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Relationship between QRS complex notch and ventricular dyssynchrony in patients with heart failure and prolonged QRS duration

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Abstract

Background: *Cardiac resynchronization therapy (CRT) has been accepted as an established therapy for advanced systolic heart failure. Electrical and mechanical dyssynchrony are usually evaluated to increase the percentage of CRT responders. We postulated that QRS notch can increase mechanical LV dyssynchrony independently of other known predictors such as left ventricular ejection fraction and QRS duration.*

Methods: *A total of 87 consecutive patients with advanced systolic heart failure and QRS duration more than 120 ms with an LBBB-like pattern in V1 were prospectively evaluated. Twelve-lead electrocardiogram was used for detection of QRS notch. Complete echocardiographic examination including tissue Doppler imaging, pulse wave Doppler and M-mode echocardiography were done for all patients.*

Results: *Eighty-seven patients, 65 male (75%) and 22 female (25%), with mean (SD) age of 56.7 (12.3) years were enrolled the study. Ischemic cardiomyopathy was the underlying heart disease in 58% of the subjects, and in the others it was idiopathic. Patients had a mean (SD) QRS duration of 155.13 (23.34) ms. QRS notch was seen in 49.4% of the patients in any of two precordial or limb leads. Interventricular mechanical delay was the only mechanical dyssynchrony index that was significantly longer in the group of patients with QRS notch. Multivariate analysis revealed that the observed association was actually caused by the effect of QRS duration, rather than the presence of notch* per se.

Conclusions: *QRS notch was not an independent predictor of higher mechanical dyssynchrony indices in patients with wide QRS complex and symptomatic systolic heart failure; however, there was a borderline association between QRS notch and interventricular delay.* (Cardiol J 2008; 15: 351–356)

Key words: QRS notch, mechanical dyssynchrony, cardiac resynchronization therapy, tissue Doppler echocardiography

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Condensed abstract

We postulated that QRS notch can increase mechanical LV dyssynchrony independently of other known predictors such as left ventricular ejection fraction and QRS duration. Patients with advanced systolic heart failure and QRS duration > 120 ms with an LBBB-like pattern in V1 were prospectively enrolled. QRS notch was seen in 49.4% of the patients. Interventricular mechanical delay was the only mechanical asynchrony index that was significantly longer in the group of patients with QRS notch. Multivariate analysis revealed that the observed association was actually caused by the effect of QRS duration, rather than presence of notch *per se*.

Introduction

Cardiac resynchronization therapy (CRT) has been accepted as an established therapy for patients with end-stage heart failure with the traditional following criteria: New York Heart Association (NYHA) class III–IV symptoms, depressed left ventricular ejection fraction (LVEF ≤ 35%) and QRS duration greater than or equal to 120 ms in the presence of optimal medical therapy [1]. Despite these criteria, approximately one-third of patients fail to respond to CRT [2, 3]. From 30% to 40% of heart failure patients with QRS duration > 120 ms do not exhibit mechanical left ventricular dyssynchrony, which may explain the non response to CRT [4]. Cardiac resynchronization therapy is a risky and expensive procedure, and we should reduce the number of nonresponders. QRS duration by itself may not adequately show left ventricular mechanical dyssynchrony [4]. One hypothesis is that QRS notch can reflect intraventricular conduction dispersion and/or delay, which may have an effect on mechanical dyssynchrony. We evaluated the effect of QRS notch on left ventricular dyssynchrony in a large group of patients with end-stage heart failure using Tissue Doppler echocardiography and prolonged QRS duration.

Methods

Study population

Between April 2005 and August 2007, a total of 87 consecutive patients with advanced heart failure were prospectively included. Inclusion criteria were as follow: NYHA class III–IV, severe left ventricular systolic dysfunction (LVEF < 35%) and QRS duration more than 120 ms.

The study was approved by the local Ethics Committee and written informed consent was obtained from all patients.

Electrocardiographic analysis

Resting 12-lead ECG (0.5–150 Hz, 25 mm/s, 10 mm/mV) was obtained for each patient. Patients with nonsinus rhythm, paced rhythm and/or non left bundle branch block (LBBB)-like pattern in ECG-V1 were excluded. Maximum QRS duration was recorded from the surface leads demonstrating the greatest values. We divided the patients into two groups, based on the presence of QRS notch. QRS notch, notching in the nadir of S wave or notching of R wave in at least two contiguous leads (Fig. 1) were analyzed by two independent readers blinded to echocardiographic data. In case of disagreement, the final diagnosis was achieved by mutual agreement.

