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For LV pacing, four is greater than two



Shortly after the turn of the millennium, cardiac resynchronization therapy (CRT) was developed as a powerful treatment for heart failure with reduced ejection fraction (HFrEF) accompanied by significant electromechanical dyssynchrony [1,2]. Despite the early success of CRT, it was clear that there was room for improvement. With early generation unipolar and bipolar LV pacing leads, there was a small but important rate of implant failure. Although implant tools improved, LV leads continued to prove more prone to dislodgement than standard endocardial pacing/defibrillation leads, and CRT pacing was also sometimes hindered by phrenic nerve stimulation (PNS) – with both of these problems leading to lead revision procedures and, occasionally, deactivation of LV pacing. Additionally, even with successful, uncomplicated implants, CRT has long been associated with a bothersome rate of clinical non-response [3].

In an effort to address some of these issues, in late 2011, the first quadripolar pacing leads were introduced to the US market, and were rapidly adopted. Single-arm observational studies of the first two quadripolar lead families showed high implant success rates, low dislodgment rates, good chronic pacing thresholds, and an ability to resolve most cases of PNS via device reprogramming [4–6]. It has, however, taken several years since the launch of quadripolar pacing leads for data to emerge proving their clinical value relative to conventional bipolar leads. In the current issue of *IPEJ*, Rijal and colleagues add to the growing literature on this topic, with a large, single-center series comparing the outcomes of CRT recipients treated with either quadripolar or bipolar leads at their center [7].

The authors scanned the ICD registry and electronic health records from their institution to identify a total of 1441 patients (292 quadripolar and 1149 bipolar) who had a CRT device implanted between January 2011 and December 2014. Baseline demographic and clinical characteristics between the two groups were comparable, except for the fact that those receiving quadripolar leads were slightly younger and had an increased incidence of diabetes mellitus. The procedures were carried out by well-experienced electrophysiologists. Both de novo and CRT upgrades were included. Quadripolar leads from both St. Jude (Quartet) and Medtronic (Attain Performa) were used.

The primary end-point was a composite of LV lead implant failure, dislodgment, or LV pacing deactivation for PNS in the first 12 months after the index procedure. Secondary outcomes included hospitalizations and mortality. For the vast majority (85%) of the patients, follow-up data for one year was available, with the overall

mean follow-up duration of almost 20 months (± 16 months).

The study found that the composite endpoint of LV lead related complications (which included failed lead placement, lead dislodgement, or lead being turned off over one year post-implantation) occurred significantly less in the quadripolar compared to the bipolar group [8 (2.7%) compared to 78 (6.8%), $p = 0.009$]. The superiority of the quadripolar lead seemed to be primarily driven by less intra-operative failures of placement (0.3% vs. 2.3%, $p = 0.03$) or early post-procedural LV lead dislodgement or deactivation for PNS. There were no statistically significant differences in the secondary endpoints of the study, although it is worth noting that both all-cause hospitalizations (31.5% vs. 37.3%, $p = 0.065$) and deaths (7.2% vs. 11.0%, $p = 0.065$) were less frequent in the quadripolar group.

Outcomes following CRT implantation with quadripolar compared with bipolar leads have been reported from several previous studies with differing designs [8–10]. As with the current study from Rijal, in all previous reports, quadripolar leads were found to have a higher freedom from implant failure and/or need for early reintervention for dislodgment or PNS than bipolar leads. The only randomized study to date, “MORE CRT” was an international multicenter study that randomized 1074 patients in a 2:1 fashion between a bipolar CRT lead system and a quadripolar system. The primary endpoint was freedom from a composite endpoint of intraoperative and post-operative LV lead-related events at 6 months, and was significantly greater in the quadripolar than the bipolar group (83.0% vs. 74.4%, $p = 0.0002$) [8].

A single center study smaller than the one from Rijal, et al. additionally found that quadripolar CRT implants were associated with a lower rate of subsequent hospitalization – and therefore lower medical costs – than bipolar CRT implants [9]. Finally, a study including all U.S. patients from a single manufacturer's database including over 23,000 patients (roughly three-fourths treated with quadripolar leads) further reported that patients receiving quadripolar leads had slightly lower mortality (5.04 vs. 6.45 deaths per 100 patient-years, hazard ratio 0.77, $p < 0.001$) than those receiving bipolar leads [10].

The current study from Rijal and colleagues provides consistent, and largely confirmatory findings compared with the prior work. It is the largest single-center series on this topic to date, and has the advantage of including both CRT-D and CRT-P devices, as well as devices from more than one manufacturer. Although the authors report negative findings on hospitalization and death, the absolute rates of these events were in fact lower with quadripolar

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implants, so the lack of nominal statistical significance on these end points may have been due to inadequate statistical power. It is curious that only about 20% of the implants in the current series utilized quadripolar leads, the use of which seemed more selective than for the rest of the US during the same timeframe [10]. Whether this more selective use of quadripolar leads could have resulted in some imbalance in the patient groups is not clear.

What is clear, from the Rijal paper and other studies that have come before it, is that the development of quadripolar leads appears to be another example of technological iteration that has provided a real step forward in optimizing the safety and effectiveness of CRT, with tangible benefits for patients. In addition to those aforementioned advantages, quadripolar leads also provide the opportunity for multi-site left ventricular pacing (“MPP”) which may help improve the clinical response to CRT in some patients [11].

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