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CLINICAL RESEARCH

The use of multisite left ventricular pacing via quadripolar lead improves acute haemodynamics and mechanical dyssynchrony assessed by radial strain speckle tracking: initial results

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Aims The objective of the present study was to evaluate the effect of multipoint pacing (MPP) on acute haemodynamics, cardiac contractility, and left ventricle (LV) dyssynchrony, in comparison with conventional cardiac resynchronization therapy (CRT).

Methods and results An open-label, non-randomized, single-centre, prospective study was designed. Twenty-seven consecutive patients were included. Evaluation of pacing configurations was performed in a random order. Transthoracic echocardiography was used to obtain haemodynamic and dyssynchrony parameters. Left ventricular ejection fraction (LVEF) was significantly superior in MPP compared with baseline (38.4 ± 1.8% vs. 26.1 ± 2.2%; $P < 0.001$), and in conventional pacing configuration compared with baseline (33.2 ± 1.8% vs. 26.1 ± 2.2%; $P = 0.007$). Cardiac index (CI) was increased by 21.8 ± 5.4% and 34.7 ± 5.1% in conventional and MPP configurations, respectively ($P = 0.19$). Percentage of acute responders (CI increase ≥10%) was 62.9 and 85.2% in conventional and MPP, respectively ($P < 0.001$). LV dyssynchrony was defined by radial strain rate parameters. Baseline anteroseptal-to-posterior wall time delay was 168 ± 21 ms. It was reduced until 70.4 ± 29 ms in conventional and −6.6 ± 11 ms in MPP (conventional vs. baseline $P = 0.04$; MPP vs. conventional $P = 0.05$). Standard deviation of the time-to-peak radial strain of the 6 LV basal segments was 101 ± 9.7, 80.3 ± 9.2, and 66 ± 8.03 ms in baseline, conventional, and MPP configurations, respectively (MPP vs. basal $P = 0.012$). Finally, we observed a positive correlation ($r = 0.69$) between reduction in dyssynchrony and CI increase ($P < 0.0001$).

Conclusion MPP showed a further reduction in LV dyssynchrony compared with conventional biventricular pacing. Moreover, MPP resulted in an additional improvement in LVEF and in CI, and this was translated into a higher number of acute responders to CRT.

Keywords Cardiac resynchronization • Multisite pacing • Dyssynchrony • Speckle tracking echocardiography

Introduction

Cardiac resynchronization therapy (CRT) is a well-accepted therapy for patients with heart failure (HF), left ventricular (LV) systolic dysfunction, and QRS prolongation. Biventricular pacing is associated with an improved quality of life, increased functional capacity, reduction in hospitalization for HF, and increased survival.[1,2] Unfortunately, a significant proportion of patients (up to 30–35%) do not respond to CRT therapy ('non-responders') adversely affecting the utility and cost-effectiveness of this form of device therapy for HF.[3] There are many suggested reasons for an inadequate response to CRT therapy such as persistence of LV dyssynchrony after CRT,

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What's new?

- The study shows the benefits of multipoint pacing (MPP) in cardiac haemodynamics in comparison with conventional cardiac resynchronization therapy (CRT). For the first time, the analysis has been performed using echocardiography unlike previous studies that used invasive haemodynamics.
- This is the first study that proposes radial strain speckle tracking to study LV dyssynchrony in a MPP cohort. In the study, MPP showed a further reduction in LV dyssynchrony compared with conventional biventricular pacing.
- The higher haemodynamic response and further reduction in dyssynchrony with MPP were associated to a greater number of acute responders to CRT.
- Finally, we observed an interesting association between higher reduction in mechanical dyssynchrony and further improvement in haemodynamics with MPP.

phrenic nerve stimulation, lead dislodgement, or suboptimal programming of device.

The search for alternatives to CRT non-responders has led several groups to examine the effect of multisite left ventricular stimulation with the requirement of placement of another pacing lead.[4] First results from these studies suggest a positive effect on left ventricular ejection fraction (LVEF) and LV volumes.[4]

The quartet lead (St. JudeMedical, Inc., Sylmar, CA, USA) is a quadripolar LV lead that with a compatible generator (Quadra Assura, St. JudeMedical, Inc.) allows multisite pacing in LV through two independent pacing pulses to the electrodes of the lead, potentially capturing a larger area of the LV along a single coronary sinus (CS) branch. Recently, benefits in acute haemodynamics[4,5] and echocardiographic measures of contractility[6] (radial strain) have been demonstrated with multipoint pacing (MPP) delivered via the quartet lead.

Radial strain evaluated by speckle-tracking analysis has been identified as a LV dyssynchrony marker and a predictor to CRT response in conventional biventricular pacing.[7] Nevertheless, the effect of MPP in dyssynchrony parameters of radial strain speckle tracking and its relationship with haemodynamic changes have not been established yet.

