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Short-Term Availability of Viable Left Ventricular Pacing Sites with Quartet™ Quadripolar Leads

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Background: Whether quadripolar leads can provide sufficient viable left ventricular pacing sites (LVPSs) for device optimization and multipoint pacing remains unclear. This study aimed to evaluate the acute and 3-month availability of viable LVPSs provided by a quadripolar LV pacing lead.

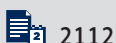
Material/Methods: A single-center cohort study evaluated consecutive patients who underwent a CRT implant with the Quartet™ LV lead under local guidelines. The availability of viable LVPSs was assessed at the pre-discharge and 3-month follow-up visit. Bipolar lead configurations, which served as the control group, were modeled by eliminating the 2 proximal electrodes on the Quartet™ LV lead.

Results: A total of 24 patients were enrolled and finished 3-month follow-up. The mean follow-up period was 93±3 days. At pre-discharge, the Quartet™ LV lead provided more viable LVPSs compared with the bipolar equivalents (median 3 [IQR 2–4] vs. median 2 [IQR 1–2], P<0.001). The percentage of patients with at least 1, 2, 3, and 4 viable LVPSs were 100% (24/24), 91.7% (22/24), 58.3% (14/24), and 33.3% (8/24) for Quartet™ leads and 91.7% (22/24), 70.8% (17/24), 0% (0/24), and 0% (0/24) for bipolar lead configurations, respectively. The median and IQR values of viable LVPSs provided by the Quartet™ LV lead remained the same (3 [IQR 2–4]) between pre-discharge and 3-month follow-up (P=0.45).

Conclusions: Compared with the bipolar equivalent, Quartet™ LV lead provides more viable LVPSs and opportunities for CRT optimization and multipoint LV pacing. The number of LVPSs provided by Quartet™ leads remained unchanged between pre-discharge and 3-month follow-up.

MeSH Keywords: **Cardiac Resynchronization Therapy • Left Ventricular Pacing Configuration • Left Ventricular Pacing Site • Quadripolar Left Ventricular Lead • True Bipolar Configuration**

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Background

Cardiac resynchronization therapy (CRT) improves heart failure (HF) symptoms, reverses myocardial remodeling, and decreases hospitalization and mortality in selected patients with HF [1,2]. However, approximately 30–40% of CRT recipients do not experience symptomatic improvement and up to 50% fail to have echocardiographic response to CRT [3,4]. The left ventricular pacing site (LVPS) has been increasingly recognized as an important determinant of CRT response in individual patients [5–10].

For patients implanted with a conventional unipolar LV lead, the LVPS cannot be changed after implant. However, the quadripolar LV lead, with its 4 pacing electrodes, has the capability to switch LVPS by device programming. Recent studies have demonstrated that CRT using a quadripolar LV lead with an optimized LVPS could improve acute hemodynamics and synchronization at implant [11–16]. More recently, multipolar pacing with quadripolar LV leads has been shown to further improve response to CRT [17]. Multipolar LV pacing can be realized only when a minimum of 2 viable LVPSs are available. However, whether the quadripolar leads can provide sufficient viable LVPSs for device optimization and multipoint pacing, both at implant and during follow-up, remains unclear.

The aim of this study was to evaluate the acute and 3-month availability of viable LVPSs provided by a quadripolar LV pacing lead.

Material and Methods

A single-center trial was performed to study the number of viable LVPSs per patient with the quadripolar LV leads when compared with modeled bipolar equivalents at pre-discharge and 3-month follow-up.

Study population

From September 2013 to September 2015, a consecutive series of heart failure patients who underwent *de novo* CRT implantation with a quadripolar LV lead (Quartet™ 1458Q, St. Jude Medical, USA) were enrolled to this study at the National Center of Cardiovascular Disease, China. Indication for CRT-D followed the guideline of the European Society of Cardiology [18]. The study protocol was approved by the Research Ethics Board of Fuwai Hospital and complied with the Declaration of Helsinki. Written informed consents were received from all patients. Demographic, clinical, and device results were collected at the time of implantation, pre-discharge, and 3-month follow-up.

