Effect of Concordance between Sites of Left Ventricular Pacing and Dyssynchrony on Acute Electrocardiographic and Echocardiographic Parameters in Patients with Heart Failure Undergoing Cardiac Resynchronization Therapy

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Summary

Background: Wide QRS complexes are associated with left ventricular (LV) dyssynchrony, but an optimal site of LV pacing has not been established.

Hypothesis: We hypothesized that concordance between the sites of LV pacing and of latest LV mechanical activation during cardiac resynchronization therapy (CRT) is associated with more favorable acute echocardiographic changes.

Methods: An analysis of 28 consecutive patients (64 ± 15 years, 46% male, 52% ischemic heart disease, LV ejection fraction 0.24 ± 0.07 , QRS 163 ± 22 ms, New York Heart Association ≥ 3 93%) implanted with biventricular (BIV) defibrillators was performed. Sites of latest LV activation were determined by tissue Doppler imaging (TDI) and speckle tracking (ST). The site of LV pacing was determined by fluoroscopy in two views. A concordance score (0–5) was created to describe the proximity of the pacing site to the site of the latest mechanical activation.

Results: Compared with the worst concordance score, a perfect score was associated with shorter QRS width with LV (187 ± 40 vs. 246 ± 8 ms, $p = 0.048$) and BIV (134 ± 19 ms vs. 179 ± 39 ms, $p = 0.05$) but not with right ventricular pacing. A perfect concordance score was also associated with a greater

acute reduction in LV volumes in systole (42 ± 36 vs. 16 ± 22 ms, $p = 0.068$) and diastole (47 ± 37 vs. 8 ± 31 ml, $p = 0.043$) 24 h after CRT device implantation.

Conclusions: A high concordance is associated with shorter QRS width with LV and BIV pacing and greater acute reduction in LV volumes. The effect of concordance on the intermediate and long-term response to BIV pacing deserves further evaluation.

Key words: concordance, left ventricular dyssynchrony, cardiac resynchronization therapy, speckle tracking, QRS width

Introduction

Prolongation of the QRS complex on the surface electrocardiogram (ECG) (≥ 120 ms) occurs in about 14 to 47% of patients with heart failure (HF)^{1–3} and is associated with worse left ventricular (LV) myocardial function and increased all-cause mortality.^{4–11}

Despite the fact that previous studies have shown that the width of the QRS complex at baseline does not reliably predict the clinical response to cardiac resynchronization therapy (CRT), and that the degree of QRS narrowing after CRT does not correlate with hemodynamic or clinical improvement,¹² QRS width ≥ 120 ms remains one of the qualifying criteria for CRT. Still, only about 70% of patients with HF seem to benefit from this therapy.^{13–17} Mechanical LV dyssynchrony is best characterized by the novel echocardiographic techniques of tissue Doppler imaging (TDI) and speckle tracking (ST) and seems to be superior to QRS width in predicting response to CRT.^{18,19}

There is a paucity of data on the effect of the pattern of LV mechanical activation in relation to the site of LV pacing on the response to CRT. Therefore, the primary aim of this study was to determine the effect of concordance between sites of latest LV mechanical activation and LV pacing on the acute echocardiographic findings in patients with HF undergoing CRT. The

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Received: June 28, 2006

Accepted with revision: August 11, 2006

secondary aim was to assess the effect of concordance on ECG findings during biventricular (BIV), LV, and right ventricular (RV) pacing.

Methods

Population

Twenty-eight consecutive patients implanted with a CRT-defibrillator (CRT-D) for standard indications at the University of Pittsburgh Medical Center were included in this analysis. The patients' electronic medical records and cardiac electrophysiology clinic records were analyzed for baseline demographics, ECG data, clinical characteristics including New York Heart Association (NYHA) class of HF, LV ejection fraction (LVEF), underlying heart disease, indication for CRT-D implantation, medications, and associated medical conditions.

Cardiac Resynchronization Therapy-Defibrillator Implantation

A CRT-D was implanted with standard right atrial and RV lead positions. The ventricular lead was placed at the RV apex in all patients. The LV pacing lead was inserted transvenously via the subclavian route. The implantation technique, type of LV lead, and manufacturer of the CRT-D were left to the discretion of the implanting physician. The LV lead was successfully implanted in an anterolateral ($n = 11$), lateral ($n = 7$), posterolateral ($n = 7$), or posterior ($n = 2$) site as determined by fluoroscopic imaging in the left anterior oblique view. In one patient, an LV lead could not be successfully implanted. QRS width was measured at baseline and during LV, RV, and BIV pacing at the time of device implantation.