The objective of the present and initial study was to evaluate the effect of MPP on acute haemodynamics, cardiac contractility, and LV dyssynchrony assessed with 2D radial strain speckle tracking in comparison with conventional CRT.

Methods

Population

An open-label, single-centre, prospective study was designed. Between December 2013 and May 2014, 27 consecutive patients who were implanted with a CRT device capable to perform MPP were prospectively included in the study. Patients were eligible to participate if they met all of the inclusion criteria and none of the exclusion criteria below.

Inclusion criteria were (i) indication for CRT-D implantation, as per current guidelines; (ii) age >18 years; and (iii) patients should be able to provide written informed consent.

Exclusion criteria were (i) patients with a life expectancy of <12 months, (ii) patients with permanent atrial fibrillation, (iii) patients who were or might potentially be pregnant, (iv) patient who had suffered any of the following in the 4 weeks prior to enrolment: acute coronary episode or coronary revascularization, and (v) patient who had primary valvular disease that has not been corrected.

The local Ethics Committee approved the study protocol, and all patients provided written informed consent to participation.

Device implantation

A biventricular pacemaker with implantable defibrillator was implanted. The biventricular device used was Quadra Assura ICD, St. Jude Medical, Inc. Right atrial and right ventricular leads were placed routinely. Following coronary venography, a LV lead (Quartet®, St. JudeMedical, Inc.) was inserted into the target vein located in the lateral or posterolateral wall of the left ventricle, where all the lead tips reached apical or mid-ventricular segments. The lead provides pace/sense capability from four electrodes (tip and three rings). The device evaluated in this study allows independent pacing from two electrodes of the quadripolar lead with multiple possible pacing vectors for each electrode and time delays between the right ventricle (RV) and the two LV pulses. The naming convention for the four LV electrodes, from distal tip electrode to proximal ring electrode, was D1, M2, M3, and P4.

At the implant, pacing vectors for, at least, three electrodes were tested for phrenic capture and capture thresholds. The vector with the best pacing parameters (more electrical LV delay within non-apical segments) and without phrenic capture was programmed as the final pacing configuration.[8] All devices were programmed in a conventional pacing configuration.

Protocol of the study

Haemodynamic evaluation was performed at first follow-up visit (3 months post-implant) to allow lead maturation and demonstration of stability while excluding implantation-related arrhythmias.

All patients were examined in the supine position in a silent environment to reduce the impact of sympathetic activation by external stimuli.

The first stage of the pacing protocol was a period of stabilization. The reference values of indexed stroke volume (iSV), cardiac index (CI), and LVEF were recorded 5 min after atrial pacing (AAI) at 90 b.p.m. In patients who were pacemaker dependent [upgraded from dual-chamber pacing (DDD)], DDD was programmed at 90 b.p.m.

Then, we proceeded to biventricular pacing stage of the protocol at 90 b.p.m. Firstly, QuickOpt™ (St. Jude Medical, Inc.) optimization method was used to provide sensed atrio-ventricular (AV) delay, paced AV delay, and inter-ventricular (VV) delay. Patients were evaluated according to two different LV pacing configurations in a random order. We compared the results from each patient obtained under standard biventricular pacing (conventional pacing) with those obtained during MPP, so each patient was his or her own control.

In conventional CRT, we evaluated the vectors using each of the four LV electrodes in extended bipolar configuration with the cathode in the LV and the RV coil used as anode. We chose the vector using the LV electrode with the longest left ventricular electric delay in relation with the beginning of the RV activation (Q-LV).[8] In all cases, this interval was ≥105 ms. Electrodes located in an apical area and those with phrenic nerve stimulation were excluded.

MPP was delivered following an anatomic strategy, by distal (D1) and proximal (P4) electrodes as a cathode in order to capture as larger area of the LV as possible. When this configuration has to be abandoned by high capture threshold (>2.5V@1 ms) or phrenic nerve stimulation, another configuration was chosen by using adjacent electrodes. The selection criterion was the maximum distance between the pacing electrodes.[5] AV and VV delays were provided by QuickOpt with a fixed delay of 10 ms between LV pacing sites.

After 5 min of stabilization, iSV, CI, and LVEF were determined. We defined an increase in CI >10% above baseline (i.e. without pacing) as a '*positive acute responder*' to CRT, according to data previously published.[9]

Echocardiographic image acquisition, haemodynamic, and dyssynchrony study

All echocardiographic studies were carried out by an experienced operator blinded to the mode of programming. IE33® imaging system equipped with an S5.1 transducer (Philips medical solutions, Eindhoven, the Netherlands) was used. The following parameters were obtained according to American Society of Echocardiography guidelines: (i) LV end-diastolic volume (LVEDV), (ii) LV end-systolic volume (LVESV), and (iii) LVEF assessed by using biplane Simpson rule. Left ventricular outflow tract (LVOT)-velocity time integral (VTI) multiplied by the calculated two-dimensional (2D) area of LVOT was used to assess iSV and CI.