Implantation procedure

Technical aspects of leads and device implantation were described in detail previously [19]. Briefly, the coronary sinus (CS) was cannulated from left subclavian or cephalic entry site using a commercially available long peelable guiding sheath. LV pacing lead was positioned in the venous system, preferably in the lateral or posterolateral vein. The right atrial (RA) and right ventricular (RV) leads were placed regularly at the RA appendage and the RV apex. The quadripolar leads were connected to the Unify Quadra (model CD3249-40[Q]) CRT-D device (St Jude Medical). Fluoroscopy was used to assess the final position of the LV pacing lead.

Lead characteristics

The quadripolar electrode was named from distal to proximal: D1 (the distal electrode), M2 and M3 (the 2 middle electrodes), and P4 (the proximal electrode). It offered 10 left ventricular pacing configurations (LVPCs): D1-M2, D1-P4, D1-RV coil, M2-P4, M2-RV coil, M3-M2, M3-P4, M3-RV coil, P4-M2, P4-RV coil, where the first electrode represents the cathode and the second electrode represents the anode. In this study, we used the 2 distal electrodes of the Quartet™ lead to model a conventional bipolar lead. The spacing between these 2 electrodes is 20 mm, which is similar to the typical spacing of commercially available bipolar leads (St Jude Medical, Quickflex 1258: 20 mm, Medtronic Attain Ability 4196: 21 mm). These LVPCs were further divided into 2 groups according to LV pacing polarity. Patients with quadripolar LV leads programmed to pace between LV electrodes were further identified as True Bipolar while those programmed to pace between a LV electrode and RV coil were identified as Extended Bipolar. An illustration of all possible LVPSs and LVPCs are summarized in Table 1 and Figure 1.

Threshold testing and definition of the viable LVPS

Threshold testing was performed with a stepwise decrease of the pacing amplitude starting at 7.5 V until loss of LV capture and loss of palpable diaphragmatic contractions for phrenic nerve threshold with a pulse width of 0.5 ms. Before discharge and at 3-month follow-up, the same parameters were reassessed for all of the 10 LVPCs during biventricular pacing.

A viable LVPS was defined as an anatomical location where the electrode on the LV lead had at least 1 pacing configuration (0.5 ms pulse width) with pacing threshold ≤ 2.5 V and freedom from PNS at twice the pacing threshold in 2 predefined body positions: sitting and lying on the left side.

Table 1. List of included LVPSs, LVPCs, and True Bipolar LVPCs for Quartet™ and its bipolar equivalents.

Quartet™ leads			Bipolar leads		
LVPSs	LVPCs	True Bipolar LVPCs	LVPSs	LVPCs	True Bipolar LVPCs
D1	D1-M2	D1-M2	D1	D1-M2	D1-M2
	D1-P4	D1-P4		–	–
	D1-RV coil	–		D1-RV coil	–
M2	M2-P4	M2-P4	M2	–	–
	M2-RV coil	–		M2-RV coil	–
M3	M3-M2	M3-M2	M3	–	–
	M3-P4	M3-P4		–	–
	M3-RV coil	–		–	–
P4	P4-M2	P4-M2	P4	–	–
	P4-RV coil	–		–	–

LVPS – left ventricular pacing site; LVPC – left ventricular pacing configuration.

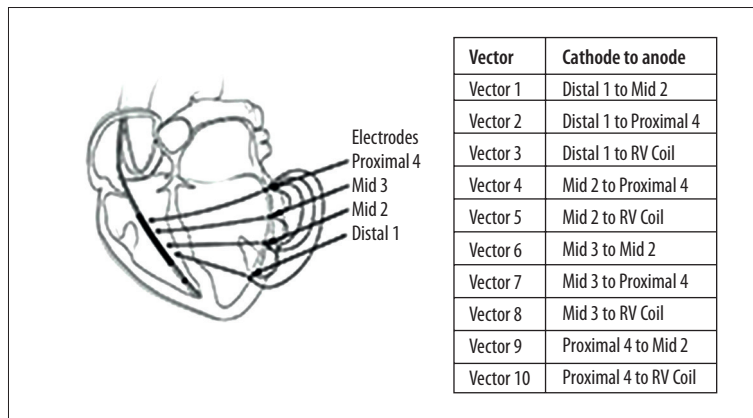


Figure 1. Possible LVPSs and LVPCs programmable with the Quartet™ LV lead.

