Problems and troubleshooting in regular follow-up of patients with cardiac resynchronization therapy

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Biventricular pacing is an efficient treatment to improve symptoms and clinical outcome in patients with drug-refractory heart failure, low left ventricular ejection fraction and wide QRS. The basis of the treatment is the permanent delivery of biventricular pacing. During the follow-up of biventricular devices the assessment of permanent biventricular capture is fundamental. This requires a tailored programming with respect to the patient’s activity and age, and thus also careful evaluations during an exercise test as well as adequate programming in case of cardiac arrhythmias.

Keywords  Cardiac resynchronization therapy • Heart failure • Exercise test

Introduction

Cardiac resynchronization therapy (CRT) is a recommended treatment for patients with moderate to severe (drug-refractory) heart failure with left ventricular (LV) systolic dysfunction and evidence of ventricular dyssynchrony defined by a QRS duration ≥ 120 ms.1,2 Cardiac resynchronization therapy improves symptoms, exercise tolerance, and quality of life and has shown a significant improvement in morbidity and mortality.3—7 However, the problem of non-response to CRT remains crucial with a stable prevalence of 30% of non-responders for clinical response and 45% for echocardiographic response.8 Several solutions can be proposed to improve the responder rate, including better selection of candidates to CRT, an optimal positioning of the LV lead, and/or the optimization of the therapy delivery. Recent data in CRT patients with permanent atrial fibrillation or stable sinus rhythm underlined the importance of (almost) permanent biventricular pacing with a cut-off value of 93% to improve the patients’ outcome.9,10 We will focus here on the importance of assessing the presence of permanent biventricular pacing during routine follow-up of patients implanted with a CRT device.

Initial device programming to maximize permanent biventricular pacing

After implantation of the CRT device, initial programming includes the choice of the pacing mode (VDD, DDD, DDDR or VVIR in case of permanent atrial fibrillation), lower and upper rate limits, AV delay after atrial sensing and pacing and rate limits to activate anti-tachycardia therapy in case of implantation of a CRT-D. Most of the published data involve patients with normal sinus rhythm with atrial-synchronous biventricular pacing (VDD mode). However, some patients with associated sinus node dysfunction or atrial chronotropic incompetence require sensor-driven pacing modes (DDDR mode). Usually the AV delay is initially programmed empirically with a range of 80–120 ms during atrial sensing with an additional offset of 30 to 50 ms during atrial pacing. An optimization of the AV delay should be performed before discharge if possible and should always provide complete biventricular capture. A common reason of loss of biventricular capture is related to sensing atrial rate close to the programmed maximal tracking rate.11 Upper rate behaviour of biventricular pacemakers may take the form of a traditional pacemaker Wenckebach response or the equivalent of fixed-ratio block as in conventional antibradydycardia pacemakers defined by the programmed upper tracking rate and the total atrial refractory period (TARP). When the atrial rate exceeds the programmed upper rate but the P–P interval remains longer than the TARP, the pacemaker exhibits a Wenckebach response. If the P–P interval becomes shorter than the TARP (which is equal to the sum of the prevailing AV delay and the post-ventricular atrial refractory period or PVARP), 2:1 block (in patients with AV block) occurs whenever every other atrial event falls in (PVARP). Initial programming of the CRT device should provide an upper rate with respect to the patient’s activity and age.

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How to detect loss of biventricular capture

During follow-up, confirmation of biventricular capture has to be assessed regularly with the analysis of the surface ECG which is compared with the ECG templates recorded at the time of implantation. The loss of biventricular capture under a number of circumstances has to be avoided by appropriate and careful programming.

The diagnosis of loss of biventricular capture is easy if the situation is stable (not intermittent), and is documented with analysis of the QRS complexes on the surface ECG. If the loss of biventricular capture is transient, the diagnosis is more difficult and may require different techniques such as exercise testing or evaluation of the percentage of biventricular pacing obtained from memorized monitoring capabilities of the biventricular devices, or a 24-h Holter recording or via telecardiology with some devices.

How to assess permanent biventricular during exercise

A patient with a CRT device will exercise, so that the assessment of biventricular capture should include exercise testing. There are many reasons why biventricular capture may fail during exercise: loss of atrial sensing, frequent premature ventricular complexes (PVCs), atrial tachy-arrhythmias, and spontaneous AV conduction that is more rapid than the programmed AV delay. Generally, RV and LV pacing channels are programmed in the bipolar mode and to better identify atrial and ventricular spikes reprogramming ventricular and atrial pacing into the unipolar mode may be useful as illustrated in Figure 1. The shape of atrial and ventricular complexes is similar with the two pacing modes (unipolar and bipolar). The analysis of ventricular complexes is of major importance to assess biventricular capture during exercise. Changes of the QRS complex during exercise may suggest (as illustrated in Figure 2) the loss of capture in one ventricle. The programmed AV delay at rest but also the adaptation of the AV delay during exercise needs to be assessed carefully. Figure 3 illustrates adequate programming of the AV delay at rest and during exercise. Conversely, in Figure 4, the rate-adaptive AV delay was not optimized during exercise resulting in the loss of LV capture. The loss of biventricular capture during exercise due to an excessively long

Figure 1 Temporary switching from a bipolar configuration (left panel) to a unipolar configuration (right panel) during exercise testing to improve the identification of the ventricular spikes.