For radial strain speckle-tracking analysis, standard 2D basal and mid-LV short-axis images were acquired and analysed offline using available software QLAB® (Philips Medical Imaging, Eindhoven, the Netherlands). All images were recorded with a frame rate of >40 Hz. From an end-systolic frame, a region of interest was traced along the endocardial border, just within the endocardium. Particular care was taken to adjust tracking of all segments. A second larger concentric circle was then automatically generated and manually adjusted near the epicardium such that the area of interest included the entire myocardial wall. The width of the epicardial circle was either increased or decreased where necessary to account for variation in wall thickness. The image was then played so that tracking in the region of interest could be fine-tuned by visual assessment to ensure that all wall segments tracked appropriately throughout the cardiac cycle and that the sectors defining each wall segment were adjusted appropriately.

Radial strain analysis was performed in order to identify the site of the latest mechanical activation, to assess the sequence of LV mechanical activation, and to obtain markers of LV dyssynchrony.[10] The basal and mid-LV short-axis views were divided into six segments, and the time-to-peak radial strain was assessed for each segment. As a measure of regional LV activation, the time from Q-wave of the electrocardiogram (ECG) to peak radial strain of the 12 LV segments was measured and recorded. The latest activated segment was therefore identified.

Radial dyssynchrony by speckle-tracking strain was defined as the time-to-peak difference between the anteroseptal and posterior wall segmental peak strains (AS-P delay), *Figure 1*. An established cut-off value of 130 ms indicates significant LV radial speckle-tracking dyssynchrony, as previously described.[10] We finally measured the standard deviation of the time-to-peak radial strain of the six LV segments (RS-SD6).

Statistical analysis

Data was analysed using SPSS Statistics 18® (SPSS, Inc., Chicago, USA).

Mean ± standard deviation was reported for continuous data and frequencies and percentage for categorical data. In 10 randomly selected patients, haemodynamic and strain measurements were repeated in a blinded fashion by the same investigator to assess intra-observer variability.

First of all, we assessed normality of data distribution with Kolmogorov–Smirnov and Shapiro–Wilk tests. Then, ANOVA test was used to compare CI, iSV, LVEF, and their increase. Radial strain parameters were also compared with ANOVA test. The Levene test was used to test variance homogeneity. Finally, we used the Bonferroni correction to adjust for multiple comparisons and considered P-value < 0.05 significant. Student's t-test was used to compare strain parameters between acute haemodynamic responders and non-responders. Finally, Pearson's test was used to study the correlation between LV dyssynchrony defined by radial strain derived parameters and haemodynamic response to biventricular pacing.

Results

Patient demographics and electrical data

Final analysis was performed with 27 patients who met the inclusion criteria. The mean age was 65 ± 5 years, and the majority of patients (21, 78%) were men. Baseline characteristics of the study population are summarized in *Table 1*. The aetiology of HF was dilated cardiomyopathy in 16 patients (59%) and ischaemic cardiomyopathy in 11 (41%). All patients had HF symptoms consistent with New York Heart Association (NYHA) Class II (10, 37%), Class III (16, 59%), and ambulatory Class IV (1, 4%) at the time of CRT device implantation. More than 80% of patients were treated with beta-blockers and angiotensin-converting enzyme inhibitors. In all patients, ECG showed a left bundle branch block (LBBB) or a paced QRS with an average width of 165 ± 6 ms.

All patients had successful implantation of the LV lead. One patient (4%) presented a LV lead dislodgement occurred prior to haemodynamic evaluation that required reintervention. Periprocedural parameters are shown in *Table 2*. LV lead placement was lateral in 22 (81%) patients and posterolateral in 5 (19%) patients. All the lead tips reached apical or mid-ventricular segments. In conventional CRT, the electrode with the longest electric delay (Q-LV) was selected as a cathode of stimulation. The electrode used was D1 in 10 (37%) patients, M2 in 4 (15%) patients, M3 in 8 (29%) patients, and P4 in 5 (20%) patients.

Three months after implantation, 22 patients (78%) had improved their NYHA functional class.

