Slowing down the heart rate in permanent atrial fibrillation

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This editorial refers to ‘Calcium channel blockers improve exercise capacity and reduce N-terminal Pro-B-type natriuretic peptide levels compared with beta-blockers in patients with permanent atrial fibrillation1’, by S.R. Ulimoen et al., on page 517

Ventricular rate control for atrial fibrillation (AF) is almost as old as the first records of the disease. While digitalis has been the focus of classical observations, this substance is currently losing relevance as a rate-controlling drug due to its side effects.8 A substudy of RATAF which has been conducted by the study authors of this paper, showed that calcium channel blockers work favourably in terms of peak oxygen uptake compared with beta-blockers.9 This is an important and novel finding supporting the use of calcium channel blockers in patients with permanent AF and no or minimal structural heart disease. In this study, patients (aged a median of 71 years) were treated with four different rate-controlling drug regimens in a randomized and investigator-blinded order, demonstrating superiority of diltiazem or verapamil treatment. In terms of patient characteristics, only 41.7% of patients in this trial had arterial hypertension. This is unusually low for an AF population. For instance, the prevalence of hypertension in a recent large trial of dronedarone in patients with permanent AF was 84.6%.2 Nevertheless, patients had mildly elevated mean blood pressure and near normal systolic ejection fraction (EF), providing information on the type of patient included in the trial. With this study, there is now evidence for first-line use of calcium channel blockers to control ventricular rate in patients with no or minimal structural heart disease (Figure 1A).

Patients with relevant structural heart disease in terms of ischaemic cardiomyopathy or HF were excluded from RATAF.3 It is nevertheless important to look at a target heart rate and drugs for rate control for such patients as rate control is an important treatment option in HF patients.4 AF occurs frequently with HF or underlying ischaemic heart disease, and even more so with worse functional class.10 Beta-blocker therapy is established and clearly beneficial in patients with ischaemic heart disease or systolic HF.11 Accordingly, the question of the type of drug to be used in permanent AF with HF will remain controversial until addressed in a prospective randomized trial. It can be speculated that calcium channel antagonists may be inferior to beta-blockers in HF.

There is good evidence that the target resting heart rate should be <110 b.p.m. in patients with permanent AF (excluding those with unstable HF, recent cardiac surgery, or stroke).12 In the ‘Rate-control Efficacy in Permanent Atrial Fibrillation: a Comparison between Lenient versus Strict Rate-control II’ (RACE-II) study, patients with reduced systolic left ventricular function (EF <40%) were only a minority (15.1% of 614 patients). However, HF defined as New York Heart Association (NYHA) functional class >II or EF <40% or previous HF hospitalization was present in 47%. Using this definition, a recent post-hoc analysis of RACE-II demonstrated a similar

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References


Outcome of lenient rate control in stable HF.13 In order to interpret these results in the context of the present data, the high prevalence of beta-blocker therapy (65.6% alone or in combination) in RACE-II has to be kept in mind (Figure 1B).

Rate control therapy in permanent AF may need to be tailored to the type of underlying cardiac disease. It is necessary to differentiate between various target heart rates and means to achieve these in specific patient populations. For patients with no or minimal structural heart disease, the present study suggests that calcium channel blockers should be used as first-line treatment. There is a need for trials on drugs and target heart rates for patients with permanent AF and relevant structural heart disease.

Figure 1 This schematic represents an approach to rate control in haemodynamically stable patients with permanent AF. Lenient rate control is defined as <110 b.p.m. at rest. Drugs suggested for first-line use are green, and alternative (or additional) drugs are yellow. (A) It is reasonable to initiate lenient rate control with a calcium channel blocker in patients with permanent AF with no or minimal structural disease. Should symptoms persist, a stricter rate control approach or use of an alternative drug may be indicated. (B) Patients with relevant structural heart disease [heart failure patients with preserved or reduced systolic left ventricular function (ejection fraction <40%) or patients with ischaemic heart disease] may potentially benefit more from initial beta-blocker treatment.