An unusual cause of poor response to cardiac resynchronisation therapy

Claire Martin (EP Fellow, Barts Health NHS Trust)
Parag Gajendragadkar (Cardiology Registrar, Papworth Hospital NHS Foundation Trust)
Peter Pugh (Cardiology Consultant, Cambridge University Hospitals NHS Foundation Trust)

clairemartin@gmail.com

Clinical Introduction

A patient with severely impaired left ventricular (LV) systolic function due to ischaemic cardiomyopathy and NYHA Class III symptoms presented with collapse and was found to have non-sustained ventricular tachycardia. The ECG demonstrated sinus rhythm with first-degree AV block and a widened QRS complex. On this basis, a cardiac resynchronisation therapy-defibrillator (CRT-D) device was implanted. Leads were introduced via the left subclavian vein to the right ventricular (RV) apex and right atrial (RA) appendage. Initial active fix parameters were: RA - threshold 0.25V, impedance 513Ω, P 2.3mV; dual coil RV - threshold 0.75V, impedance 513Ω, R 16.5mV. A Medtronic 4194 bipolar LV lead was positioned in a secure position in a posterolateral tributary of the coronary sinus (threshold 2.75V, impedance 855Ω). Pacing parameters at the 3 month check were unchanged with no device therapies. The patient initially improved clinically following CRT, but by 6 months their breathlessness had returned. ECGs immediately post-device insertion (Fig1A) and at 6 months (Fig1B) are shown, as well as a chest radiograph at 6 months (Fig1C).

Fig 1 ECGs immediately post-device insertion (A) and at 6 months (B); PA chest radiograph at 6 months (C).

Clinical Question
What investigation/therapy would you suggest next?

1. Refer for echo optimization of AV and VV delays
2. Refer for premature ventricular contraction (PVC) ablation
3. Increase LV pacing output
4. Refer for lead repositioning
5. Increase diuretics
6. Check full blood count

Answer

ECG (Fig 1A) demonstrates biventricular pacing whilst (Fig 1B) demonstrates a change in morphology consistent with lone RV pacing. A pacing check confirmed there was no LV capture at maximum output. (Fig 1C) shows that the LV lead has been withdrawn out of the vascular system entirely and is curled up around the generator. The patient was therefore admitted for repositioning of the LV lead. Whilst other factors such as suboptimal medical therapy, anaemia, suboptimal AV timing and arrhythmias may all contribute to non-response, they will not be the main factor on this occasion. Whilst the non-response here is due to a lack of LV capture, this is due to gross lead displacement and therefore will not be improved by increasing LV output. It is worth noting, however, that the patient does have a high PVC burden on both ECGs, which will both decrease the effective bi-ventricular pacing percentage, and indeed may have contributed to the aetiology of the LV impairment. If the patient remains symptomatic despite lead repositioning, a trial of amiodarone to suppress the ectopy or referral for PVC ablation may be advised (see ‘Discussion’ below).

The most likely explanation for the lead displacement is ‘Twiddler’s Syndrome’. First described in 1968, this refers to malfunction of a pacemaker due to the patient’s deliberate or subconscious manipulation of the pulse generator (1). Elderly and obese patients appear to be at increased risk because the presence of loose subcutaneous tissue allows for easier rotation (2). Creating a small pocket, suturing the device to the fascia or use of a Dacron pouch can help minimise this.

Discussion

Around one third of patients currently do not respond to CRT based on the current guidelines, and more than 40% do not show a LV reverse modelling response. In some of these cases, this could be improved with better patient management; Mullens et al (3) identified common reasons for CRT non-response (Fig 2). One difficulty is that clinical trials evaluating the effects of CRT have used different outcome measures. Early clinical trials used clinical parameters such as NYHA functional class, 6 minute walk test and quality of life assessments. Clinical end point was a decrease in heart failure (HF) hospitalizations (4). More recently, studies have used improvement in
echocardiography parameters such as LV ejection fraction (EF) and decrease in end-diastolic and end-systolic LV volumes, which are more objective and are correlated with long term mortality benefit (5, 6).

From a practical perspective, there are several things to check when managing a patient who has not responded to CRT. Interrogation of the device will reveal whether the LV is capturing. A rise in threshold may be caused by lead malfunction or displacement, as in our case presented here. LV lead location is also an important factor in determining CRT response. The LV lead should ideally be positioned in a basal to mid-lateral or posterolateral position. LV lead position anteriorly is associated with worse prognosis and non-response (7), and lead reposition may be considered in these cases. If transvenous options are limited, an epicardial approach via a mini-thoracotomy might be considered. Some centres also perform transeptal endocardial LV lead implantation, although patients then require lifelong anticoagulation, and there is so far limited data on whether it might cause mitral regurgitation. Some studies have suggested that right ventricular (RV) lead position may also play a role in CRT response, with high septal RV lead positioning preferred over apical positioning.

It is useful to perform a 12 lead ECG, with pacing off, with RV only pacing and biventricular (Bi-V) pacing. The aim would be for the Bi-V paced ECG to have a narrower QRS without a left bundle branch block pattern. QRS duration and morphology will depend on the paced timings as well as lead location. AV and VV delay optimisation should be performed in all non-responders. This may be performed either with echocardiography or guided by the device. If done via echocardiography, the AV delay can be optimising through measurement of the transmitral filling profile. The SMART AV trial showed that patients with normal AV-delay did not derive benefit from echo-guided or device-guided AV-optimization compared to the empiric settings; however, patients with prolonged AV-conduction were not included in this prospective, randomized study (7). Other data suggest patients with prolonged AV-interval to derive benefit from AV-delay optimization (8).

Additional assessment includes measurement of LV interventricular and intraventricular mechanical dyssynchrony. Interventricular mechanical dyssynchrony is measured as the difference of the aortic and pulmonary pre-ejection interval and its immediate decrease shows effective resynchronization. Intraventricular dyssynchrony can be evaluated by tissue Doppler imaging or by strain dyssynchrony based on speckle tracking. VV-optimization is a useful tool to correct intraventricular dyssynchrony, and is usually achieved through optimising LV stroke volume.
It is also important to ascertain whether the patient is in normal SR or AF. AF may lead to tachycardia with loss of LV pacing or fusion/pseudofusion beats with ineffective resynchronization. It is vital to control the ventricular rate, with AV node ablation necessary if medication is inadequate. The role of pulmonary vein isolation in such patients is currently unclear and the subject of ongoing trials. Frequent PVCs, more often observed in patients with ischaemic cardiomyopathy, may also cause non-response, and require treatment with antiarrhythmics, or consideration of PVC ablation. Interrogation of the device will demonstrate the AF or PVC burden; Bi-V pacing percentage must be higher than 90% to ensure optimal CRT. However, fusion and pseudofusion may not be detected by the device, and so the reported Bi-V pacing percentage may be falsely high.

Finally, it is important not to forget to examine comorbidities such as diabetes, ischaemic heart disease, and vascular and cerebral diseases, which carry an increased risk of pool renal function, anaemia and hypotension, which are in turn associated with poor prognosis in CRT recipients. Optimal treatment of these factors may improve CRT response. Non-responders may be on inadequate medical therapy for their HF. Medications may be discontinued as HF worsens or if they develop renal dysfunction, and it is also importance to check for patient compliance for prescribed medications.

References