For MPP vector combination selection, a combination of D1-RV and P4-RV was used in 23 (85%) patients, and a combination of M2-RV and P4-RV in 4 (15%) patients because of the presence of

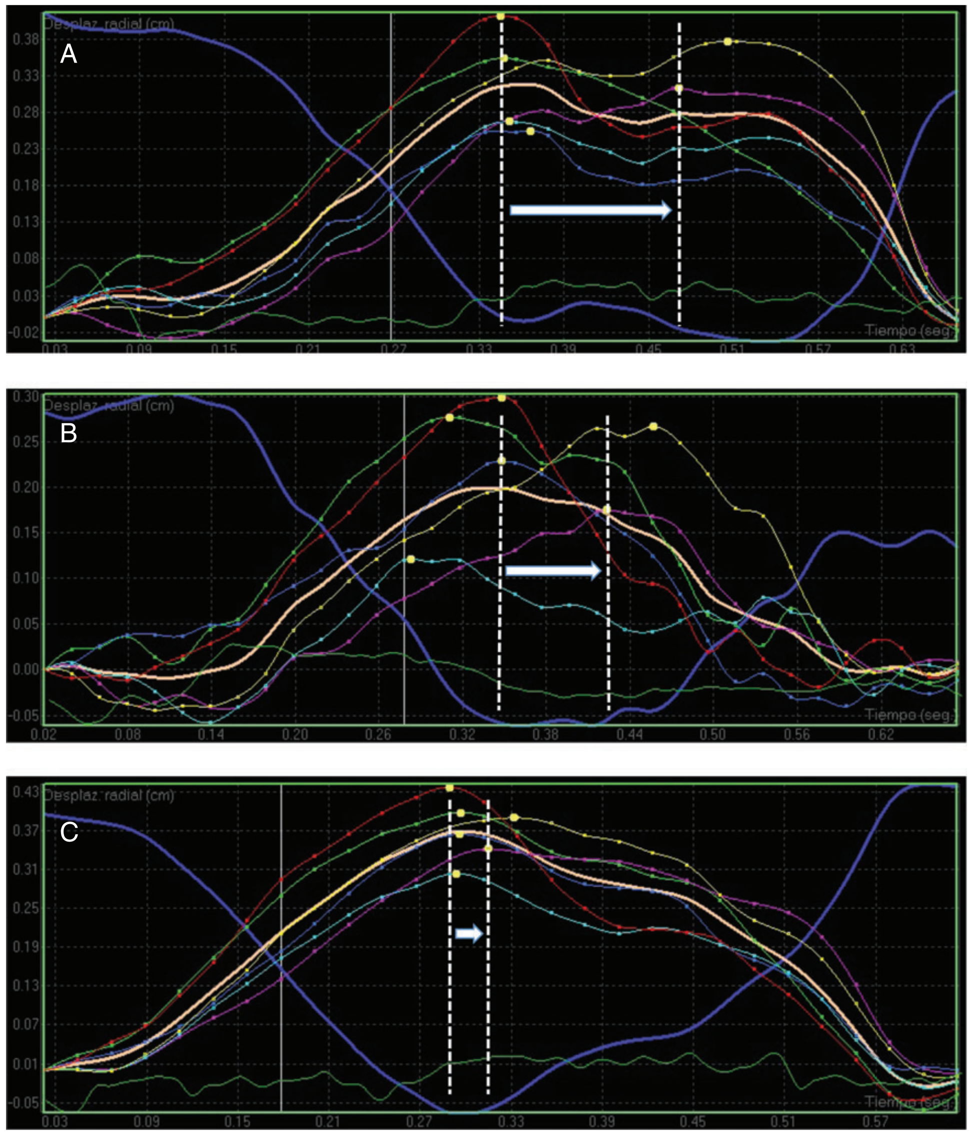

Figure 1 (representative figure) Example of LV dyssynchrony analysis from mid-ventricular short-axis views in a patient with LBBB. Dyssynchrony is shown as time difference (*white arrow*) between time-to-peak speckle-tracking radial strain in anterior septum (*red curve*) and posterior wall peak speckle-tracking strain (*purple curve*). (*A*) In baseline conditions, this patient exhibited significant LV dyssynchrony (QRS width 175 ms). Furthermore, there was a delayed mechanical activation of the posterior wall compared with the anteroseptum (AS-P delay 134 ms). (*B*) With conventional biventricular pacing configuration, a decrease in the value of LV dyssynchrony was showed (AS-P delay 80 ms). (*C*) With MPP configuration, a higher decrease in LV dyssynchrony was showed (AS-P delay 34 ms) by earlier mechanical activation of the posterior wall that is synchronized to the timing of mechanical activation of the anteroseptal wall.

phrenic nerve stimulation or high pacing threshold in D1-RV configuration.

Haemodynamic response according to LV pacing configuration

Haemodynamic data (CI) collected from all patients in basal conditions and after biventricular (conventional and multipoint) pacing are shown in *Figure 2A*. CI was 2.02 ± 0.17, 2.46 ± 0.21, and 2.72 ± 0.25 L/min/m^2 in baseline, conventional, and MPP configurations, respectively (P = ns). The mean increase in CI with regard to reference values conditions was 21.8 ± 5.4 and 34.7 ± 5.1% in conventional and MPP configurations, respectively (*Figure 3A*). It was significant only when comparing MPP and baseline condition ($P = 0.017$).

