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## Correlation of QRS duration with intraventricular mechanical dyssynchrony on tissue Doppler imaging in heart failure

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### Abstract

**Introductions:** Wide QRS complex with left bundle branch block morphology is one of the three criteria for cardiac resynchronization therapy (CRT) in heart failure (HF) patients who do not improve on medical management. This study investigates to find out to what extent the wide QRS duration correlates with the intraventricular mechanical dyssynchrony (IVMD) as measured by Tissue Doppler Imaging (TDI) echocardiography.

**Methods:** The HF patients of dilated or ischemic cardiomyopathy with ejection fraction  $\leq 35\%$  admitted in the medical ward of Patan Hospital, Nepal from March to August 2017 were enrolled in the study. They were divided into two groups, narrow QRS duration of  $<120\text{ms}$  (Gr1) and wide QRS duration of  $\geq 120\text{ms}$  (Gr2). TDI was performed to measure time to peak systolic velocity of the left ventricular walls. The IVMD, defined as 60 ms (millisecond) or greater difference in time to peak velocity between any two points of the left ventricular walls, was compared in both groups.

**Results:** There were 26 patients, 18 in group-1, and eight in Gr2. In Gr1, IVMD was observed 13/18 (72%) patients and in group-2 in 7/8 (87%) patients, ( $\chi^2 = 0.70$ ,  $p = 0.403$ ). There was no significant difference of IVMD between Gr1 and Gr2 ( $73 \pm 36\text{ms}$  vs  $97 \pm 38\text{ms}$ ,  $t = 1.54$ ,  $p = 0.136$ ).

**Conclusions:** Assessment of intraventricular mechanical dyssynchrony (IVMD) by Tissue Doppler Imaging (TDI) is probably superior to QRS duration in heart failure patients.

**Keywords:** cardiac resynchronization therapy, cardiomyopathy, heart failure, intraventricular mechanical delay, tissue Doppler imaging, QRS duration

## Introductions

One third of patients with congestive heart failure (HF) have some form of intraventricular conduction abnormality that is manifested as a wide QRS duration on the electrocardiogram.<sup>1</sup> Wide QRS ( $\geq 120$  ms, millisecond) implies electrical dyssynchrony of ventricular contraction, and it has been taken as one of the three criteria required for implantation of cardiac resynchronization therapy (CRT) device in HF patients. The other two criteria are severe left ventricular dysfunction, ejection fraction (EF)  $\leq 35\%$ , and not responding to optimal medical management.

The treatment guidelines, and CRT are based on Multisite Stimulation in Cardiomyopathy (MUSTIC),<sup>2</sup> and Multicentre In Sync Randomized Clinical Evaluation (MIRACLE)<sup>3</sup> trials. Despite the selection criteria, 32% of patients in the MIRACLE trial had no change or had deterioration in the New York Heart Association (NYHA) class after CRT. Other studies have reported a 20 to 30% non-response rate after CRT.<sup>4</sup> Thus, the role of wide QRS, whether it is equivalent to mechanical dyssynchrony is not sure.

This study aims to measure the degree of intraventricular conduction delay in HF patients, and analyse the correlation between the QRS duration on standard 12-lead electrocardiogram (ECG) and intraventricular mechanical dyssynchrony (IVMD) using Tissue Doppler Imaging (TDI).

## Methods

This was a cross sectional study conducted at Patan Hospital, Patan Academy of Health Sciences (PAHS), Nepal, from March to August 2017. The HF patients admitted in the medical ward with the diagnosis of dilated cardiomyopathy (DCM) or ischemic cardiomyopathy (ICM) with ejection fraction (EF) of  $\leq 35\%$  were included in the study. Informed consent was obtained from patients. According to QRS duration patients were divided into two groups: QRS duration

$< 120$  ms (Gr1), and QRS duration of  $\geq 120$  ms with or without left bundle branch block (LBBB) (Gr2). The exclusion criteria were: (1) non-sinus rhythm; (2) previous pacemaker implantation; and (3) valvular heart disease. All patients underwent a standard 12-lead electrocardiogram (ECG) and an echocardiographic examination which included a specific evaluation of intraventricular dyssynchrony by tissue Doppler imaging (TDI).

