Rate control was more cost effective than rhythm control in persistent atrial fibrillation


Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ IM/Ambulatory care ★★★★★★★ Internal medicine ★★★★★★★★

**Question**
In patients with persistent atrial fibrillation, is rate control more cost effective than rhythm control for reducing cardiovascular morbidity and mortality?

**METHODS**

**Design**: cost effectiveness analysis (from a societal perspective) of a randomised controlled trial (Rate Control versus Electrical cardioversion (RACE)).

**Allocation**: concealed.

**Blinding**: blinded (outcome assessors and monitoring committee).

**Follow up period**: mean 2.3 years.

**Setting**: 31 centres in the Netherlands.

**Patients**: 522 patients who had recurrent persistent atrial fibrillation or flutter, 1–2 electrical cardioversions during the previous 2 years, and no contraindications to oral anticoagulation. Exclusion criteria: arrhythmia lasting >1 year, New York Heart Association class IV heart failure, current or previous treatment with amiodarone, or use of a pacemaker.

**Intervention**: rate control (n = 256) or rhythm control (n = 266). Rate control included use of digitals, a non-dihydropyridine calcium channel blocker, and a β blocker, alone or in combination. Target resting heart rate was <100 beats/minute. Patients in the rhythm control group received serial electrical cardioversion and serial antiarrhythmic drugs using sotalol, 160–320 mg/day, as the first choice, followed by class IC antiarrhythmic drugs, with amiodarone used as the last choice.

**Outcomes**: incremental cost savings per avoided composite endpoint (ie, death from cardiovascular causes, heart failure, thromboembolic complications, bleeding, need for pacemaker implantation, or severe effects of antiarrhythmic drugs). Costs of care (including cardioversions, medications, outpatient visits, hospital admissions, general practitioner visits, thrombosis laboratory, professional help, informal care, and travel costs) (discounted at a rate of 4%) were estimated in 2000 European euros.

**Patient follow up**: 82% of patients (mean age 69 y, 63% men) were included in the intention to treat cost effectiveness analysis.

*See glossary.

**MAIN RESULTS**
The groups did not differ for the composite endpoint; however, rate control was more cost effective than rhythm control (table).

**CONCLUSION**
In patients with persistent atrial fibrillation, rate control was more cost effective than rhythm control for reducing cardiovascular morbidity and mortality.

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**Rate control vs rhythm control in persistent atrial fibrillation at mean 2.3 years**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Rate control</th>
<th>Rhythm control</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite endpoint</td>
<td>17.9%</td>
<td>21.2%</td>
<td>–3.7% (–11.2 to 3.9)</td>
</tr>
<tr>
<td>Cost effectiveness ratio</td>
<td>€7386</td>
<td>€8284</td>
<td>€24 944</td>
</tr>
</tbody>
</table>

*Composite endpoint = death from cardiovascular causes, heart failure, thromboembolic complications, bleeding, need for pacemaker implantation, or severe effects of antiarrhythmic drugs. CI defined in glossary.

†Difference not significant.

**Commentary**

The RACE trial by Hagens et al did not identify a strategy-dependent difference in efficacy outcomes between patients randomised to receive efforts to maintain sinus rhythm or continue with rate control. This negative result was also seen in the 4000 patient Atrial Fibrillation Follow up Investigation of Rhythm Management (AFFIRM) Study. In RACE, 36% of patients in the rhythm control group were in sinus rhythm by the time the study ended compared with 9% in the rate control group. Given the neutral intention to treat differences for mortality and health related quality of life (QOL), the well done study by Hagens et al assessed costs in a “straight up” comparison without the need to adjust costs per QOL improvement. As seen in a similar AFFIRM analysis, the rhythm control strategy was more expensive. Furthermore, the costs did not differ when data were analysed by efficacy (ie, who is, or is not, in sinus rhythm) as opposed to a strict intention to treat analysis. In an efficacy analysis, however, a weighted QOL approach may be needed because both the RACE and AFFIRM trials have shown a QOL benefit associated with achieving sinus rhythm in their respective efficacy analyses.

For the older RACE and AFFIRM types of patients, no clear QOL mortality, and now cost based reason exists to support a strategy aimed at maintaining sinus rhythm.

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