Rate-control vs. rhythm-control in patients with atrial fibrillation: a meta-analysis
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CRD summary
This review looked at two strategies for treating atrial fibrillation: rate control by means of drugs compared with rhythm control by cardioversion followed by prophylactic drugs. The authors found that rate control was associated with a lower risk of death or thromboembolic stroke. Although information on some aspects of the review process was missing, the conclusions are likely to be reliable.

Authors' objectives
To assess the effects of a rhythm control strategy versus a rate control strategy in the treatment of atrial fibrillation (AF).

Searching
BioMed Central, the Cochrane CENTRAL Register, Current Contents, MEDLINE and the meta Register of Controlled Trials were searched to January 2005; the search terms were given. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared the effects of pharmacological therapy, aimed at ventricular rate control, with those of pharmacological or electrophysiological methods of restoring and maintaining sinus rhythm were eligible for inclusion. In the included studies, rate control involved the use of diltiazem, beta-blockers, digitalis, calcium antagonists, or their combinations, or atrioventricular node ablation/modification with or without pacemaker implantation. Rhythm control consisted of electrical or pharmacological cardioversion, followed by prophylaxis with amiodarone, sotalol, class 1 anti-arrhythmics, flecainide, propafenone, disopyramide, moricizine, procainamide, quinidine, sotalol, or their combination.

Participants included in the review
Studies on people with first or recurrent AF were eligible for inclusion. Any studies where there were severe imbalances in major baseline characteristics between the study groups were excluded. Details of exclusion criteria for the included studies were given in the paper. These included NYHA class IV heart failure, recent myocardial infarction, valvular disease, previous pacemaker, sick sinus syndrome, bundle branch block, Wolf Parkinson White syndrome, thyroid dysfunction, pregnancy, contraindications to anti-arrhythmics or anticoagulants, and so on. The mean ages of the participants ranged from 60.8 to 69.7 years, and between 61.3 and 73% of the participants were men.

Outcomes assessed in the review
Only studies that analysed data on an intention-to-treat basis were eligible for inclusion. Those studies where less than 80% of participants were followed-up were excluded. Follow-up in the included studies ranged from 1 to 3.5 years. The outcomes of interest were all-cause death, thromboembolic stroke, a combined outcome of death or thromboembolic stroke, major bleeds (intracranial or extracranial) and systemic embolism. Definitions of these outcomes were taken as defined in the individual studies.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Quality was assessed using methods suggested in the Cochrane Handbook. The studies were graded A (highest) to C
The authors did not state how many reviewers performed the quality assessment.

Data extraction

Two independent reviewers extracted the data. Any differences were resolved by consensus. Published reviews were searched for data not available in the original articles.

Methods of synthesis

How were the studies combined?

Pooled odds ratios (ORs), with 95% confidence intervals (CIs), were calculated using a random-effects model. Pooled random-effects risk differences were calculated and used to estimate power and the numbers-needed-to-treat per year (NNT), with 95% CI. Funnel plots were used to check the possibility of publication bias.

How were differences between studies investigated?

Heterogeneity was assessed using the Cochran Q test and I² statistic. Subgroup analyses were conducted according to mean age and mean length of follow-up.

Results of the review

Five RCTs (5,239 participants) were included.

A rate control strategy, compared with a rhythm control strategy, was associated with a significantly lower risk for the combined outcome of death or thromboembolic stroke (OR 0.85, 95% CI: 0.73, 0.98, P=0.03) and a non significant reduction in death (OR 0.87, 95% CI: 0.74, 1.02, P=0.09) and thromboembolic stroke (OR 0.8, 95% CI: 0.6, 1.07). The NNT was 50 in order to avoid one death and 100 in order to avoid one thromboembolic stroke.

Both strategies resulted in similar rates of major bleeds (OR 1.12, 95% CI: 0.82, 1.53, P=0.47), intracranial bleeds (OR 1.16, 95% CI: 0.64, 2.10, P=0.6), extracranial bleeds (OR 1.09, 95% CI: 0.94, 1.41, P=0.5) and systemic embolism (OR 0.93, 95% CI: 0.43, 2.02, P=0.90).

The rate control strategy was associated with a significant decrease in the risk of the combined end point in studies where the mean age was 65 years or older (3 trials; OR 0.86, 95% CI: 0.74, 0.99, P=0.04; NNT 50), and in studies where the mean age was 65 years or older and the mean follow-up was at least 20 months (2 trials; OR 0.85, 95% CI: 0.74, 0.99, P=0.04; NNT 50). In studies with a mean follow-up of less than 20 months, there was a lower risk of thromboembolic stroke with the rate control strategy (3 trials; OR 0.18, 95% CI: 0.04, 0.82, P=0.03; NNT 33). There was no significant increase in major bleeds.

No significant heterogeneity was found in any of the analyses. No relevant inconsistency was found (I² less than 25%), apart from thromboembolic stroke with showed moderate inconsistency (I² greater than 50%)

Funnel plots suggested the possibility of publication bias.

Authors' conclusions

An initial rate control strategy is associated with a better prognosis than a rhythm control strategy.

CRD commentary

The inclusion criteria for this review were clearly stated. Several relevant databases were searched without language restrictions, but the search for unpublished studies was somewhat limited. The methods by which studies were selected for the review were not described, and although quality was assessed the authors did not describe this process. It is possible for error or bias to be introduced into a review during these stages. The statistical pooling of data was appropriate, heterogeneity was assessed, and useful subgroup analyses were performed to look at differences between the studies. The authors' conclusions are supported by the data in the review, although the finding cannot be extrapolated to patients younger than 60 years and some other important groups. Another analysis of this topic came to...
similar conclusions although it reported the outcomes rather differently (see Other Publications of Related Interest).

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: Any new therapeutic strategies should be tested against rate control strategies.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.