Statistical analysis

SAS 9.3 (SAS Institute, Inc, Cary, NC) was used for data analysis. Continuous variables are reported as mean ± standard deviation when normally distributed, as median and inter-quartile range when not normally distributed, and were compared using the *t* test and Wilcoxon signed-rank test, respectively. Categorical variables are summarized by the count and percentage (%) and compared using chi-square analysis or Fisher exact test. P values <0.05 were considered statistically significant.

Results

Baseline patient characteristics

All enrolled patients completed study follow-up and were included in final analysis. Of the 24 patients, the mean age was

54.6±9.4 years, all were in sinus rhythm, QRS duration was 163.8±23.5ms, 17 (70.8%) were male, 4(16.7%) had an ischemic heart disease etiology and 21(87.5%) presented with concomitant left bundle branch block. The mean left ventricular ejection fraction was 27.5±4.5%. The characteristics of the patient population are shown in Table 2.

Procedural data

The LV lead positions (defined as the position of the distal electrode) were classified along the short axis of the LV as anterolateral in 2 patients (8.3%), lateral in 5 patients (20.8%), posterolateral in 16 patients (66.7%), posterior in 1 patient (4.2%), along the long axis as apical in 10 patients (41.7%), midventricular in 11 patients (45.8%), and basal in 3 patients (12.5%) (Table 2).

Table 2. Baseline characteristics of the study population (n=24).

Characteristics	n (%) / Mean ±SD	
Age	54.6±9.4 years	
Sex		
Male	17	(70.8%)
Female	7	(29.2%)
Primary disease		
Ischemic	4	(16.7%)
Nonischemic	20	(83.3%)
ICD indication		
Primary prevention	18	(75.0%)
Secondary prevention	6	(25.0%)
LVEF	27.5±4.5%	
NYHA class		
Class II	12	(50.0%)
Class III	11	(45.8%)
Class IV	1	(4.2%)
LV lead position		
LAO projection		
Anterolateral	2	(8.3%)
Lateral	5	(20.8%)
Posterolateral	16	(66.7%)
Posterior	1	(4.2%)
RAO projection		
Apical	10	(41.7%)
Midventricular	11	(45.8%)
Basal	3	(12.5%)

ICD – implantable cardioverter defibrillator; LVEF – left ventricular ejection fraction; NYHA – New York Heart Association; SD – standard deviation.

Follow-up

The mean follow-up period was 93±3 days. During the observation period, a dislodgement of the LV lead was noted and subsequently repositioned. One patient experienced rise in LV capture threshold and another patient experienced PNS that required an LVPC change with device programming. No other significant implant-related complications were observed during the follow-up.

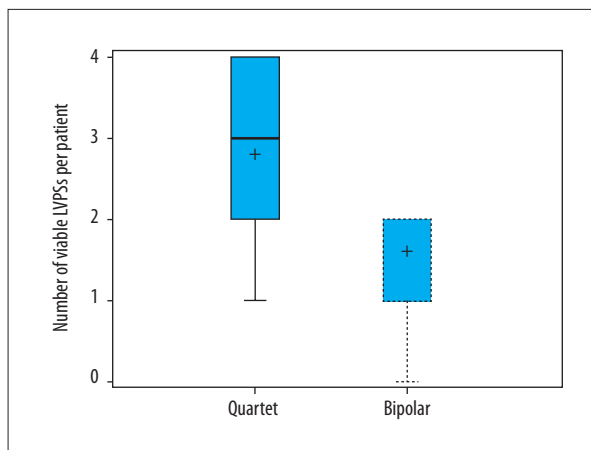


Figure 2. Number of viable LVPSs per patient at pre-discharge.