LVEF was significantly superior in MPP compared with baseline (38.4 ± 1.8% vs. 26.1 ± 2.2%; $P < 0.001$; *Figure 2B*) and in conventional CRT compared with baseline (33.2 ± 1.8% vs. 26.1 ± 2.2%; $P = 0.007$). Difference between conventional CRT and MPP did not reach statistical significance ($P = 0.2$). When comparing the increase in LVEF of each patient in conventional CRT and MPP with

Table 1 Baseline characteristics of the study population ($n = 27$)

Men, *n* (%)	21 (78)
Age (years)	65 ± 5
NYHA class	2.65 ± 0.16
II, *n* (%)	10 (37)
III, *n* (%)	16 (59)
IV, *n* (%)	1 (4)
Aetiology	
Ischaemic	11 (41)
Non-ischaemic	16 (59)
LVEF (%)	24.3 ± 1.8
Medical therapy	
ACE inhibitors, *n* (%)	23 (85)
β-Blockers, *n* (%)	24 (89)
Loop diuretics, *n* (%)	22 (81)
ARA, *n* (%)	13 (48)
QRS duration (ms)	165.6 ± 5.8
LBBB	23 (85)
Upgrading	4 (15)

NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; ACE, angiotensin converter enzyme; ARA, aldosterone receptor antagonist; LBBB, left bundle branch block.

Table 2 Implant details

Implant success	27 (100)
Duration (min)	80.25 ± 2.9
Time of fluoroscopy (min)	10 ± 1.5
LV lead position	
Lateral, *n* (%)	22 (81)
Posterolateral, *n* (%)	5 (19)
RV lead position	
Apical, *n* (%)	5 (19)
Septal, *n* (%)	22 (81)
RV lead threshold (V@0.5 ms)	0.55 ± 0.32
LV lead threshold (V@0.5 ms)	1.01 ± 0.13
LV pacing cathode	
D1, *n* (%)	10 (37)
M2, *n* (%)	4 (15)
M3, *n* (%)	8 (29)
P4, *n* (%)	5 (19)
PNS, *n* (%)	8 (29)
Pneumothorax, *n* (%)	0 (0)
Lead dislocation, *n* (%)	1 (4)

LV, left ventricle; RV, right ventricle; PNS, phrenic nerve stimulation.

regard to baseline, we found an increase of 33.1 ± 7% ($P = 0.03$) and 50.4 ± 9% ($P < 0.0001$), respectively (*Figure 3*B).

Percentage of acute haemodynamic responders to CRT (increase in CI > 10%) was superior in MPP configuration than in conventional LV pacing configuration (62 ± 9% vs. 85.2 ± 7%, $P < 0.001$, *Figure 4*).

LV dyssynchrony parameters derived from radial strain

Analysis of radial strain data for intra-observer variability showed an excellent agreement. Intra-class correlation coefficients were 0.92 (0.89–0.95) and 0.93 (0.91–0.95) for time to peak of anteroseptal and posterior segments, respectively, and 0.93 (0.9–0.96) for RS-SD6.

Radial strain assessed by speckle tracking was used to assess LV dyssynchrony. Time to peak in posterior segment was 473.4 ± 17, 384.45 ± 16, and 289.3 ± 21 ms in baseline, conventional CRT, and MPP configurations, respectively. We found statistical significance when comparing MPP vs. baseline condition ($P < 0.001$), conventional CRT vs. baseline condition ($P = 0.003$), and conventional CRT vs. MPP ($P = 0.002$), *Figure 5A*.

We calculated the difference between time-to-peak strain of the anteroseptal and posterior segments (AS-P delay). AS-P delay was 168.6 ± 21, 70.4 ± 29, and −6.6 ± 11 ms in baseline, conventional CRT, and MPP configurations, respectively (conventional CRT vs. baseline $P = 0.04$; MPP vs. basal $P < 0.001$; MPP vs. conventional CRT $P = 0.05$), *Figure 5B*. The change in AS-P delay was 69.4 ± 30% in conventional CRT and 123.9 ± 23% in MPP configurations.

Standard deviation of the time-to-peak radial strain of the 6 LV basal segments (RS-SD6) was obtained; RS-SD6 was 101 ± 9.7, 80.3 ± 9.2, and 66 ± 8.03 ms in baseline, conventional CRT, and MPP configurations, respectively (conventional vs. baseline $P = 0.34$, MPP vs. baseline $P = 0.012$).

Correlation between LV dyssynchrony parameters and haemodynamic response

We compared sequences of LV mechanical activation in acute haemodynamic responders and in non-responders. In particular, acute responders experienced LV resynchronization (AS-P delay 30.5 ± 19 ms in acute responders group vs. 112.2 ± 30 ms in non-responders group; $P = 0.071$) in relation to an earlier activation of the posterior segment (328 ± 97 vs. 389 ± 100 ms to peak strain; $P = 0.08$).

