

Editorial

Is Left Ventricular Endocardial Pacing the Future for Cardiac Resynchronization Therapy?



¿El marcapasos endocárdico ventricular izquierdo es el futuro de la terapia de resincronización cardiaca?

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Cardiac resynchronization therapy (CRT) is a well-established treatment for heart failure patients with left ventricular (LV) systolic dysfunction and asynchronous LV contraction. This treatment improves quality of life and reduces heart failure-related hospitalizations and mortality.¹ “Conventional” CRT relies upon percutaneous access to the LV epicardial surface via the coronary sinus and venous tributaries. Venous anatomy and phrenic nerve location dictate the LV pacing site and can result in suboptimal clinical outcomes.²

Most patients who receive CRT report symptom improvement, but 20% to 30% of patients demonstrate no objective clinical benefit³ whilst 5% to 10% of conventional implants fail.⁴ ‘Nonresponders’ and those with unsuitable coronary venous anatomy post a significant clinical challenge. The Alternate Site Cardiac Resynchronization (ALSYNC) study has demonstrated that LV endocardial pacing (LVEP) can be safely achieved percutaneously and this treatment has emerged as the solution for this patient group.⁵

The ALSYNC study was a prospective multicenter evaluation of a novel atrial transseptal LV endocardial lead delivery system. Recruited patients included CRT nonresponders, patients with suboptimal coronary sinus anatomy, and those with previously failed epicardial LV lead implants. A steerable guide catheter, introduced via the subclavian vein, acted as the delivery platform for a radiofrequency puncture of the interatrial septum. A guidewire supported advancement of a lead delivery catheter across the septum and mitral valve, facilitating targeted placement of an endocardial LV pacing lead.

The primary endpoint of achieving LVEP whilst demonstrating freedom from complications at 6 months’ postimplant was achieved in 82.2% (95% confidence interval [95%CI], 75.6%–88.8%). Six months postimplant, 55% of patients had achieved a 15% reduction in LV end systolic volume ($P \leq .0001$), 64% had a 5% increase in LV ejection fraction ($P \leq .0001$), and 59% had functional improvement in New York Heart Association (NYHA) class

($P \leq .0001$). The overall percentage of NYHA class III/IV patients in the cohort fell from 76% at implant to 30% after 6 months of LVEP. Importantly, those previously deemed as CRT “nonresponders” showed similar improvements, with 52% reporting an improvement in NYHA class and 61% showing a greater than 5% increase in ejection fraction.

These results are compelling. However, LVEP should not be limited to this patient cohort. Endocardial LV pacing offers several additional advantages over conventional epicardial pacing and may well represent the future of CRT for all patients requiring resynchronization.

Left ventricular endocardial pacing offers choice of pacing site across the LV endocardial surface and introduces the potential for more physiological septal pacing. Various lead locations may also be tested at implant, allowing assessment of the location yielding the greatest benefit to cardiac function prior to position selection, although acute hemodynamic response may not necessarily indicate long-term outcome. Capture thresholds are lower with endocardial pacing with a considerable reduction in the risk of phrenic nerve capture.⁶

Optimal site endocardial pacing has been consistently shown to enhance hemodynamic LV performance compared with conventional coronary sinus site stimulation and is associated with better LV filling and systolic function.^{7–9} “Nonresponder” rates are also significantly lower in the studied LVEP population.⁹

Normal electrical activation of the myocardium is reversed in epicardial pacing. Basic science studies show that this results in increased transmural dispersion and QT prolongation, generating both the substrate and trigger for the development of reentrant ventricular arrhythmias.¹⁰ An increase in QT dispersion has been shown to predict sudden cardiac death risk.¹¹ Epicardial-based CRT may be proarrhythmic in certain individuals. Certainly, CRT does not reduce risk of sudden cardiac death, despite significant reductions in heart failure-related death and improvements in LV systolic function.¹² Left ventricular endocardial pacing may provide a more physiological wave front of myocardial depolarisation and obviate the proarrhythmic effect.

The main clinical drawbacks of LVEP are the potential for thromboembolic events and the long-term effects on mitral valve function. Mid-term follow-up has demonstrated that with

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adequate anticoagulation there is no increase in thromboembolic complications.^{5,13} At 6 to 12 months postimplant, there is also no evidence of pacing lead-induced mitral valve damage or increased mitral regurgitation.^{5,13} Patients requiring CRT, even in the absence of atrial fibrillation, are at high risk of thromboembolism. The long-term impact of an endovascular LV lead to this pre-existing risk remains unknown. The potential need for LV endocardial lead extraction may also present a challenge to the long-term safety of LVEP.

The entirely subcutaneous implantable cardioverter defibrillator and the leadless pacemaker have changed the landscape of device therapy in recent years. Endocardial LV pacing offers the potential for wireless CRT, which cannot currently be achieved with current epicardial systems. Wireless CRT would confer significant benefits over systems reliant upon transvenous components.

Leadless LV endocardial devices have been successfully implanted and used for CRT in combination with transvenous right ventricular systems.¹⁴ There is a growing body of evidence to indicate that leadless LV endocardial stimulation for CRT is both feasible and safe.^{15–17} The future of CRT may in fact consist of entirely leadless devices, offering superior hemodynamic response through the use of LVEP sites.

CONFLICTS OF INTEREST

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