td>
<td>-11</td>
<td>0.32 (0.22-0.46) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>Other treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium supplementation</td>
<td>774/2688 (28.8)</td>
<td>-5</td>
<td>0.53 (0.42-0.68) &lt;.001</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>173/934 (18.5)</td>
<td>-7</td>
<td>0.49 (0.40-0.60) &lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; CI, confidence interval; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, odds ratio.

*A score of less than 14 indicates low risk; a score of 14 to 31, medium risk; and a score higher than 31, high risk.
†The ORs are adjusted for the factors included in the final model and presented in this table.
‡The OR is for a 10-year change and may be extrapolated.
# Perioperative optimization of beta-blockers

* $N = 125$ patients chronically treated with $\beta$-blockers and undergoing conventional cardiac surgery

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>POD 0</th>
<th>POD 1</th>
<th>POD 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-blocker administered</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 1</td>
<td>73 (100)</td>
<td>3 (4)</td>
<td>31 (42)</td>
<td>47 (64)</td>
</tr>
<tr>
<td>Phase 2</td>
<td>52 (100)</td>
<td>0 (0)</td>
<td>39 (75)*</td>
<td>52 (100)*</td>
</tr>
</tbody>
</table>

| **Therapeutic goal reached** |       |       |       |       |
| Phase 1              | 49 (67)     | 1 (1) | 24 (33) | 37 (51) |
| Phase 2              | 35 (67)     | 0 (0) | 39 (75)* | 50 (96)* |

Values are number (%)  
* $P < 0.001$ vs. phase 1  

+79% +56%  
+127% +88%

_Fellahi et al., J Cardiothorac Vasc Anesth 2015;29:32-37_
Early postoperative beta-blocker strategy

From the morning of POD 1 to the ICU discharge
Patients chronically treated with beta-blockers

Therapeutic goal: 60 < HR < 90 b/min and SBP > 100 mmHg
Prevention of AF

Settings with a high-incidence of AF (> 20%)
- Cardiac surgery
- General thoracic surgery
- Severe sepsis/septic shock

Risk/benefit and cost/benefit ratios in favor

Prevention strategy
- Treatment of associated factors
- Optimization of perioperative beta-blocker therapy
- Magnesium 1.5-3 g/d or more during 1 to 4 days
Intraoperative magnesium administration does not reduce postoperative atrial fibrillation after cardiac surgery

Double-blind, placebo-controlled trial including 389 adult patients scheduled for conventional cardiac surgery with CPB: Mg = 100 mg/kg intraoperative vs. placebo

POAF: 42% (95% CI: 35-50) Mg group vs. 38% (95% CI: 31-45) placebo group, \( P = 0.40 \)
aOR = 1.09 (95% CI: 0.69-1.72), \( P = 0.73 \)

![Figure 2. Serum concentration of magnesium at the 5 measurement time points. Data are represented as mean ± SD. *\( P < 0.001 \). ICU = intensive care unit.](image)
## Postoperative AF treatment

<table>
<thead>
<tr>
<th></th>
<th>Total on 8 months N = 74</th>
<th>Months 1 to 4 N = 40</th>
<th>Months 5 to 8 N = 34</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amiodarone</strong></td>
<td>37 (50)</td>
<td>19 (48)</td>
<td>18 (53)</td>
<td>0.721</td>
</tr>
<tr>
<td><strong>Magnesium</strong></td>
<td>41 (55)</td>
<td>21 (53)</td>
<td>20 (59)</td>
<td>0.730</td>
</tr>
<tr>
<td><strong>Beta-blockers</strong></td>
<td>17 (23)</td>
<td>4 (10)</td>
<td>13 (38)</td>
<td>0.005</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Electrical cardioversion</td>
<td>3 (4)</td>
<td>2 (5)</td>
<td>1 (3)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Values are number (%)  

Fellahi 2014, unpublished data
POAF treatment: is there a role for magnesium?

De Oliveira, J Cardiothorac Vasc Anesth 2012
Amiodarone in POAF treatment
A benefit/risk analysis

Advantages

- Good hemodynamic tolerance (oral form +++)
- Can be used when LVEF is altered and/or in patients receiving positive inotropic agents

Disadvantages

- Numerous side effects
- Low classes of recommendation and levels of evidence
- Contraindicated in COPD, ARDS and pneumonectomy
From 2005 to 2015

What about recommendations?

Cardiac surgery > Thoracic surgery > General surgery > ICU
ACCP guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery

Pharmacologic control of ventricular rate

*Chest 2005; 128: 56S-60S*

1. Because of the hyperadrenergic state after surgery, **betablockers are recommended as the first line of therapy** for patients with AF who do not require urgent cardioversion  *moderate recommendation*

2. Calcium channel blockers are recommended as second-line therapeutic agents  *moderate recommendation*

3. Digoxin and amiodarone have little efficacy  *no recommendation possible*

Pharmacologic control of rhythm

*Chest 2005; 128: 48S-55S*

1. Based on limited available evidence, **amiodarone** is recommended for pharmacologic conversion of postoperative AF in patients with depressed LV function who do not need urgent electrical conversion  *weak recommendation*

2. Betablockers may be efficacious in achieving AF conversion but the evidence is limited and weak  *no recommendation possible*
ESC Task Force guidelines for the management of AF

*Eur Heart J* 2010; 31: 2369-2429.