Tissue Doppler Imaging and Speckle Tracking

As previously described,^{18, 20–26} patients had routine echocardiographic, tissue Doppler, and ST studies prior to and 24 h post CRT (Vivid 7 GE-Vingmed, Horten, Norway). Complete echocardiographic data were available in 21 patients prior to and after CRT. Sites of latest LV mechanical activation by ST were anterolateral ($n = 6$), lateral ($n = 3$), posterolateral ($n = 8$), and posterior ($n = 11$). Determination of LV lead positions and sites of latest LV mechanical activation by ST were determined independently by blinded observers.

Concordance Score

A concordance score between the site of LV pacing and the site of latest LV mechanical activation was developed. The LV was divided into four areas in the left anterior oblique view (anterolateral, lateral, posterolateral, and posterior) (Fig. 1), and into three areas in the right anterior oblique view (basal, mid, and apical). The concordance score was defined as the sum of the scores in these two views. The scores for each view are shown in Table I. In brief, in the left anterior oblique view, if the pacing site coincided with the site of latest mechanical activation, a score of 3 was given. This score was reduced by

FIG. 1 Classification of the regions of left ventricular lead placement and mechanical activation adopted in this study. In the left anterior oblique view of the coronary sinus vasculature, the regions were divided into anterolateral, lateral, posterolateral, and posterior zones. Of note, the left ventricular regions were further divided into basal, mid, and apical zones in the right anterior oblique views. The position of the lead was determined according to the location of its pacing tip.

1 point if the pacing site was adjacent to the site of latest mechanical activation, by 2 points if one zone separated the 2 sites, and by 3 points (score of 0) if 2 zones separated the sites. Similarly, in the right anterior oblique view, the scores ranged from 0 to 2. The concordance score, therefore, ranged from 0 (complete discordance) to 5 (perfect concordance).

Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Sciences 14.0 (SPSS Inc., Chicago, Ill., USA). Continuous variables were expressed as mean $\pm$ standard deviation or median depending on the assumption of normality of the variable. Categorical variables were reported as percentages. Chi-square analysis was used to compare each variable in the groups and one-way analysis of variance was performed for more than two-group analyses with least significant difference post hoc test. Pearson's correlation coefficient "r" was used as a measure of linear association between two variables. P values ≤ 0.05 were considered statistically significant.

TABLE I Concordance score between sites of left ventricular pacing and latest mechanical activation defined by its left anterior oblique (LAO) and right anterior oblique (RAO) components

LAO view	LAO score	RAO view	RAO score
Same site	3	Same site	2
1 Site off	2	1 Site off	1
2 Sites off	1	2 Sites off	0
3 Sites off	0		

Concordance score = LAO score + RAO score.

TABLE II Baseline characteristics of patients population grouped by site of latest left ventricular mechanical activation

	Lateral wall (n = 9)	Posterior wall (n = 19)
Age (years)	64 ± 13	65 ± 16
Male gender (%)	44	47
NYHA		
Class 2 (%)	0	10
Class 3 (%)	89	63
Class 4 (%)	11	27
Serum sodium	141 ± 4	140 ± 2
Serum creatinine	1.0 ± 0.2	1.2 ± 0.4
LBBB (%)	89	95
Coronary disease (%)	44	53
Ace inhibitors (%)	89	90
Beta blockers (%)	78	74
Class III drugs (%)	18	13
Diabetes mellitus (%)	44	42
Dyslipidemia (%)	78	74
LVEF (%)	25 ± 8	23 ± 7

Abbreviations: NYHA = New York Heart Association, LBBB = left bundle-branch block, ACE = angiotensin-converting enzyme, LVEF = left ventricular ejection fraction.

Results

Baseline Demographics

Twenty-eight consecutive patients (64 ± 15 years, 46% male, 52% with ischemic heart disease, LVEF 0.24 ± 0.07, QRS 163 ± 22 ms, 93% with NYHA HF class ≥ 3) received a CRT-D and underwent echocardiography with TDI and ST at the University of Pittsburgh. Table II shows the baseline demographics for the cohort of patients divided by site of latest LV mechanical activation as determined by ST. For the purpose of this analysis, the sites were grouped into two categories: lateral (anterolateral and lateral) and posterior (posterolateral and posterior). Although not based on physiologic criteria, this categorization divides the coronary sinus territory into two equal regions in the left anterior oblique view. There were no significant differences noted in this patient population with regard to age, gender, medications, etiology, or severity of HF by site of latest mechanical activation.

Latest Mechanical Activation and Electrocardiographic Parameters

QRS duration at baseline was compared with sites of latest mechanical activation by ST (lateral vs. posterior). The baseline QRS was significantly greater if the site of latest activation was in the lateral wall compared with the posterior wall (176 ± 11 vs. 156 ± 24 ms, $p = 0.024$).

