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Editorial

Further insights into CRT delivered through a trans septal LV endocardial lead☆

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Cardiac resynchronization therapy (CRT) is an effective electrical therapy for patients with drug refractory heart failure symptoms, severely impaired left ventricular systolic function and prolonged QRS duration measured by surface ECG. Improvement in quality of life, exercise tolerance, heart failure hospitalizations and mortality have all been demonstrated; however, a sizeable proportion of patients fail to derive benefit [1].

Conventional CRT involves LV lead placement into an epicardial venous target of which there are, on average 2–3 viable veins per patient. A spectrum of venous tributaries with different length, tortuosity and angulation exist, sometimes with the added difficulty of a valve which may obstruct the successful passage of a lead. Therefore, the constraints of the epicardial venous system are an important and insurmountable limitation of current day CRT. Recently, both animal and clinical data have suggested endocardial LV stimulation for biventricular pacing may confer superior benefit to conventional epicardial LV stimulation. Access to all of the endocardium, superior haemodynamics [2] and more physiological transmural activation [3] are some of the potential advantages.

Biffi et al. describe a subanalysis of ALSYNC (Alternate Site Cardiac Resynchronization), a prospective feasibility and safety study of a transeptal endocardial LV lead for CRT in patients who were either non responders to conventional therapy or unable to be treated due to a failed LV lead implant [4]. Biffi et al. divided the 118 attempted implants into those who were prior non responders (NR) to conventional CRT (n28) and those CRT naive patients who had a failed LV (fLV) implant (n90). There were no major differences in the demographics and associated cardiovascular comorbidities comparing the two groups. The prevalence of ischemic etiology, left bundle branch block (LBBB), mean QRS duration, LVEF and NYHA scores were similar. However, the NR group had larger LV chamber size (LVEDD 70 ± 12 vs. 65 ± 9, $p = 0.025$) and a higher proportion were anticoagulated (96% vs 72%, $p = 0.008$) despite similar prevalence of AF, suggesting this subgroup may have had more advanced disease.

During mean follow up of 19 ± 9 months, NR underwent significantly less LV volume reduction and LVEF improvement, compared with those who were CRT naïve through fLV placement. Furthermore, the proportion of patients achieving super responder status (LVESVi reduction of >30%) was greater in the fLV group compared with NR (40% vs 5%). These outcomes are indeed intuitive given one group has already received biventricular pacing and the other group is CRT naïve. In keeping with other published data, non ischemic etiology produced a higher degree of reverse remodelling than ischemics in the CRT naïve group. In the NR group, volumetric response was quantitatively less than in the fLV group, however more interestingly there appeared to be more of a reduction in LV size in the ischemic cohort compared with the non ischemic group. This may reflect that LV endocardial pacing may be a highly attractive option for the ischemic cohort who have the most to gain from this approach, given their CRT response rate is arguably poor with a conventional epicardial LV lead [1]. Our group has previously demonstrated that LV endocardial pacing may offer superior haemodynamic and electrical effects compared with LV epicardial pacing when delivering biventricular pacing in ischemic patients with suboptimal response to CRT. Whilst this may in part be due to the unrestricted access to a larger surface area, LV endocardial stimulation also appears to be more physiological and optimal than the epicardium at the same site [5].

CRT delivered with LV endocardial pacing certainly provides an opportunity for improvement in a population whom until now have had limited alternatives. 47% of the 28 non responders were converted to echo responders after 6 months of therapy which remains impressive. Interestingly however, implanting physicians in the ALSYNC study employed empirical lead positioning (on the lateral wall) rather than any targeted approach. Given recent published data on the merit of LV lead targeting away from scar [6] and toward dyssynchrony [7], it

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would be interesting to hypothesise whether the improvements in response would have been even more impressive if an image or substrate guided approach was used. Echocardiography, cardiac CT, nuclear perfusion or cardiac MRI can all be used to identify the optimal substrate and site for LV stimulation. Furthermore, image co-registration (between MRI/CT and X-Ray) can help to identify and display favourable and suboptimal locations which correlate to local electrical parameters, in order to guide the implanter toward the optimal site [8]. Whilst small and limited clinical studies have suggested potential benefit, a larger randomised study is required to evaluate whether an image guided approach translates into greater CRT response compared with a conventional approach using X-ray.

Finally, whilst LV endocardial stimulation may benefit patients unable to respond to conventional CRT, permanent positioning of a lead in the left ventricle confers a thromboembolic stroke risk despite anticoagulation and disruption of the mitral valve apparatus [9]. Avoiding these pitfalls with wireless LV endocardial stimulation may be an alternative. Wireless LV Endocardial CRT (WiSE-CRT, EBR Systems) is a new, disruptive technology comprising a 9 mm electrode with nitinol barbs which is implanted directly the LV endocardium through a transcatheter, retrograde aortic approach. This is powered by an ultrasound transmitter and attached battery pack which are implanted separately in the chest wall. The device requires a co-implant from an existing pacemaker and whilst sensing the signal from the right ventricle, delivers a near simultaneous stimulus from the LV endocardial electrode to provide biventricular pacing. Published evidence to date suggests this technology may be highly effective in a similar group of patients unable to respond to conventional CRT [10]. A larger randomised controlled study is underway to scrutinise the efficacy of this system in patients unable to achieve or benefit from conventional CRT (SOLVE CRT, NCT 02922036).

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