### Recommendations for post-operative AF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral β-blockers are recommended to prevent post-operative AF for patients undergoing cardiac surgery in the absence of contraindications.</td>
<td>I</td>
<td>A</td>
<td>186, 187</td>
</tr>
<tr>
<td>If used, β-blockers (or other oral antiarrhythmic drugs for AF management) are recommended to be continued until the day of surgery.</td>
<td>I</td>
<td>B</td>
<td>187, 196</td>
</tr>
<tr>
<td>Ventricular rate control is recommended in patients with AF without haemodynamic instability.</td>
<td>I</td>
<td>B</td>
<td>196</td>
</tr>
<tr>
<td>Restoration of sinus rhythm by DCC is recommended in patients who develop post-operative AF and are haemodynamically unstable.</td>
<td>I</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Pre-operative administration of amiodarone should be considered as prophylactic therapy for patients at high risk for post-operative AF.</td>
<td>IIa</td>
<td>A</td>
<td>186–188</td>
</tr>
<tr>
<td>Unless contraindicated, antiarrhythmic/anticoagulation medication for post-operative AF should be considered when the duration of AF is ≥48 h.</td>
<td>IIa</td>
<td>A</td>
<td>195</td>
</tr>
</tbody>
</table>

- If sinus rhythm is restored successfully, duration of anticoagulation should be for a minimum of 4 weeks but more prolonged in the presence of stroke risk factors.
- Antiarrhythmic medications should be considered for recurrent or refractory postoperative AF in an attempt to maintain sinus rhythm.
- Sotalol may be considered for prevention of AF after cardiac surgery, but is associated with risk of proarrhythmia.
- Biventricular pacing may be considered for prevention of AF after cardiac surgery.
- Corticosteroids may be considered in order to reduce the incidence of AF after cardiac surgery, but are associated with risk.
Option 1 « Rate control »
Selective beta-1 blockers should be considered first (class I, level B), then calcium channel antagonists (diltiazem, verapamil) (class I, level B)

Option 2 « Rhythm control »
Amiodarone can be used (class IIa, level B)

No consensus is currently available suggesting one option is superior to the other. Because postoperative AF is transient and beta-blockers or diltiazem are safer than amiodarone, the option 1 should be preferred as a first-line therapy.
### Postoperative cardiac and thoracic surgery

- **Beta blocker is recommended to treat postoperative AF unless contraindicated**
  - **Category**: I
  - **Grade**: A

- **A nondihydropyridine calcium channel blocker is recommended when a beta blocker is inadequate to achieve rate control with postoperative AF**
  - **Category**: I
  - **Grade**: B

- **Preoperative amiodarone reduces AF with cardiac surgery and is reasonable as prophylactic therapy for high risk of postoperative AF**
  - **Category**: IIa
  - **Grade**: A

- **It is reasonable to restore sinus rhythm pharmacologically with ibutilide or direct-current cardioversion with postoperative AF**
  - **Category**: IIa
  - **Grade**: B

- **It is reasonable to administer antiarrhythmic medications to maintain sinus rhythm with recurrent or refractory postoperative AF**
  - **Category**: IIa
  - **Grade**: B

- **It is reasonable to administer antithrombotic medications for postoperative AF**
  - **Category**: IIa
  - **Grade**: B

- **It is reasonable to manage new-onset postoperative AF with rate control and anticoagulation with cardioversion if AF does not revert spontaneously to sinus rhythm during follow-up**
  - **Category**: IIa
  - **Grade**: C

- **Prophylactic sotalol may be considered for patients with AF risk following cardiac surgery**
  - **Category**: IIb
  - **Grade**: B

- **Colchicine may be considered postoperatively to reduce AF following cardiac surgery**
  - **Category**: IIb
  - **Grade**: B
5.4.2. Management of supraventricular arrhythmias and atrial fibrillation in the perioperative period

« The goal is usually ventricular rate control. Betablockers and calcium channel blockers are the drugs of choice. Betablockers have been shown to accelerate the conversion of atrial fibrillation to sinus rhythm in the ICU after non-cardiac surgery. »
### Rate Control

1. **Esmolol iv**  
   *Dosage*: 500 µg/kg over 1 min  
   *Maintenance*: 50-300 µg/kg/min  
   *Oral Shift*: bisoprolol 2.5-10 mg daily

2. **Diltiazem iv**  
   *Dosage*: 0.25 mg/kg over 2 min  
   *Maintenance*: 5-15 mg/h  
   *Oral Shift*: 120-360 mg daily

3. **Amiodarone iv/oral**  
   *Dosage*: 300 mg over 60 min  
   *Maintenance*: 10-50 mg/h  
   *Oral Shift*: 100-200 mg daily

4. **Digitalis**

### Rhythm Control

**Electrical cardioversion**

1. **Propafenone iv/oral**  
   *Dosage*: 2 mg/kg iv over 10 min  
   *Maintenance*: 450-600 mg daily

2. **Flecainide iv/oral**  
   *Dosage*: 2 mg/kg iv over 10 min  
   *Maintenance*: 200-300 mg daily

3. **Amiodarone iv/oral**  
   *Dosage*: 300 mg over 60 min  
   *Maintenance*: 10-50 mg/h

4. **Dronedarone, vernakalant**

**Prevention of recurrence with amiodarone or flecainide or propafenone**

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**AF** without hypotension before day 7 *(paroxysmal AF)*

**AF** with hypotension or prolonged beyond day 7 *(persistent AF)*
Anticoagulation is recommended if POAF lasts more than 48h, whatever the CHADS score and methods employed to convert to sinus rhythm (I-B)

- Warfarin is indicated (INR 2.0-3.0) and must be maintained during 4 weeks following return to sinus rhythm (I-B)

- New oral drugs should be considered (IIa-C)
Postoperative AF is frequent in the perioperative setting
Beta-blocker therapy is the only patient-related chronic factor that can be optimized by practitioners
Medical treatment of POAF often differs from international recommendations and could be markedly improved by written protocols
Selective Beta 1-blockers are the first line of therapy in both prevention and treatment of POAF