



# Atrial fibrillation: rhythm versus rate control

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*Consideration should be given to whether rhythm control or rate control is best when treating patients with atrial fibrillation.*

**A**trial fibrillation (AF) is an emerging cardiovascular epidemic and imposes a substantial burden of morbidity, mortality and economic cost on Australian society. The incidence and prevalence of AF increases with age, with a prevalence of 8% in people older than 80 years.<sup>1-3</sup> The age-adjusted incidence increased significantly from the 1960s to the 1980s, and increased further from 1980 to 2000.<sup>4,5</sup> The lifetime risk of AF in patients over the age of 40 years is 25%.<sup>6</sup>

AF is a chronic disease associated with symptoms of palpitations, dyspnoea and fatigue, and is an important cause of heart failure and stroke.<sup>7,8</sup> The presence of AF confers a twofold increased risk of death across all age groups.<sup>9</sup>

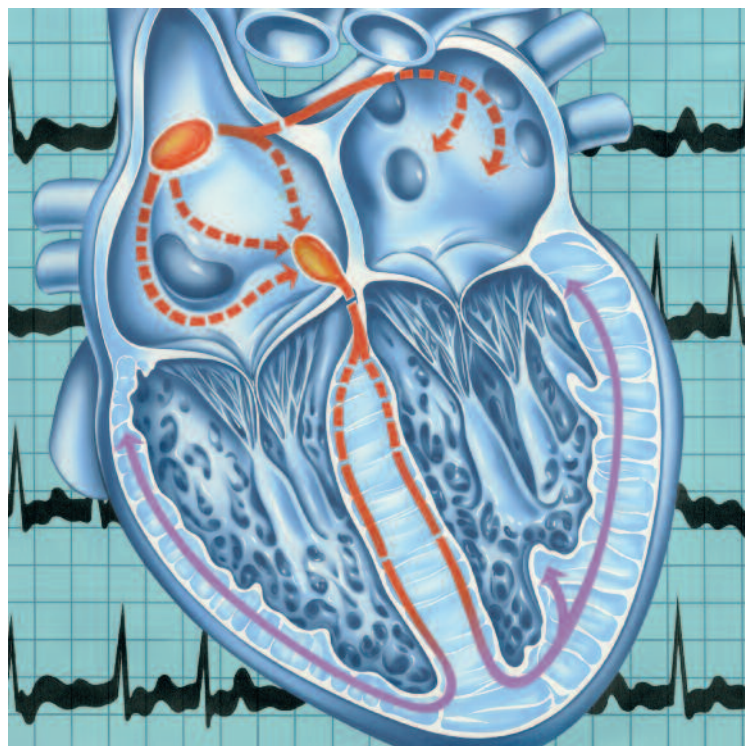
The clinician must consider two important factors in the management of patients with AF:

- rhythm versus rate control
- stroke prophylaxis.

The aim of the present review is to address the issues surrounding sinus rhythm restoration as opposed to accepting AF and controlling ventricular rate.

## Rhythm control

The proposed benefits of restoring sinus rhythm include symptom resolution, reduction in stroke risk and survival advantage. The tools currently available for rhythm control include medication, electrical cardioversion and catheter ablation. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study was a landmark multicentre study that provided an evidence base for guiding decision-making in minimally symptomatic or asymptomatic older patients with AF.<sup>10</sup> This study randomised 4060 patients to a rate-control versus rhythm-control strategy. Treatment for the rhythm-control group largely consisted of electrical cardioversion and pharmacotherapy (amiodarone in 63% and sotalol in 41%). The rate-control group received pharmacotherapy with rate-controlling drugs such as  $\beta$ -blockers. There was no significant difference in mortality between the pharmacological rate-control and rhythm-control arms; catheter ablation was not included due to its relative novelty at the time the trial was conducted.<sup>10</sup> However,



## Key points

- The management of patients with atrial fibrillation (AF) may be considered at two levels: rhythm control versus rate control; and the protection against stroke and embolic events.
- Rhythm control may be achieved through antiarrhythmic drugs such as flecainide, sotalol or amiodarone; however, it may be limited by efficacy, tolerance and proarrhythmia.
- Catheter ablation for AF may provide long-term freedom from AF in the absence of antiarrhythmic medication and is most effective in patients with paroxysmal AF in the absence of structural heart disease.
- Rate control may be achieved through atrioventricular nodal blocking medications or pacemaker implant followed by atrioventricular node ablation.