Figure 2 Left panel: Biventricularly paced QRS complexes with unipolar configuration at rest. During exercise testing, the loss of biventricular pacing was diagnosed by the modifications of the QRS complexes and the loss of ventricular spikes (right panel).

Figure 3 Left panel shows the surface ECG recording at rest with unipolar atrial and ventricular spikes and an AV delay of 150 ms. In the right panel it is shown that during exercise the heart rate increases and the AV delay shortens providing permanent biventricular capture.
Figure 4 (A) Twelve-lead surface ECG recorded during an exercise test in a patient implanted with a CRT pacemaker. The patient did not improve after CRT implantation and pacemaker interrogation showed a low percentage of ventricular pacing, around 60%. An exercise test performed on a treadmill showed that the programmed AV delay was longer than the spontaneous PR interval resulting in loss of CRT. In the same patient, programming a shorter AV delay during exercise resulted in permanent biventricular capture during exercise associated with a significant improvement in symptoms (B).

Figure 5 (A) Six-minute walking test performed in a patient implanted with a biventricular pacemaker. Inadequate programming of the AV delay resulted in the absence of biventricular pacing as illustrated on the ECG channel and the markers channels (AP: atrial pace, RVS: right ventricular sense, LVS: left ventricular sense). (B) Optimization of the AV interval provided permanent biventricular capture with right ventricular pacing (RVP) and left ventricular pacing (LVP).
programmed AV delay may be also assessed using the device tele-
markers (Figure 5). In patients with permanent atrial fibrillation and
without AV node ablation, exercise testing has to be performed to
verify the constancy of biventricular capture. In these patients,
apparent adequate biventricular capture at rest may not be a
reliable marker of satisfactory biventricular capture because intrin-
sic AV conduction on exercise may inhibit biventricular capture
when the spontaneous ventricular rate exceeds the sensor-driven
pacemaker rate (Figure 6).

Haemodynamic deterioration during exercise may sometimes
be due to a loss of atrial sensing with preservation of biventricular
capture, a situation that requires reprogramming of the atrial sen-
sitivity (Figure 7).

Finally, the evaluation of a patient with a rate-adaptive pace-
maker has to consider the type of rate-adaptive sensor. For ex-
ample patients with an activity sensor may not exhibit an
increase of heart rate during exercise performed on a bicycle.

Figure 6 (A) Twelve-lead surface ECG in a patient with permanent atrial fibrillation implanted with a biventricular pacemaker. At rest, biven-
tricular pacing is provided with QRS duration of 130 ms. The patient complained of fatigue as soon as he started exercise. (B) Twelve-lead ECG
in the same patient during an exercise test on a treadmill. Intrinsic ventricular rate with a left bundle branch block pattern was observed result-
ing in the loss of CRT. After AV node ablation, the patient received permanent biventricular pacing resulting in functional improvement.

Figure 7 Example of a loss in atrial sensing during exercise (arrows) in a heart failure patient during an exercise test. The
surface ECG at rest showed an appropriate detection of the
atria. Increase in atrial sensing resulted in appropriate detection
of the atria during further exercise testing.
but an exercise test performed on a treadmill without changing the sensor settings may demonstrate better adaptation of the heart rate (Figure 8).

**Programming and paroxysmal atrial arrhythmias**

In patients with severe heart failure, atrial arrhythmias and especially atrial fibrillation occur in up to 40% with a significant correlation with the severity of heart failure. The occurrence of atrial fibrillation in CRT patients may produce major hemodynamic deterioration due to the loss of the atrial contribution to cardiac output. Atrial fibrillation may also interfere with programming functions of the CRT device. Atrial arrhythmias may cause loss of biventricular pacing during rapid spontaneous ventricular rates or induce excessively rapid ventricular pacing during atrial tracking. Atrial arrhythmias may be the cause of poor resynchronization in up to 20% of CRT patients.

In case of paroxysmal atrial fibrillation, the mode-switching activation may avoid a rapid ventricular rate in patients with AV block. New features are available in the most recent devices to optimize the percentage of ventricular pacing with little or no increase in the daily mean heart rate and thus to promote delivery of CRT during atrial fibrillation or atrial tachy-arrhythmias episodes.

**Programming and permanent atrial fibrillation**

In permanent atrial fibrillation, continual biventricular capture has to be assessed at rest and during exercise as previously emphasized. Usually in permanent atrial fibrillation, patients without spontaneous or radiofrequency-induced AV block, ventricular rate control is achieved with beta-blockers, calcium blockers, or digoxin, alone or in combination. At rest, the rate control with these drugs may be effective but it may be unsatisfactory as soon as the patient starts exercise. In these patients with a low percentage of paced ventricular cycles, radiofrequency AV node ablation is recommended to optimize CRT delivery. Some cardiologists have suggested the use of routine AV node ablation at the time of CRT implantation or 1 month later after verification of proper device function. Gasparini et al. showed the superior effect of CRT on exercise tolerance, disease progression and survival in patients with atrial fibrillation and AV node ablation.

**Conclusion**

The clinical follow-up of CRT patients requires a multidisciplinary approach. Programming of CRT devices has to be carefully evaluated to ensure continual biventricular capture at rest and during exercise. With the technical improvement of recent CRT devices and appropriate fine-tuning of devices with specific algorithms designed to improve CRT delivery, we can reasonably expect that the relatively high number of partial or complete non-responders will decrease. However, programming of a CRT device remains complex and needs tailoring to the individual patient.

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