Finally, we studied the correlation between LV dyssynchrony and haemodynamic response. We found a positive correlation of 0.69 between mean per cent change in AS-P delay and the relative increase in CI, which showed statistical significance ($P = 0.001$, *Figure 6*).

Discussion

The present and initial study is the first comprehensive evaluation with radial strain speckle tracking to assess LV dyssynchrony in a cohort of MPP CRT patients. We also studied haemodynamic response associated with MPP. The main findings of this study are that in comparison with conventional CRT: (i) MPP decreased further the LV dyssynchrony measured by radial strain rate, (ii) MPP resulted in a higher improvement in LVEF and CI, (iii) this was translated into a higher number of acute responders to CRT, and finally,

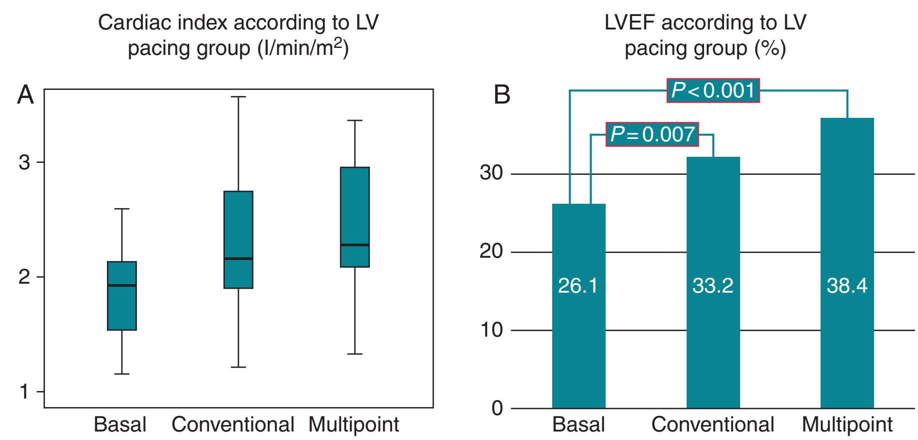

Figure 2 (*A*) Haemodynamic evaluation expressed by CI with regard to pacing configuration (baseline, conventional, and MPP). (*B*) LVEF according to pacing configuration. Comparison of different study groups in relation to the measurements obtained in the non-paced state.

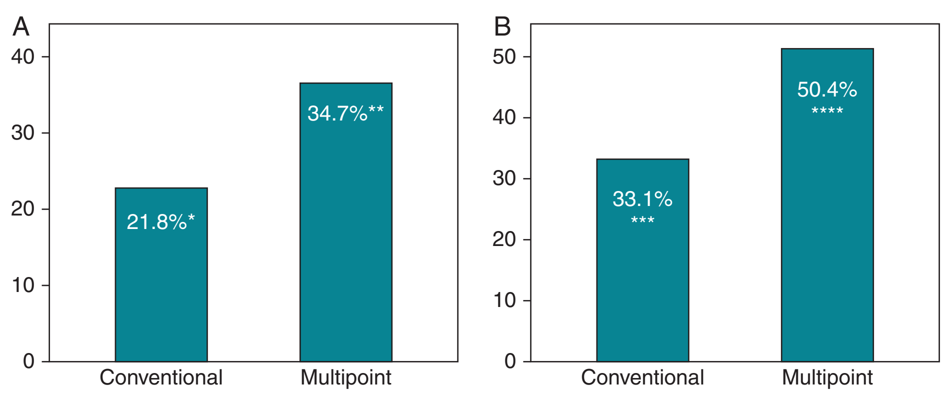

Figure 3 Mean per cent change in CI (*A*) and in LVEF (*B*) between the different biventricular pacing configurations in relation to baseline measurements. $*P$ = NS, $**P = 0.017$, $***P = 0.03$, and $****P < 0.0001$.

(iv) an association was observed between higher reduction in dyssynchrony and further improvement in haemodynamics.