Echocardiographic analysis

A complete M-mode, two-dimensional and tissue Doppler imaging (TDI) were performed using an ultrasonographic machine (Vivid 7, General Electric, Wauwatosa, WI, USA). Images were obtained using a 3.5 MHz transducer at a depth of 16 cm in the parasternal and apical views (standard long axis and two and four chamber views). Left ventricular end-systolic and diastolic dimensions and volumes and left ventricular ejection fraction were calculated using the biplane Simpson's technique. The echocardiographers measured the delay between the septum systolic motion and left posterior wall (septal-to-posterior wall motion delay [SPWMD]). This parameter is a global ventricular asynchrony index and calculated as the shortest interval between the maximal posterior wall displacement of the septum and the maximal displacement of the left posterior wall using a mono-dimensional short-axis view at the papillary muscle level [5]. The cut-off value was defined as more than 130 ms. The aortic pre-ejection time was obtained by pulse-wave Doppler recordings in apical five chamber view and calculated from the beginning of QRS complex to the beginning of the aortic flow velocity. The pulmonary pre-ejection time was measured from the beginning of QRS complex to the beginning of pulmonary flow velocity curve recorded in the left parasternal view. The difference between the two values was considered as the interventricular mechanical delay (IVMD); according to previous studies, an IVMD > 40 ms was selected as the cut-off value for interventricular dyssynchrony [6]. Colour TDI was used to obtain the apical views (four chambers and two chambers). Both the basal and mid segments

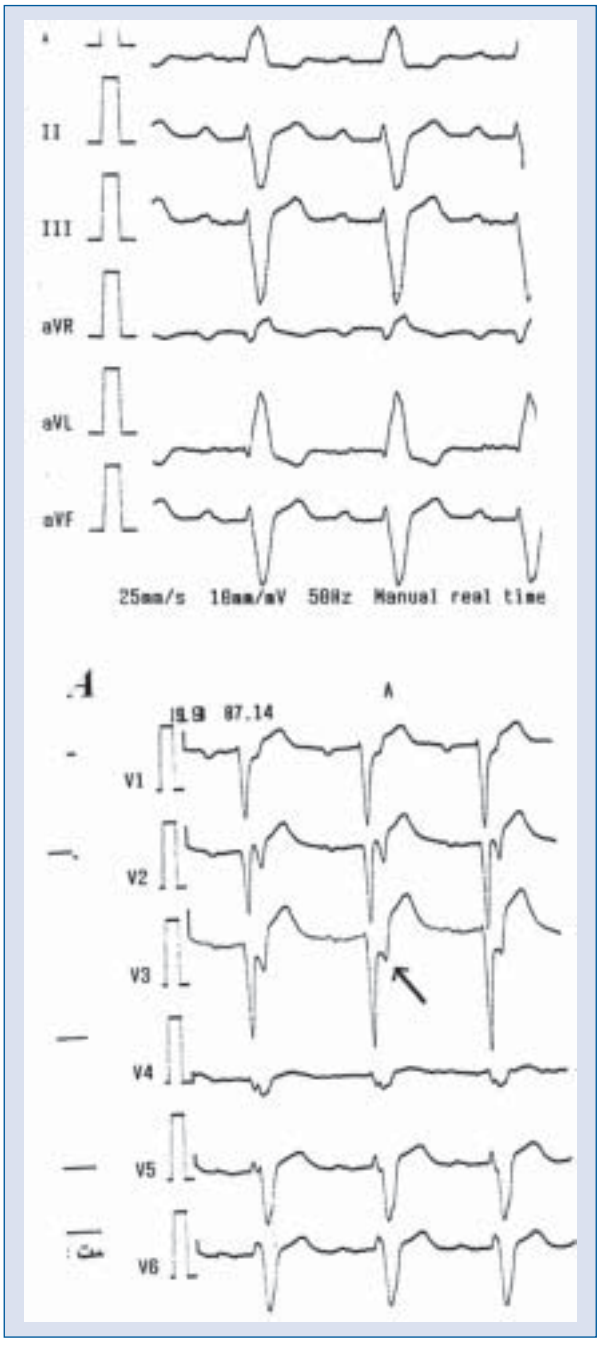

Figure 1. Sinus rhythm with left bundle branch block pattern in V1. Note the QRS notch in V1–V4 (black arrow).

