Physiologic pacing: where pacing mode selection reflects the indication

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Results of recent trials suggest that in patients with left ventricular dysfunction, interventricular synchrony is possibly more important than atrioventricular synchrony. In patients with AV block and conduction system disease, alternatives to right ventricular apical pacing are therefore needed.

In this issue of *Heart*, Kristensen and colleagues report that AAIR pacing reduces the development of atrial fibrillation compared to DDDR pacing in patients with sinus node dysfunction.1 Their study design focuses attention on right ventricular pacing as the potential cause of atrial structural remodelling that, in turn, leads to an increased risk of atrial fibrillation. The results of this study have important implications for rational pacemaker selection.

Five randomised trials comparing “physiologic” pacing to ventricular pacing, involving over 5000 patients, have not shown a reduction in mortality, stroke, or heart failure.7 Although this was a small study, and had a much higher rate of stroke and mortality than the other randomised trials, it raised suspicion that atrial pacing and dual chamber pacing are not equally “physiologic”.

Both atrial and dual chamber pacing preserve atrioventricular (AV) synchrony and permit atrial stimulation. However, dual chamber pacing frequently results in right ventricular stimulation, which in patients with sinus node dysfunction is often unnecessary. The use of dual chamber pacing in these patients may result in a more physiologic AV delay but at the price of inducing asynchronous ventricular activation.

Patients with isolated sinus node disease usually have a normal QRS complex; however, with right ventricular pacing, they develop a left bundle branch type QRS complex with sequential activation of the right and left ventricles. This asynchronous activation pattern reduces cardiac output compared to normal conduction over the His-Purkinje system.9

**INTERVENTRICAL SYNCHRONY**

The clinical importance of interventricular synchrony is beginning to be clarified with the results of the DAVID8 and COMPANION10 trials in patients with left ventricular dysfunction. The DAVID trial was designed to show a benefit from the use of dual chamber defibrillators in patients with heart failure, of whom 82% had normal baseline QRS durations. The use of dual chamber defibrillators did produce a shorter AV delay, but was associated with an increase in the percentage of time that the ventricle was paced from 2.9% to 55.7%, and an unexpected, significant increase in the outcome of death or hospitalisation for heart failure.9

The COMPANION trial enrolled patients with heart failure and a prolonged QRS duration that were randomised to one of three groups: optimal medical treatment, optimal medical treatment plus a biventricular pacemaker, or optimal medical treatment plus a biventricular defibrillator.10 In these patients, simultaneous pacing of the right and left ventricles (biventricular pacing) has been shown to restore a more normal ventricular activation sequence and improve the efficiency of the heart.11 In COMPANION, patients with biventricular pacemakers or defibrillators had a 20% reduction in cardiac mortality or admission for heart failure. Mortality was reduced by 40% in patients receiving biventricular defibrillators and by 15% in patients receiving biventricular pacemakers. Thus, analysis of the results of DAVID and COMPANION suggest that in patients with left ventricular dysfunction, interventricular synchrony is possibly more important than AV synchrony.

Post-hoc analysis of the MOST trial also points to the importance of ventricular synchrony in patients with standard bradycardic indications for pacing. This study compared dual chamber versus ventricular pacing in patients with sinus node dysfunction, and found no reduction in stroke-free survival with dual chamber pacing.12 Subsequent analysis demonstrated an increased incidence of atrial fibrillation and heart failure hospitalisations with increasing frequency of ventricular stimulation by the pacemaker.12 When empirically programmed AV synchrony was maintained, ventricular asynchrony induced by ventricular pacing increased the risk of heart failure and atrial fibrillation.

**Abbreviations:** AV, atrioventricular; COMPANION, comparison of medical therapy, pacing and defibrillation in heart failure; DAVID, dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator; MOST, mode selection trial

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RIGHT VENTRICULAR PACING LEADS TO ADVERSE OUTCOMES

The current study by Kristensen and colleagues\(^1\) clearly supports the concept that right ventricular pacing leads to adverse outcomes. Patients were randomised to one of three pacing modes, which resulted in different frequencies of ventricular pacing: AAI (0%), DDDR-long AV delay (17%), and DDDR-short AV delay (90%). There was a corresponding, significant increase in atrial fibrillation: AAI (3%/year), DDDR-long (8.2%/year), and DDDR-short (11.7%/year), and a trend for fewer thromboembolic events: AAI (1.9%/year), DDDR-long (2.2%/year), and DDDR-short (4.0%/year).\(^3\)

Previous randomised trials have already shown a 20% reduction in atrial fibrillation using dual chamber pacing compared to ventricular pacing.\(^2\)\(^3\) The loss of AV synchrony with ventricular pacing has been shown to cause left atrial enlargement,\(^13\) which is a known risk factor for the development of atrial fibrillation.\(^14\) However, the study by Kristensen and colleagues\(^1\) suggests that even in patients with preserved AV synchrony, interventricular synchrony remains important for the development of atrial fibrillation. This also appears to be mediated through left atrial enlargement, as they found a significant increase in left atrial size over time in patients randomised to DDDR-long or DDDR-short, but not AAI.\(^2\)

Despite showing a reduction in atrial fibrillation, the two largest randomised trials comparing dual chamber to ventricular pacing did not show a reduction in thromboembolic events.\(^2\)\(^3\) This may reflect the low rate of stroke (3.3% over 3–5 years) in these trials, or their relatively short follow up. Alternatively, the use of dual chamber rather than atrial pacing may have minimised the reduction in atrial fibrillation because of the apparent detrimental effects of right ventricular stimulation.

EMBOLIC RISK

The embolic risk of patients in the study by Kristensen and colleagues\(^1\) was much higher than previous pacing trials; however, it is likely comparable when one considers that this is a much smaller study with wide confidence intervals for the estimated risk of stroke. Nevertheless, it illustrates why measures to reduce atrial fibrillation and stroke in this group are particularly needed. Although the methodology used to diagnose atrial fibrillation was insensitive, 12 of the 14 patients experiencing stroke had a history of the tachycardia-bradycardia syndrome, and two had atrial fibrillation documented during follow up. Thus, atrial fibrillation preceded stroke in the majority of patients. However, only one of 14 patients who had a stroke were receiving warfarin at the time of their event. This may explain the high rate of stroke in this trial, but it also underscores the potential rewards of the prevention of atrial fibrillation and atrial enlargement through pacing mode selection.

Despite this potential advantage, the use of atrial pacing has been limited, by concern about the development of AV block. However, the authors have shown that with appropriate patient selection, this risk is less than 2%/year over a follow up of 4.6 years.\(^8\) This small risk is more than offset by the reduction in atrial fibrillation and stroke.

The results of this study support the logic of choosing a mode of pacing which specifically targets the underlying bradyarrhythmia. In the case of sinus node dysfunction, this means atrial pacing, with an effort to avoid ventricular stimulation. In patients with AV block and conduction system disease, alternatives to right ventricular apical pacing are needed to address the issue of ventricular synchrony. Clearly, the conventional dual chamber pacemaker is not the pinnacle of physiologic pacing, and we must continue to refine this technology.

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