Rate Control

One year living with the 2010 EHRA/ESC atrial fibrillation guidelines: need for an update?
Madrid 27-06-2011

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Disclosures of H. Crijns

- consulting fees from Medacorp, Astra Zeneca, sanofi-aventis, Boehringer-Ingelheim, Merck
- research grants from Boehringer-Ingelheim, St. Jude Medical, Boston Scientific, Merck
- lecture fees from Astra Zeneca, sanofi-aventis, Boehringer-Ingelheim, Merck
Aims of Rate Control

- Decrease AF Symptoms
- Reduce risk of Cardiomyopathy
## Recommendations for rate and rhythm control of AF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate control should be the initial approach in elderly patients with AF and minor symptoms (EHRA score 1).</td>
<td>I</td>
<td>A</td>
<td>86-87, 90</td>
</tr>
<tr>
<td>Rate control should be continued throughout a rhythm control approach to ensure adequate control of the ventricular rate during recurrences of AF.</td>
<td>I</td>
<td>A</td>
<td>86</td>
</tr>
</tbody>
</table>
Among all rhythm control patients 54% were also on typical rate control drugs. 52% was on amiodarone or sotalol. Overall, 84% had some type of rate control drug.
Recommendations for acute rate control
## Recommendations for acute rate control

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref. &lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the acute setting in the absence of pre-excitation, i.v. administration of β-blockers or non-dihydropyridine calcium channel antagonists is recommended to slow the ventricular response to AF, exercising caution in patients with hypotension or heart failure.</td>
<td>I</td>
<td>A</td>
<td>100</td>
</tr>
</tbody>
</table>

<sup>a</sup> Class of recommendation.  
<sup>b</sup> Level of evidence.  
<sup>c</sup> Reference number.
## Recommendations for acute rate control

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<tr>
<td>In the acute setting, i.v. administration of digitalis or amiodarone is recommended to control the heart rate in patients with AF and concomitant heart failure, or in the setting of hypotension.</td>
<td>I</td>
<td>B</td>
<td>101</td>
</tr>
</tbody>
</table>

Acute rate control with **amiodarone** or **digitalis** in recent onset AF and hemodynamic compromise

**Table 1  Characteristics of patients**

<table>
<thead>
<tr>
<th></th>
<th>Digoxin group (n=24)</th>
<th>Amiodarone group (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>~ 1 mg in 4 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>70 ± 6</td>
<td>70 ± 8</td>
</tr>
<tr>
<td>Men:women</td>
<td>21:3</td>
<td>22:4</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>61 ± 11</td>
<td>60 ± 11</td>
</tr>
<tr>
<td>NYHA Fc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>8 (33%)</td>
<td>9 (35%)</td>
</tr>
<tr>
<td>III</td>
<td>5 (21%)</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>IV</td>
<td>11 (46%)</td>
<td>14 (54%)</td>
</tr>
<tr>
<td>Chamber size*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVIDs (mm)</td>
<td>44 ± 15</td>
<td>42 ± 13</td>
</tr>
<tr>
<td>LVIDd (mm)</td>
<td>61 ± 13</td>
<td>57 ± 11</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>49 ± 9</td>
<td>47 ± 10</td>
</tr>
<tr>
<td>Consecutive treatments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine/dobutamine</td>
<td>7 (29%)</td>
<td>10 (38%)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>11 (46%)</td>
<td>12 (46%)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>12 (50%)</td>
<td>12 (46%)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>5 (21%)</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>Ca blockers</td>
<td>2 (8%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>β-blockers</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Bronchodilators</td>
<td>3 (13%)</td>
<td>3 (11%)</td>
</tr>
</tbody>
</table>

**Conversion to SR at 24 hrs**
- Digoxin 71%
- Amiodarone 92%

**Figure 2** The changes in heart rates following administration of digoxin or amiodarone in patients who completed the study (24 h). The difference between both curves was tested with two-way analysis of variance (P=0.0001), followed by Student’s t-test for comparisons between both groups at specific observation periods. The amplitude of reduction was significantly different at 1 h until 8 h after medication. *P<0.05 between both groups; **P<0.01 between both groups.
Recommendations for long-term rate control
### Recommendations for long-term rate control

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</tr>
</thead>
<tbody>
<tr>
<td>Rate control using pharmacological agents (β-blockers, non-dihydropyridine calcium channel antagonists, digitalis, or a combination thereof) is recommended in patients with paroxysmal, persistent, or permanent AF. The choice of medication should be individualized and the dose modulated to avoid bradycardia.</td>
<td>I</td>
<td>B</td>
<td>100</td>
</tr>
</tbody>
</table>
Individualize the choice of rate control medication.
‘The optimal heart rate target during AF is unknown’

Portrait of Paul Gachet - attending physician of Vincent van Gogh

www.escardio.org/EHRA
Rate response in persistent AF patients with Normal and Reduced exercise tolerance

- 73 patients (33 women)
- 59 yrs (range 29-81)
- VHD 27 pts
- CAD 10 pts
- Hypertension 11 pts
- CHD/iCMP 11 pts
- lone AF 14 pts
- AF duration 28 months

- digoxin 47 pts
- verap/diltiazem 22 pts
- beta-blockers 8 pts
- amiodarone 10 pts
- ACE-i 17 pts

Optimal Rate Control

Rate control

No or tolerable symptoms

Accept lenient rate control

Symptoms

More strict rate control

Exercise test if excessive heart rate is anticipated during exercise

24 h ECG for safety

It is reasonable to initiate treatment with a lenient rate control protocol aimed at a resting heart rate <110 bpm.