were assessed in each view. In this way, the following segments were interrogated: septal, lateral, inferior, posterior, anteroseptal and anterior at both the basal and middle levels. The regional pre-ejection period was measured for all segments from the beginning of QRS to the peak myocardial sustained systolic velocity (Ts). From these data, the following parameters were derived: intraventricular dyssynchrony, defined as the maximal difference between peak systolic velocities of any 2 of the 12 segments and the cut-off value for it, based on previous studies, is ≥ 100 ms [6]. Another parameter is total dyssynchrony index, defined as the standard deviation (SD) of the electromechanical delay in 12 left ventricle segments, Ts-SD (six basal, six mid-segmental model). Total dyssynchrony index (Ts-SD) cut-off value is more than 31.4 ms [7]. We also assessed another echocardiographic determinant of ventricular dyssynchrony as an electromechanical delay on TDI between the septum and lateral wall: the so-called the septal to lateral mechanical delay (SLMD). The cut-off value for this dyssynchrony index is more than 60 ms [5, 8]. All echocardiographic measurements were performed by two independent echocardiographers who were blinded to the clinical status of the patients.

Statistical analysis

Results are expressed as mean (SD) for interval and frequency (relative frequency) for categorical data. Independent sample t and chi-square tests were used for comparison between the two groups. Pearson correlation coefficient (r) was used to find the linear correlation between interval data. P value less than 0.05 was considered statistically significant. Multiple regression models were fitted to determine the associations between the presence of notches in patient ECGs and dyssynchrony indices, adjusted for: duration of QRS, left ventricular ejection fraction and underlying heart diseases. STATA 8 SE (STATA Corporation, Texas, USA) was used for statistical analysis.

Results

Eighty-seven patients, 65 male (75%) and 22 female (25%), with mean ± SD age of 56.7 ± 12.3 years (range 31 to 79) were enrolled the study. The underlying heart disease in 50 patients (58%) was ischemic and in 37 patients (42%) was idiopathic. Mean (SD) ejection fraction of the left ventricle was 18% (6%). Mean (SD) left ventricular end diastolic volume was 207.10 (68.11) ml. Patients had a mean (SD) QRS duration of 155.13 (23.34) ms. All included patients were categorized into two groups based on the presence or absence of QRS notch. QRS notch was seen in 49.4% of the patients (19.5% in precordial leads, 17.3% in limb leads and 12.6% in both).

Baseline data, with comparisons between the two groups of patients with and without notches in their ECG, is presented in Table 1. Patients with ischemic heart diseases had more QRS notches in

Table 1. Comparison of baseline data in patients with and without QRS notch.

Characteristics	Presence of QRS notch (n = 43)	Absence of QRS notch (n = 44)	p
Age	56.23 ± 12.46	57.16 ± 12.16	0.726
Men	32 (74%)	33 (75%)	0.950
Ischemic heart disease	31 (72%)	19 (44%)	0.006
Left ventricular ejection fraction	17.96 ± 5.27	17.85 ± 5.86	0.948
Left ventricular end-diastolic volume	204.72 ± 66.35	209.43 ± 70.48	0.749
QRS duration	166.51 ± 19.13	144.02 ± 21.83	< 0.001

Table 2. Comparison of echocardiographic dyssynchrony indices in patients with and without QRS notch.

Dyssynchrony indices	Presence of QRS notch (n = 43)	Absence of QRS notch (n = 44)	p
Intraventricular dyssynchrony	91.07 ± 31.12	89.84 ± 30.37	0.853
Inter-ventricular mechanical delay	55.51 ± 23.89	37.84 ± 16.42	< 0.001
Total dyssynchrony index (Ts-SD)	34.21 ± 12.38	34.74 ± 12.61	0.844
Septum to posterior wall mechanical delay	127.88 ± 66.20	116.90 ± 61.08	0.424
Septum to lateral mechanical delay	57.51 ± 44.12	57.86 ± 33.32	0.967

their ECG, compared to idiopathic heart diseases (odds ratio: 3.40, 95% confidence interval: 1.39–8.31; p = 0.006). Also, the mean of QRS duration in patients with notch was significantly greater than in patients without notch (p < 0.001). No other significant differences were found.

A comparison between the mean of the dyssynchrony indices in patients with and without notches in their ECG are shown in Table 2. Inter-ventricular mechanical delay was statistically greater in patients with QRS notch (p < 0.001). The mean of other indices had no statistically significant difference in the two groups (all p > 0.4). Pearson correlation coefficient was used to evaluate linear correlation between dyssynchrony indices and other interval variables. The only relatively important correlation was seen between inter-ventricular mechanical delay and QRS duration (r = 0.60, p < 0.001). Other correlations had correlation coefficients less than 0.5.