The usefulness of CRT in patients with systolic HF and electromechanical dyssynchrony is well established. Unfortunately, a significant proportion of patients do not respond to CRT adversely affecting the utility and cost-effectiveness of this therapy for HF.[3] Suboptimal LV lead position and persistent mechanical dyssynchrony despite correct biventricular pacing have been some of the reasons suggested to explain the absence of response to CRT. Several reports have indicated that there is an important variability in the ventricular activation pattern, the region of maximal electrical delay, and the distribution of mechanical dyssynchrony, even in LBBB patients.[11,12] In addition, the presence of lines of functional conduction block in the LV can induce slow conduction of the electrical wavefront, limiting the ability of a lateral LV lead to reduce the mechanical dyssynchrony. Finally, in patients with ischaemic cardiomyopathy, the presence of transmural scars in the lateral wall may limit the benefit from CRT when pacing in vicinity.[12] As a consequence, intraventricular and inter-ventricular dyssynchrony could persist in 25–30% of patients during CRT.[13] Multisite LV pacing has been advocated to enhance the likelihood of response to CRT by stimulating and capturing a broader area of the LV. Theoretically, this mode of pacing could induce a more simultaneous activation of the LV. First studies using multiple leads in different coronary veins showed that multisite pacing was superior to conventional CRT pacing.[14] However, this technique has several potential drawbacks including early battery drain, the absence of suitable CS branches to cannulate and stimulate with adequate electrical parameters limiting the practical use of this technique in a significant proportion of patients. Recently, the introduction of quadripolar leads connected to a device with dedicated software has facilitated multipoint, single-branch pacing, with the introduction of a single lead. First studies with this new modality of LV pacing have reported benefits in terms of haemodynamic improvement in comparison with conventional biventricular pacing.[4,5]

Consistently with previous series, our study offers new evidence in relation to benefits of MPP for CRT in a series of patients with systolic HF. MPP delivered from a single CS branch improved LV function and haemodynamic as demonstrated by greater improvement in LVEF and in CI in comparison with conventional pacing. Activation of MPP was associated to an immediate increase in LVEF of 12 absolute points on average in comparison with baseline LVEF and an increase of 35% in CI, values that doubled those obtained with conventional pacing. These results offered a responder rate to CRT (considering improvement of 10% in CI) of 63 and 85% for conventional pacing vs. MPP.

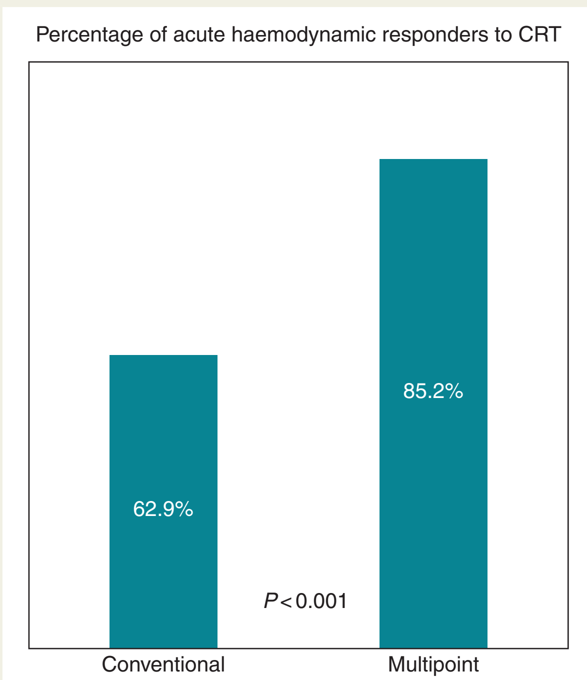

Figure 4 Acute responder rates to CRT (considered by a 10% improvement in CI) categorized by biventricular pacing configuration.

If this improvement will be translated into follow-up, clinical benefits are a question that remains elusive. Evidence for a strong relation between acute haemodynamics response and long-term outcome is sparse with conflicting results. In an invasive haemodynamic study from Duckett *et al.*,[15] a greater increase than 10% in dP/dt_{max} was associated with a clinical improvement as well as reverse remodelling. De Roest *et al.*[16] showed that long-term echocardiographic responders demonstrated a significant acute improvement in pump function compared with baseline, whereas long-term non-responders showed no acute improvement compared with baseline.

The current study has shown, for the first time, that MPP reduces dyssynchrony evaluated by radial strain speckle tracking more than conventional pacing. It has been reported that radial strain measurements can provide a reliable measurement of LV dyssynchrony and LV mechanical activation sequence in patients with HF.[17] Moreover, radial strain speckle tracking could predict midterm LV reverse remodelling and long-term outcomes after CRT.[7]

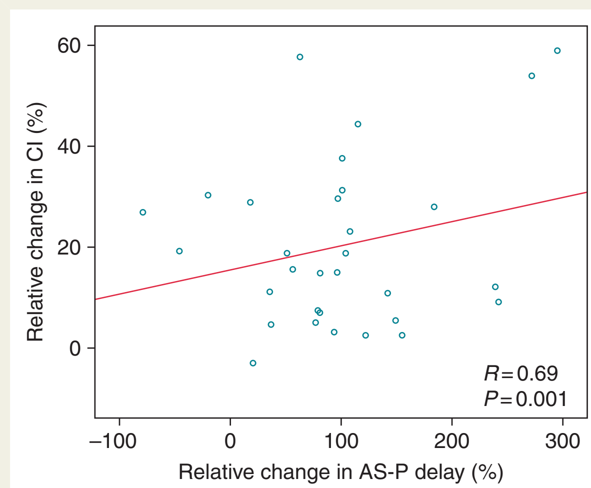

Figure 6 Correlation between mean per cent reduction in LV dyssynchrony (AS-P per cent change) and mean per cent haemodynamic change (CI per cent increase).

