Heart rates in cardiac resynchronization: the art of optimal device programming

Alexander H. Maass* and Dirk J. van Veldhuisen

Department of Cardiology, University Medical Center Groningen, University of Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands

Received 28 October 2010; accepted after revision 11 November 2010; online publish-ahead-of-print 24 December 2010

This editorial refers to ‘Acute haemodynamic effects of increase in paced heart rate in heart failure patients recorded with an implantable haemodynamic monitor’ by M. Stählberg et al., on page 237.

Cardiac resynchronization therapy (CRT) has become the standard therapy for patients with decreased systolic left ventricular (LV) function with the indication extending most recently also to the less symptomatic patients. Implantation rates in Europe have steadily increased with a clear difference between countries. Objective response rates with significant reverse LV remodelling have remained at 50–70% depending on the definition. Reverse remodelling, however, is the pre-requisite for decreasing hard clinical endpoints. Optimal delivery of CRT rests on three legs: (i) patient selection, (ii) optimal implantation, and (iii) optimal device programming. Although the first and, to lesser extent, the second point have been extensively studied, optimal device programming remains obscure, mostly due to time-consuming procedures for optimization and complex interdependence of the several parameters. Randomized studies are scarce and evidence is only available for optimal atrioventricular (AV) intervals. Heart rates have become critical in heart failure patients with the goal to ‘go as low as possible’. If the heart rate per se needs to be low or if this is merely a surrogate for efficient suppression of neurohormonal activation remains controversial even though more data with the selective sinus node inhibitor ivabradine become available. Furthermore, it is unclear what optimal heart rates at exercise are. Chronotropic incompetence has been associated with adverse outcome in heart failure patients.

The optimal heart rates in CRT patients have not been systematically studied. Stählberg et al. present data on the effect of intrinsic or paced increase in heart rates in patients with ambulatory measurements of right ventricle (RV) haemodynamics. Even though this is a small non-randomized study, it adds important information through the methodology that allows haemodynamic measurements via an implanted haemodynamic monitor. The authors were able to demonstrate a positive force frequency relationship (FFR) with increments in paced heart rate. They tested higher heart rates at rest and also performed an exercise test to put these results into a physiological perspective. Haemodynamic measurements were restricted to the RV. If dp/dt in the RV also reflects LV, contractility in heart failure patients remains obscure. Cardiac output measurements and filling pressures, however, can be reliably tested and give information on LV function. This mechanistic study can give rise to clinical studies further investigating haemodynamics, metabolism, and clinical outcome with different heart rates.

What is known about programming of heart rates in CRT patients? Obviously, intrinsic heart rates should not exceed the programmed upper rate of the device to prevent loss of biventricular stimulation at this moment. We have previously shown that if this occurrence of heart rates above the upper tracking or sensor rates at submaximal exercise is associated with non-response to CRT. The importance of chronotropic competence is still controversial. There is conflicting evidence about the influence of atrial pacing on cardiac output. Bernheim et al. have demonstrated better diastolic filling and myocardial performance with VDD vs. DDD pacing. In contrast, Gold et al. showed increased contractility in patients with atrial pacing at optimal AV delays that were significantly longer with atrial pacing than intrinsic conduction. It has further been shown that patients with the highest percentage of atrial pacing have the highest incidence of atrial fibrillation. New-onset atrial fibrillation in turn has been associated with non-response to CRT. Increase in heart rate could be offset by a decrease in stroke volume that can be demonstrated at higher heart rates. Atrial pacing can induce or enhance atrial dysynchrony. We have shown that chronotropic response is associated with non-response to CRT. A causal relationship remains obscure in the absence of a randomized study demonstrating the superiority of a rate sensor modus in chronotropically incompetent patients. Smaller studies, however, point at improvements with atrial pacing in these patients. Tse et al. demonstrated increased performance on cardiopulmonary exercise testing with rate adaptive pacing in chronotropically incompetent patients. Chronotropic
incompetence could on the other hand be a surrogate marker of irreversibility of LV dysfunction such as has been demonstrated for contractile reserve.14 There are still patients who fulfil all positive predictors for response to CRT, such as broad QRS with a left bundle branch block and non-ischaeimic cardiomyopathy but still do not respond to resynchronization. To identify these patients obviously has socioeconomic implications as well as for the individual patients as they undergo a futile treatment with risk for significant complications.

Optimal atrial pacing is dependent on a good rate sensor. As of yet a physiological sensor is not present in CRT devices. There is controversy over what the optimal sensor would be. Physiological sensors that could be incorporated are a QT-interval sensor, peak endocardial acceleration, or closed loop stimulation. The latter two measurements can also be used for the optimization of device timing such as AV and VV intervals. How to programme these intervals at higher heart rates is also an area of controversy. In contrast to what happens in patients without heart failure where physiologically intrinsic PR intervals shorten, in resynchronization, AV delays might even have to be programmed longer if there is atrial pacing.15 In a more comprehensive analysis, AV delays at higher heart rates need to be individualized with longer delays in some patients, shorter delays in others, and patients in which the delays can be kept constant.16

Patients with persistent or permanent atrial fibrillation are also dependent on optimal heart rate programming. In patients without AV node ablation, programming is tailored to ensure biventricular pacing. We have shown that this needs to be present at rest but also at exercise reflecting activities of daily life.8 The group of patients with AF after AV node ablation is obviously chronotropically incompetent and depends on good sensor programming even though there is no evidence supporting this hypothesis. What the optimal maximal sensor heart rate is remains obscure. Further studies are needed proving the optimal heart rate in terms of haemodynamics but also metabolism as there needs to be an optimal balance of increase in cardiac output without offset by a lack of energy delivery.

A possible extension of CRT to patients with LV function >35%17 or even those with heart failure with preserved ejection fraction (EF) has recently been suggested18 as they have an almost similarly poor prognosis as those with a low LVEF, but treatment options for these patients are scarce.19 In these patients, optimal programming of AV intervals and heart rate might be even more critical as the improvement in diastolic filling is possibly the main mechanism of response.18

Heart rate programming in cardiac resynchronization including all of its pitfalls such as sensors and AV delays with intrinsic conduction and atrial pacing as well as dynamic programming of AV delays is an art that rests mostly on observational studies and personal experience. Patient-tailored programming with the help of exercise testing will become more important with the broadening indications that will most certainly lead to a further increase in CRT implantations.

Conflict of interest: D.J.V. has received consultancy fees from Medtronic and Biotronik and is the Principal (Co-)Investigator of the DDT-HF Study. A.H.M. has received lecture fees from Medtronic, Biotronik, Boston Scientific, and Sorin.

References