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within the AFFIRM study, subgroup analysis demonstrated a significant reduction in mortality in the rhythm-control group who maintained sinus rhythm, with the overall benefits offset by the detrimental effects of pharmacotherapy.<sup>11</sup>

Antiarrhythmic drugs have limited efficacy in maintaining sinus rhythm, and introduce a risk of proarrhythmia particularly in patients with heart failure. Currently available medications include sotalol, flecainide and amiodarone. Sotalol use may be limited by the presence of fatigue, diarrhoea, bradycardia or QT prolongation. Flecainide is of equivalent efficacy and its use may be considered following the exclusion of structural heart disease by echocardiography and coronary ischaemia. In older patients, an exercise test should be considered before commencing flecainide. Amiodarone is the most effective agent in maintaining sinus rhythm, but its use is limited by potential toxicities. Novel antiarrhythmics, such as dronedarone, show promise; however, safety concerns remain about hepatic toxicity and increased mortality in patients with symptomatic heart failure and persistent AF populations.

The pulmonary vein isolation technique has evolved after the landmark observation by Haissaguerre and colleagues, recognising the pulmonary veins as the responsible triggers for the majority of AF episodes.<sup>12</sup> Catheter ablation is performed via a femoral venous approach and involves double transseptal access to deliver encircling ablation lesions to the antral aspect of the pulmonary veins with the endpoint of electrical isolation. Catheter ablation should be considered in patients with recurrent symptomatic AF despite use of antiarrhythmic medication. It is more effective at restoring sinus rhythm than pharmacotherapy; however, it is invasive, time-consuming, may need to be repeated and can be associated with significant complications. The best results are achieved in patients with paroxysmal AF in the absence of structural heart disease. Patients with persistent AF or structural heart disease may require more extensive atrial ablation or substrate modification to improve procedural outcomes.

Patient characteristics are important in guiding the decision process and include the presence of symptoms, patient age, comorbidities, reversible factors, duration of AF, presence of structural heart disease and left atrial size. Generally an attempt at rhythm control should be considered in symptomatic patients and when AF is associated with a significant decline in ventricular function. In contrast, older asymptomatic patients with significant left atrial enlargement may be better managed by rate control.

### Rate control

Ventricular rate control is effective in reducing symptoms associated with AF. This generally involves the use of atrioventricular (AV) nodal blocking drugs to slow the penetration of fibrillatory impulses to the ventricle. The principle medications include  $\beta$ -blockers, calcium channel blockers and digoxin. Amiodarone and sotalol also possess AV nodal slowing properties, but they are better considered as rhythm-control agents. If ventricular rate control cannot be achieved by pharmacotherapy then pacemaker implant followed by AV node ablation is an option. An ablate and pace strategy is associated with

improvements in quality of life, exercise duration and ventricular function.

The heart rate target for ventricular rate control has been determined as being arbitrarily equivalent to sinus rhythm. It can also be determined by physician experience of the heart rate needed to achieve amelioration of symptoms and avoidance of tachycardia-mediated cardiomyopathy. The definition of adequate rate control in the AFFIRM study was a resting heart rate of less than 80 bpm and a heart rate of less than 110 bpm during a six-minute walk test. However, subgroup analysis within the rate-control arm did not demonstrate a survival advantage in patients with lower average heart rates. This uncertainty prompted the initiative of the multi-centre Rate Control Efficacy in Permanent Atrial Fibrillation (RACE) II trial, which randomised 614 patients with permanent AF to either a lenient (resting heart rate of <110 bpm) or strict (heart rate of <80 bpm at rest and <110 bpm with moderate exercise) heart rate control strategy.<sup>13</sup> Lenient rate control was as effective as strict rate control in patients with equivalent qualities of life and was easier to achieve. Although intensive rate control to achieve a specified heart rate 'number' is probably not necessary, there are important caveats to the interpretation of this study. Patients with tachycardia-mediated cardiomyopathy and more severe symptoms were most likely underrepresented in this study.

### Conclusion

Patient symptoms are important in guiding the physician's choice between rate control and rhythm control in patients with AF. Randomised clinical trials have not demonstrated a survival advantage for rhythm control or strict ventricular rate control. Stroke prophylaxis must be considered in all patients with AF. **CT**

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