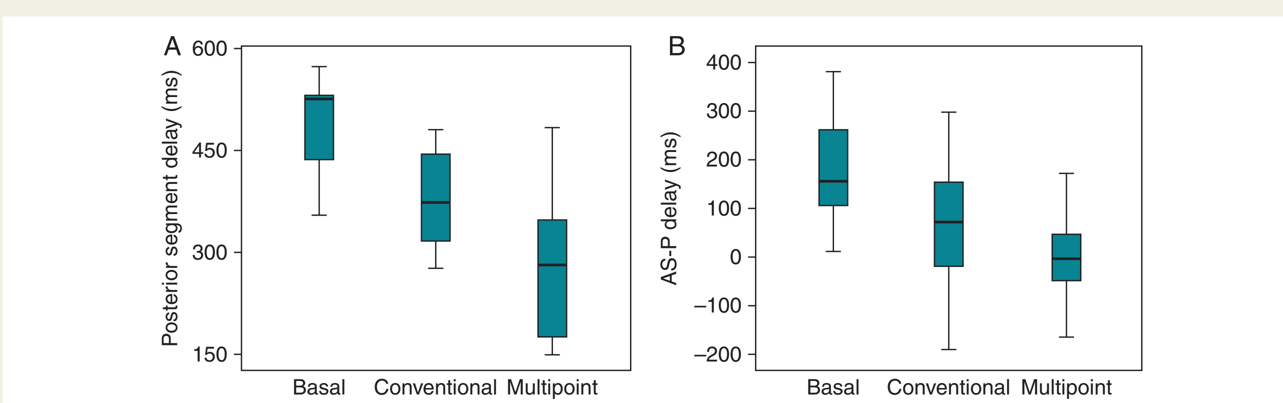

Figure 5 (*A*) Mean time-to-peak radial speckle-tracking strain in posterior wall segment in baseline condition, conventional, and MPP configurations. (*B*) LV dyssynchrony (AS-P delay) in baseline condition, conventional, and MPP configurations.

Patients evaluated in our study had a baseline mean peak strain delay of 168 ms indicating a significant LV dyssynchrony. Importantly, MPP acutely decreased dyssynchrony indexes higher than conventional pacing. If this additional reduction in LV dyssynchrony may have prognostic implications is also speculative. In a study using colour-coded Tissue Doppler Imaging, Bleeker *et al.*[18] reported that immediately post-implantation, responders to CRT (>10% reduction in LVESV) showed a significant reduction in LV dyssynchrony, while non-responders did not show a significant reduction in LV dyssynchrony. In 121 patients with HF treated with a CRT device, Imanishi *et al.*[19] showed that an acute reduction of >33% in LV dyssynchrony was associated to a greater survival free of HF hospitalizations and mortality.

Finally, we observed an important correlation between reduction in LV dyssynchrony and the relative increase in CI. This observation supports the suggested mechanism of the therapeutic benefit of CRT in HF patients as the correction for mechanical dyssynchrony.[20] MPP, by capturing a larger area of the LV and normalizing the propagation wavefront around the pacing sites including areas of slow conduction or scar tissue, would reduce further the dyssynchrony in LV activation, and this would be followed by a higher improvement in CI and in LVEF.

The observed acute effects of MPP in haemodynamics together with the higher ability of MPP in reducing acutely dyssynchrony could have important implications for patients with poor response to CRT as many ischaemic patients and may allow speculating a positive long-term impact in HF patients outcomes.

Study limitations

Our study has several limitations; first, it is a single-centre, non-randomized study of a relatively small number of patients. In fact, the failure to demonstrate significant differences in some comparisons between conventional group and baseline conditions and between conventional and MPP configurations is likely due to the small study population. Second, this is an acute study. Although the results are important and significant in favour to MPP, it is not possible to assume that they will be translated into long-term clinical benefits. Third, All haemodynamic measurements were conducted in the supine position at rest; thus, no information is available under exercise conditions. Only well-designed, prospective, and randomized clinical trials will confirm the question if MPP will improve morbidity and mortality of HF patients.

Conclusion

To our knowledge, this is the first study that proposes radial strain speckle tracking to study LV dyssynchrony in a MPP cohort. MPP showed a further reduction in LV dyssynchrony compared with conventional biventricular pacing. Moreover, MPP resulted in an additional improvement in LVEF and in CI, and this was translated into a higher number of acute responders to CRT. Finally, we observed an association between higher reduction in mechanical dyssynchrony and further improvement in haemodynamics with MPP. Ongoing studies are evaluating if these acute benefits translate to a better medium- to long-term outcomes for CRT patients.

Conflict of interest: none declared.

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