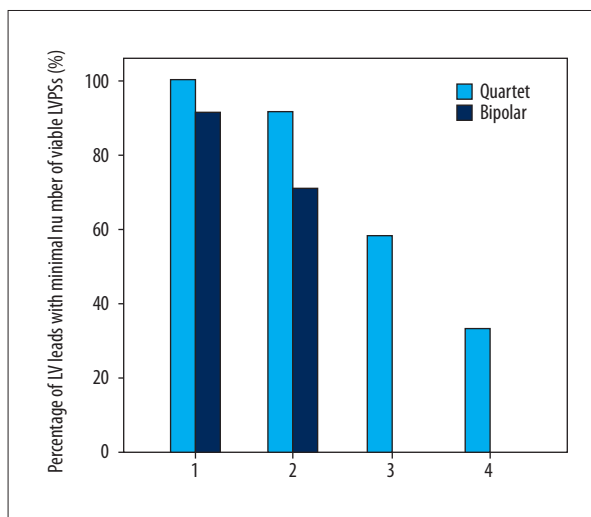


Figure 3. Percentage of patients with at least 1, 2, 3, or 4 viable LVPSs at pre-discharge.

Viable LVPSs at pre-discharge (Quartet™ vs. Bipolar)

The Quartet™ LV lead provided more viable LVPSs compared with the bipolar equivalents (median 3 [IQR 2–4] vs. median 2 [IQR 1–2] at pre-discharge (P<0.001) (Figure 2). The percentage of patients with at least 1, 2, 3, and 4 viable LVPSs were 100% (24/24), 91.7% (22/24), 58.3% (14/24), and 33.3% (8/24) for Quartet™ and 91.7% (22/24, P=0.49), 70.8% (17/24, P=0.14), 0% (0/24, P<0.001), and 0% (0/24, P=0.002) for the bipolar equivalent, respectively (Figure 3).

Viable LVPSs with True Bipolar configuration (Quartet™ vs. Bipolar)

When only considering the True Bipolar configurations, the Quartet™ LV lead provided more viable LVPSs compared with the bipolar equivalents (median 2 [IQR 1–3] vs. median 0.5 [IQR 0–1]) at pre-discharge (P<0.001) (Figure 4). The percentage of

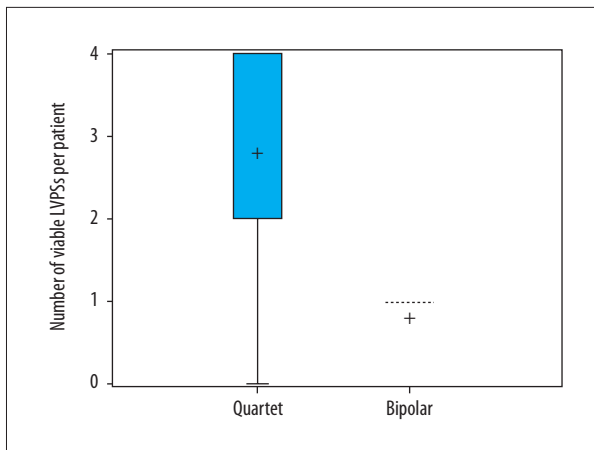


Figure 4. Number of viable LVPSs per patient when only considering the True Bipolar configurations.

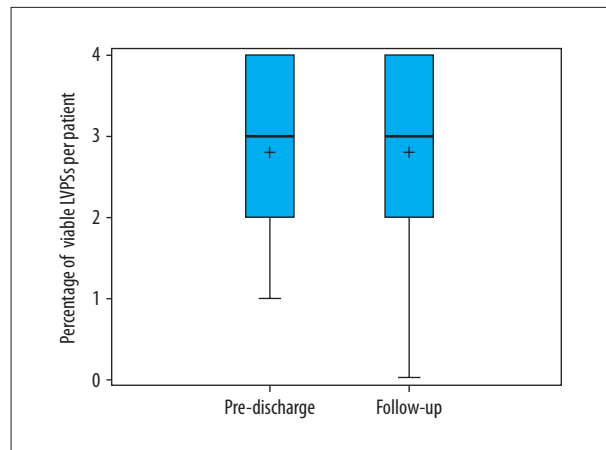


Figure 6. The number of viable LVPSs per patient for Quartet™ LV leads at pre-discharge and 3-month follow-up.