Multivariate analysis

A multiple regression model was fitted for each dyssynchrony index (as a dependent variable) to determine the associations between that index and the presence of notch, adjusted for other confounders. After adjustment for duration of QRS, left ventricular ejection fraction and underlying heart diseases, no association was observed between the presence of ECG notch and the values of echocardiographic dyssynchrony indices. Bivariate analysis proposed a relationship between IVMD and QRS notch; however, multivariate analysis revealed that the observed association is actually caused by the effect of QRS duration, rather than the presence of notch per se. Table 3 shows the parameters of this model.

Table 3. Adjusted association between inter-ventricular mechanical delay (IVMD) and presence of QRS notch in a multiple linear regression model (R^2 = 0.39).

	Coefficient (95% CI)	p
Presence of QRS notch	8.05 (–0.79–16.89)	0.074
Left ventricular ejection fraction	–0.18 (–0.90–0.53)	0.607
Underlying heart disease*	–6.61 (–14.78–1.56)	0.111
Duration of QRS	0.51 (0.32–0.71)	< 0.001

*including ischemic and idiopathic cardiomyopathies

Discussion

Electrical dyssynchrony as the main index of ventricular dyssynchrony (QRS duration equal to or

more than 120 ms) has been used for patient selection in all major trials. A wide QRS complex, reflecting left-sided intraventricular conduction delay in patients with heart failure, is associated with more advanced myocardial disease, worse left ventricle function, poorer prognosis and a higher all-cause mortality rate [9]. Despite this strategy, there is a report that shows that 27% of patients are nonresponders to CRT at six months of follow-up [2]. Bleeker et al. [10] evaluated the role of the QRS complex as a marker of mechanical left ventricular dyssynchrony. They showed that 30–40% of patients with a wide QRS complex, predominantly reflecting left-sided conduction delay, did not show mechanical left ventricular dyssynchrony. These data correlate with the reported percentage of nonresponders to CRT selected on the basis of QRS duration. Mechanical dyssynchrony can be seen more frequently in the presence of inhomogeneous activation of the ventricles. QRS complex fragmentation (presence of notch in R and/or S waves) on the surface 12-lead ECG has been implicated with abnormal activation of the ventricles due to myocardial scar and/or ischemia [11, 12]. These studies suggest that different morphologies of QRS fragmentation are caused by a shifting of the QRS vector during depolarization around the areas of scarred or ischemic myocardium, depending on their extent and location in the ventricles. In our study, we found QRS fragmentation and increased global depolarization time (QRS duration) in patients with ischemic vs. idiopathic cardiomyopathy (161 ± 21 *vs*. 147 ± 23 ms; p = 0.005). Nevertheless, in this study, QRS notch, as a marker for inhomogeneous ventricular activation, especially in the left ventricle, did not have an independent effect on mechanical dyssynchrony indices. Global ventricular asynchrony index (SPWMD) and intraventricular asynchrony indices (intraventricular dyssynchrony, total dyssynchrony index, Ts-SD, and SLMD) were not affected by QRS notch (Table 2). These findings can be explained by more extensive myocardial scar tissue in patients with QRS fragmentation in their surface ECG because scar tissue can prevent meticulous echocardiography analysis. Interventricular asynchrony, which is measured by pulse wave Doppler echocardiography, is much less affected by ventricular myocardial scar. In multivariate analysis, QRS notch could not be a marker of interventricular mechanical delay, independent of QRD duration; however, a noticeable trend toward significance was found (p = 0.074). An increase in the number of patients may reveal QRS notch effect on interventricular mechanical delay.

Limitation of the study

In our study all included patients had a wide QRS complex. QRS notch as a marker for inhomogeneous depolarization can be evaluated in patients with symptomatic systolic heart failure and narrow complex ECGs with mechanical dyssynchrony in echocardiography analysis. We did not categorize the presence of QRS notch into anterior, inferior and lateral groups, based on ECG. QRS fragmentation in different leads can show different regional myocardial electrical activation abnormality, which can be effective for mechanical dyssynchrony indices. It is possible that a larger sample size might lead to significance of the association between QRS notch and interventricular delay.

Conclusions

QRS notch was not an independent predictor of higher mechanical dyssynchrony indices in patients with wide QRS complex and symptomatic systolic heart failure; however, there was a borderline association between QRS notch and interventricular delay.

Acknowledgements

The authors do not report any conflict of interest regarding this work.

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