Editorial

Heart rate, regularity, and synchronicity in heart failure: a tale of three brothers

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This editorial refers to 'Functional impact of rate irregularity in patients with heart failure and atrial fibrillation receiving cardiac resynchronization therapy'† by V. Melenovsky et al., on page 705, and 'Comparative assessment of right, left and biventricular pacing in patients with permanent atrial fibrillation'‡ by M. Brignole et al., on page 712.

The electrical consequences of heart failure and their impact on disease progression have frequently been underestimated. It is long known that a significant percentage of heart failure patients develop disease of the conduction system and atrial fibrillation (AF). Conduction disturbances are not only a marker of disease progression but may lead to further haemodynamic deterioration, thus representing another vicious circle in the heart failure syndrome. It has also been recognized that AF may impair haemodynamics by the loss of atrial contribution to stroke volume, by reducing filling time especially if the ventricular response to AF is uncontrolled and by rate irregularity itself.¹ In fact, AF with rapid ventricular conduction may ultimately lead to left ventricular (LV) dysfunction, i.e. to a 'tachycardiomyopathy', which can be reversed by controlling the ventricular rate, e.g. by atrioventricular (AV) node ablation with consequent pacemaker implantation.² The elegant study from Melenovsky et al.³ shows that there are two synergistic effects of this procedure in heart failure patients: rate control and rate regularization. However, the positive effect of rate regularization is only operative at high heart rates. This may be another explanation for the negative results of studies comparing rate with rhythm control⁴ and may prove the common belief untrue that heart failure patients benefit more from sinus restoration compared with less sick patients. In fact, there are many good clinical reasons to leave a heart failure patient in AF: the recurrence rate after cardioversion is high, the drugs needed to stabilize sinus rhythm may be pro-arrhythmic especially in heart failure, and there is apparently no clear haemodynamic benefit of re-establishing sinus rhythm as long as the ventricular rate during AF is well controlled.

Melenovsky et al.³ used biventricular (BiV) pacing in order to reduce the influence of pacing-inducing ventricular dyssynchrony on haemodynamics. However, right ventricular (RV) apical pacing is usually used after AV node ablation. In the era of cardiac resynchronization therapy (CRT), we need to take a new look at this approach. With chronic RV pacing, the ventricular activation sequence resembles left bundle branch block, i.e. the RV is activated before the left ventricle (interventricular dyssynchrony) and the LV septum before the LV free wall (intraventricular dyssynchrony). Dyssynchronous ventricular activation leads to local differences in myocardial loading conditions which has detrimental effects on LV function: experimental and clinical evidence shows a reduction in stroke volume, an inhomogeneous distribution of perfusion and metabolism,⁵ and regional differences in protein expression.⁶ Therefore, patients with heart failure undergoing AV node ablation may pay a price for the procedure. This danger is real as data from several trials in patients with preserved sinus rhythm indicate that chronic RV pacing increases the likelihood of hospitalization for heart failure or death.⁷ However, it is not clear whether BiV pacing significantly improves patients after AV node ablation for chronic AF. This is highlighted by the OPSITE study presented by Brignole et al.⁸ In their study there was no significant improvement with LV pacing compared with RV pacing and only modest benefit with BiV pacing after AV node ablation for drug-refractory AF. This result is somewhat disappointing but in agreement with previous data from the MUSTIC trial.

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which failed to show any significant improvement of BiV pacing compared with RV pacing using an intention-to-treat analysis.\(^9\) The recently presented PAVE (‘Post AV node ablation Evaluation’) trial\(^10\) randomized 252 patients with chronic AF, moderate heart failure, only mildly reduced LV function, and normal baseline QRS width who underwent AV node ablation for drug-refractory AF with rapid ventricular conduction to RV vs. BiV stimulation. After 6 months, there was a significant improvement in maximum oxygen uptake and quality of life with BiV compared with RV pacing. Patients in the RV-paced group surprisingly showed no significant improvement in \(V_{\text{O2,\text{max}}}\) compared with baseline as opposed to those in the BiV group. Until the final publication of the PAVE study, it is hard to compare it with the OPSITE trial. However, the effect was only modest in both trials and the question arises whether the minor functional improvement observed justifies a significantly more complex implantation procedure. The failure rate of LV lead implantation with currently available technology is \(\sim 10\%\), complications are more frequent and radiation exposure higher. Given the risk of coronary sinus lead dislodgements, LV-only pacing can not be recommended for pacemaker-dependent patients. The superiority of BiV over LV pacing reported in the OPSITE trial is in agreement with earlier, noncontrolled trials that were in favour of BiV pacing in AF patients.\(^11\) The observation that in sinus rhythm patients, LV pacing is at least equivalent to BV pacing has been explained by fusion of paced activation with intrinsic conduction via the intact right bundle branch. Because of the lack of a triggering atrial beat, this fusion cannot be achieved during AF. Thus, LV pacing may simply replace one dyssynchrony by another in this situation. But why has it been so difficult to demonstrate clinical benefit of BiV pacing compared with RV pacing after AV nodal ablation? Both in the PAVE and OPSITE trials, patients who had a lesser degree of heart failure compared with earlier CRT trials were included. In these patients, substantial clinical improvement may be achieved by rate control and regularization alone and it may be difficult to prove additional benefit by synchronizing LV activation. Moreover, it has been previously shown that the effect of CRT is also smaller in sinus rhythm patients with less advanced heart failure.\(^12\) The apparent lack of response to BiV pacing in patients with more advanced heart failure in the OPSITE trial should be interpreted with caution because it is a subanalysis in a small number of patients. A large trial with hard endpoints in heart failure patients comparing RV with BiV pacing after AV node ablation would be desirable. It is doubtful whether such a trial will be done because current CRT guidelines do not differentiate between sinus rhythm and AF patients and many physicians feel that implantation of a BiV device is justified in an AF patient who fulfills all other accepted criteria for CRT. This opinion is supported by studies demonstrating significant improvement in AF patients with conventional dual-chamber pacemakers that are upgraded to a BiV device.\(^13\)

In summary, on the basis of the two studies, the most important goal in AF therapy seems to be adequate rate control. Despite the theoretical considerations favouring BiV pacing after AV node ablation, available data do not justify routine BiV pacemaker implantation in this setting at present. Additional criteria to evaluate mechanical dyssynchrony such as tissue Doppler echocardiography or strain rate imaging may help us to identify the patients who show clear benefit from BiV pacing in this population. Despite the fact that Brignole’s study and the data from PAVE seem to indicate that patients with lack of baseline dyssynchrony and well-preserved LV function seem to benefit more from this approach, it may be wise to restrict BiV pacing to those patients who fulfill all other criteria for an accepted CRT indication until more solid data are available.

References