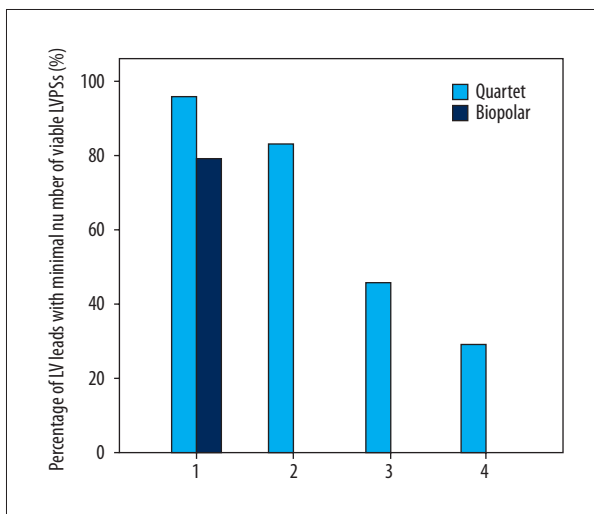


Figure 5. Percentage of patients with at least 1, 2, 3, or 4 viable LVPSs when only considering the True Bipolar configurations.

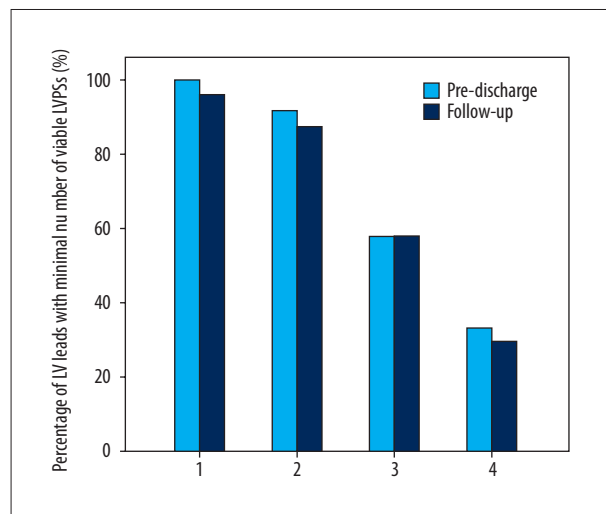


Figure 7. The percentage of Quartet™ LV leads offering at least 1, 2, 3, and 4 viable LVPSs at pre-discharge and 3-month follow-up.

patients with at least 1, 2, 3, and 4 viable LVPSs were 95.8% (23/24), 83.3% (20/24), 45.8% (11/24), and 29.2% (7/24) for Quartet™ and 79.2% (19/24, $P=0.19$), 0% (0/24, $P<0.001$), 0% (0/24, $P<0.001$), and 0% (0/24, $P=0.009$) for the bipolar equivalent, respectively (Figure 5).

Viable LVPSs with Quartet™ (Pre-discharge vs. Follow-up)

The median and IQR values of viable LVPSs provided by the Quartet™ LV lead remained the same (median 3 [IQR 2–4]) between pre-discharge and 3-month follow-up ($P=0.45$) (Figure 6). The percentage of leads offering at least 1, 2, 3, and 4 viable LVPSs were 100% (24/24), 91.7% (22/24), 58.3% (14/24), and 33.3% (8/24) at pre-discharge and 95.8% (23/24), 87.5% (21/24), 58.3% (14/24), and 29.2% (7/24) at 3-month follow-up, respectively ($P=1.0$) (Figure 7).

Discussion

This study was the first investigation of viable LVPSs provided by a commercially available quadripolar LV pacing lead. The primary findings of this study were as follows: (1) Quartet™ quadripolar LV lead provided more viable LVPSs compared with modeled bipolar configurations, especially when only considering the True Bipolar configurations. (2) The number of LVPSs provided by Quartet™ leads remained unchanged between pre-discharge and 3-month follow-up.