IIa B

It is reasonable to adopt a stricter rate control strategy when symptoms persist or tachycardia/myopathy occurs, despite lenient rate control: resting heart rate <80 bpm and heart rate during moderate exercise <110 bpm. After achieving the strict heart rate target, a 24 h Holter monitor is recommended to assess safety.

IIa B

Van Gelder IC, et al. (RACE-2), NEJM 2010

www.escardio.org/EHRA
Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

Isabelle C. Van Gelder, M.D., Hessel F. Groenveld, M.D.,
Harry J.G.M. Crijns, M.D., Ype S. Tuininga, M.D., Jan G.P. Tijssen, Ph.D.,
A. Marco Alings, M.D., Hans L. Hillege, M.D., Johanna A. Bergsma-Kadijk, M.Sc.,
Jan H. Cornel, M.D., Otto Kamp, M.D., Raymond Tukkie, M.D.,
Hans A. Bosker, M.D., Dirk J. Van Veldhuisen, M.D.,
and Maarten P. Van den Berg, M.D., for the RACE II Investigators*
Permanent AF > 80 bpm

- lenient
  - HR < 110 bpm (12 lead ECG)

- strict
  - HR < 80 bpm (12 lead ECG)
    and
  - HR < 110 bpm (at 25% of maximal exercise)

After achieving rate control target:
Holter for safety

Van Gelder IC, et al. NEJM 2010
Heart rate during study

Van Gelder IC, New Engl J Med 2010
Cumulative incidence primary outcome

Cumulative Incidence (%)

0 10 20

No. At Risk

Strict 303 282 273 262 246 212 131
Lenient 311 298 290 285 255 218 138

Van Gelder IC, et al. NEJM 2010
Optimal Rate Control

Rate control

No or tolerable symptoms

Accept lenient rate control

Symptoms

More strict rate control

Exercise test if excessive heart rate is anticipated during exercise

24 h ECG for safety

HF with preserved ejection fraction
- May need strict rate control
- Diastolic dysfunction
- Dyspnea with minimal exercise & rapid resolution at rest
- Non-DHP Ca-antagonist or beta-blocker

Van Gelder IC, et al. RACE-2, NEJM 2010
Table 15  Drugs for rate control

<table>
<thead>
<tr>
<th></th>
<th>Intravenous administration</th>
<th>Usual oral maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-Blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoprolol CR/XL</td>
<td>2.5–5 mg</td>
<td>100–200 mg o.d. (ER)</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>N/A</td>
<td>2.5–10 mg o.d.</td>
</tr>
<tr>
<td>Atenolol</td>
<td>N/A</td>
<td>25–100 mg o.d.</td>
</tr>
<tr>
<td>Esmolol</td>
<td>10 mg</td>
<td>N/A</td>
</tr>
<tr>
<td>Propranolol</td>
<td>1 mg</td>
<td>10–40 mg t.i.d.</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>N/A</td>
<td>3.125–25 mg b.i.d.</td>
</tr>
<tr>
<td><strong>Non-dihydropyridine calcium channel antagonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil</td>
<td>5 mg</td>
<td>40 mg b.d. to 360 mg (ER) o.d.</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>N/A</td>
<td>60 mg t.d.s. to 360 mg (ER) o.d.</td>
</tr>
<tr>
<td><strong>Digitalis glycosides</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.5–1 mg</td>
<td>0.125 mg–0.5 mg o.d.</td>
</tr>
<tr>
<td>Digitoxin</td>
<td>0.4–0.6 mg</td>
<td>0.05 mg–0.1 mg o.d.</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>5 mg/kg in 1 h, and 50 mg/h maintenance</td>
<td>100 mg–200 mg o.d.</td>
</tr>
<tr>
<td>Dronedarone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>N/A</td>
<td>400 mg b.i.d.</td>
</tr>
</tbody>
</table>

Sotalol is not recommended for rate control
• Dronedarone if
  – insufficient RC with conventional RC drugs
  – side effects other RC drugs
  – not in permanent AF, wait for PALLAS study

95. Hohnloser, et al. (ATHENA trial), NEJM 2009
103. Davy JM, et al. (ERATO), Am Heart J 2008

www.escardio.org/EHRA
Recommendation for atrioventricular node ablation in AF patients

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<tr>
<td>Ablation of the AV node to control heart rate should be considered when the rate cannot be controlled with pharmacological agents and when AF cannot be prevented by antiarrhythmic therapy or is associated with intolerable side effects, and direct catheter-based or surgical ablation of AF is not indicated, has failed, or is rejected.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Elderly with palpitations and underlying CVD**
- Low success rhythm control
- Side effects of drugs
  - Bradycardia
  - Syncope
  - Proarrhythmia
- Why try all this?

Recommendation for atrioventricular node ablation in AF patients

Ablation of the AV node should be considered for CRT non-responders in whom AF prevents effective biventricular stimulation and amiodarone is ineffective or contraindicated.

AVJ ablation will be applied a lot …

No randomized study available

www.escardio.org/EHRA

Conclusion

Living with the 2010 ESC/EHRA guidelines for AF, need for an update?

- Very well presented
- Recommendations for rate control in AF are well in line with clinical practice
- Several opinion-based recommendations (LoE C) need further studies
  - Rate control for AF in HF-PEF
  - AF + CHF + CRT: RC drugs versus AV junction ablation
  - Early AV junction ablation in elderly with palpitations and underlying CVD after RC failed