A lateral site of latest LV mechanical activation by ST was associated with a trend toward more longitudinal dyssyn-

TABLE III Measures of longitudinal and radial left ventricular dyssynchrony by site of latest mechanical activation

	Lateral wall	Posterior wall	p Value
Radial TDI before CRT	199 ± 157	216 ± 130	NS
Radial TDI after CRT	68 ± 47	102 ± 76	NS
Change in radial TDI	163 ± 116	91 ± 175	NS
Longitudinal TDI before CRT	238 ± 136	152 ± 89	0.055
Longitudinal TDI after CRT	135 ± 100	99 ± 75	NS
Change in longitudinal TDI	52 ± 103	49 ± 118	NS

Abbreviations: TDI = tissue Doppler imaging, CRT = cardiac resynchronization therapy, NS = not significant.

chry by TDI (238 ± 136 vs. 152 ± 89 ms, $p = 0.055$), but with no significant differences in other measures of longitudinal or radial TDI before or after CRT (Table III).

Concordance

A higher concordance score was associated with narrower QRS width with LV ($r = -0.47$, $p = 0.014$, Fig. 2A) and BIV ($r = -0.51$, $p = 0.007$, Fig. 2B), but not RV ($r = -0.17$, $p = 0.387$) pacing. Compared with the worst concordance score (score = 1), a perfect score (score = 5) was associated with shorter QRS width with LV (187 ± 40 vs. 246 ± 8 ms, $p = 0.048$) and BIV (134 ± 19 vs. 179 ± 39 ms, $p = 0.05$, Fig. 3) but not RV (198 ± 25 vs. 206 ± 28 ms, $p = 0.80$) pacing. A perfect concordance score was also associated with a greater acute reduction in LV volumes in systole (42 ± 36 vs. 16 ± 22 ms, $p = 0.068$) and diastole (47 ± 37 vs. 8 ± 31 ml, $p = 0.043$, Fig. 4).

Discussion

The findings in this study demonstrate that the more concordant the sites of latest LV mechanical activation and LV pacing, the narrower the width of the QRS complex with LV and BIV pacing, and the greater the acute reduction in LV volumes 24 h after CRT. The correlation of the concordance score with the QRS width on the surface ECG is of mechanistic interest but has minimal clinical implications.

Short-term studies have suggested that the lateral wall is a preferred site of LV stimulation to achieve effective CRT.^{27–29} However, this choice may be limited by technical difficulties such as high capture thresholds, unfavorable coronary venous anatomy, phrenic nerve stimulation, or lead instability. Gasparini *et al.* showed that a 99% implantation success rate was achieved by positioning the LV leads in the septal region when the lateral LV wall could not be effectively paced.²⁷ Ansalone *et al.* showed that in >40% of patients evaluated with TDI, the anterior portion of the left ventricle is most delayed and is therefore suitable, at least theoretically, for LV lead placement.²⁸ Ansalone *et al.* further suggested that synchronous BIV pacing can reduce the interventricular de-

FIG. 2 Correlation of concordance score with the QRS width with left ventricular (LV) (A) and biventricular (BIV) (B) pacing.

FIG. 3 Bar graph of the QRS duration with biventricular (BIV) pacing as a function of the concordance score.

FIG. 4 Bar graph of the reduction in left ventricular end-diastolic volume (LVEDV) after biventricular pacing as a function of the concordance score. CRT = cardiac resynchronization therapy.

lay caused by bundle-branch block in patients with HF, but one-third of the patients remain nonresponders, probably because of a persistent left intraventricular dyssynchrony. This dyssynchrony, which is evaluated by TDI, may be secondary to discordance between the sites of LV pacing and mechani-

cal activation.²⁹ In this study, the authors hypothesized that this discordance could result in a lack of response after CRT. Conversely, concordance may result in better hemodynamic changes and improved intraventricular resynchronization.²⁸

Our data suggest that the site of LV pacing is an important determinant of the width of the QRS complex and of the acute echocardiographic response after CRT. We have introduced in this study a new scoring system for the level of concordance between LV latest activation and pacing sites. We demonstrate a dose-dependent decrease in QRS width with BIV and LV pacing as the concordance score increases. Acute echocardiographic benefits after CRT seem to require a more stringent definition of concordance, since only the highest concordance score (score = 5) predicted a greater acute reduction in end-systolic and end-diastolic LV volumes 24 h after CRT.

Limitations

First, this is an acute study looking at the importance of pacing the left ventricle at the site of latest mechanical activation in predicting acute echocardiographic response. No information is available from our dataset on the long-term clinical significance of our findings in patients with end-stage HF. Second, determining the optimal pacing site does not necessarily translate into being able to pace chronically at that site. Our current study does not address the feasibility of targeting specific areas for LV lead positioning during CRT device implantations. Finally, the number of patients included in this analysis is relatively small, and confirmation of our results in a larger cohort of patients is needed.

Conclusion

We introduce in this study a new scoring system for the level of concordance between the sites of latest LV activation and pacing. This concordance score is associated with narrower QRS complexes during LV and BIV pacing and predicts favorable acute echocardiographic response to CRT.

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