The number of LVPCs with quadripolar LV leads has been previously studied by O'Donnell et al. in patients receiving CRT [20]. They found that the Quartet™ quadripolar LV lead resulted in significantly increased numbers of viable LVPCs compared with modeled bipolar or tripolar configurations. Unlike

their previous work, our study focused on the number of viable LVPSs, which has been associated with the effectiveness of CRT [9,21]. The number of viable LVPCs, on the other hand, is associated with reduction in the hazard of PNS or unsatisfactory LV capture thresholds [22].

Selecting a better LVPS using the quadripolar lead is expected to further improve the effectiveness of CRT. Using invasive measurement of the LV dP/dt, Asbach et al. showed that LVPS selection affected acute hemodynamic response, yielding an additional average 10% increase in LV dP/dt when comparing best and worst LVPSs, with significant interindividual differences [23]. Bencardino et al. found that selecting a better LVPS with quadripolar leads on the basis of QRS shortening was associated with an improvement of LVEF greater than that observed in patients receiving a bipolar LV lead [16]. Moreover, Beharhas et al. further demonstrated that the use of quadripolar LV leads with an optimized LVPS for CRT was associated with lower overall mortality [24]. However, the additional benefits of the quadripolar leads discussed above are dependent on the number of viable LVPSs available. In this study, we found that the Quartet™ LV lead provided more viable LVPSs and thus more opportunities for LVPS optimization and, potentially, multipoint LV pacing when compared with the bipolar equivalent. More than half of the patients implanted with the Quartet™ LV leads had 3 or 4 viable LVPSs, which cannot be achieved with the bipolar equivalents.

As noted by Abu Sham'a et al. [25], LV pacing with an RV ring as the anode may cause local capture at the RV ring site, resulting in anodal pacing, which is a phenomenon that has been associated with worse short-term clinical outcomes with CRT [25–29]. Sina Jamé et al. recently analyzed the association between the LV lead pacing polarity and clinical outcomes. They found that True Bipolar LV pacing configuration, rather than unipolar or Extended Bipolar pacing, is associated with a significantly lower risk of HF/death and all-cause mortality in CRT-D patients with LBBB [30]. Therefore, we also compared the number of viable LVPSs provided by the Quartet™ leads and the bipolar equivalents when only considering the True Bipolar configurations. We found that although a bipolar lead could provide a second viable LVPS in 70.8% of the patients at pre-discharge, it failed to provide a second LVPS when only considering the True Bipolar configurations. By contrast, the Quartet™ lead still provided a second LVPS in at least half the patients when only considering the True Bipolar configurations.

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Multipoint LV pacing in a single coronary sinus (CS) branch from a quadripolar LV lead is another strategy to improve CRT response and LV function [32,32]. However, LV capture threshold and phrenic nerve stimulation thresholds vary over time [33]. A recent study involving 22 subjects receiving multipoint LV pacing found that during a 3-month follow-up 4.5% (1/22) of patients were reprogrammed to conventional biventricular pacing because of a lack of sufficient viable LVPSs [32]. In the present study, no significant differences on LVPSs were found between pre-discharge and 3-month follow-up, emphasizing that long-term multipoint LV pacing can be achieved.

Limitations

A number of potential limitations need to be mentioned. First, this was a single-center study with a relatively small number of patients and 3-month follow-up period. The results in the first 3 months after implant will need to be reassessed at longer-term follow-up in larger series. Second, our analysis comes from comparisons of Quartet™ lead with its bipolar modeled equivalents, rather than a real bipolar lead, so the finding of superiority of Quartet™ leads over conventional bipolar leads should be interpreted with caution. Finally, the study included data from a single quadripolar lead design because the Quartet™ lead was the only commercially available quadripolar LV lead in China at the time data were collected. As a result, our analysis was limited to the pacing vectors available for the Quartet™ lead, which uses only M2, P4, and the RV coil as anode. The results of this study may not be applicable to other quadripolar lead designs introduced later to the market.

Conclusions

Compared with the bipolar equivalent, the Quartet™ quadripolar LV lead provides more viable LVPSs and opportunities for CRT optimization and, potentially, multipoint LV pacing. The number of LVPSs provided by Quartet™ leads remained unchanged between pre-discharge and 3-month follow-up.

Conflict of interest

The authors declare that they have no conflict of interest.

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