Standard 12-lead ECGs were acquired at a paper speed of 25 mm/s and a scale of 10 mm/mV. The measurements, QRS duration (recorded from the surface leads demonstrating the greatest values) and the assessment of QRS axis and morphology were performed. The typical ECG features of LBBB is QRS duration  $\geq 120$  ms, no Q-wave but slurred, broad R waves in leads I, aVl and V6 and rS or QS deflections in lead V1. Prolongation of QRS which was not associated with the typical features of bundle branch blocks was considered as "non-specific intraventricular conduction delay".

A complete M-mode, 2-D and Doppler evaluation were performed using a Philips EPIQ 7C ultrasonographic equipment. Left ventricular end-diastolic and end-systolic volumes and left ventricular EF were calculated using the Simpson's method.

The TDI were performed in the apical views (four chamber, two chamber, and long axis) for the long axis motion of the LV. Two-dimensional echocardiography with tissue Doppler colour imaging was performed with a 2.5 or 3.5 MHz phase array transducer. A colour Doppler frame scanning rate of 100–140 Hz was used. At least three consecutive beats were stored and the images were digitized and analyzed off-line, (Figure 1a,b,c). Myocardial regional velocity curves were constructed from the digitized images. For detail assessment of regional myocardial function, the sampling window was placed at the myocardial segment of interest.

In each view, both the basal and mid-segments were assessed. In this way, the following twelve segments were interrogated: septal, antero-septal, anterior, lateral, inferior, and posterior segments at both basal and middle levels. For the measurement of timing, the beginning of the QRS complex was used as the reference point, where the time to peak myocardial sustained systolic ( $T_s$ ) velocities was quantified. For the assessment of synchronicity,  $T_s$  of all 12 LV segments were measured and the maximal difference in  $T_s$  between any two of the LV segments was calculated. Intraventricular dyssynchrony was considered to be present if any of the

measurements showed a difference of equal or greater than 60 ms.

Data were analyzed using a statistical software (SPSS 16). The data were expressed as mean $\pm$ SD for the continuous variables, and as absolute or relative frequencies for categorical variables. Independent t-test was performed to compare the means of continuous variables. Categorical data between the two groups were compared by the Fisher exact test. Spearman's coefficient was calculated to evaluate correlations between QRS duration and IVMD, and IVMD and other echocardiographic parameters. The  $p < 0.05$  was considered significant.

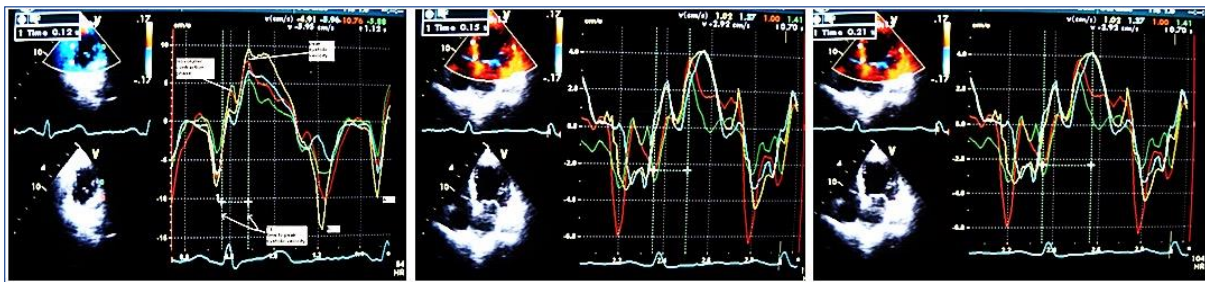


Figure 1. a) Evaluation of intraventricular dyssynchrony by placing sample volumes on the septum (yellow and blue curves) and lateral wall (green and red curves). Data from a normal individual showing complete intraventricular synchrony. b&c) Intraventricular dyssynchrony of 60 ms between the septum (blue and yellow curves) and the lateral wall (green and red curves)

## Results

Out of 26 HF patients, 18/26 (69.2%) had QRS duration  $< 120$  ms (Gr1), and 8/26 (30.8%)  $\geq 120$  ms with or without LBBB (Gr2), (Table 1).

Echocardiographic characteristics, the systolic synchronicity was impaired in patients with HF of both groups. The IVMD  $73 \pm 36$  ms in (Gr1) and  $97 \pm 38$  ms (Gr2) was not significantly different, ( $\chi^2 = 0.70$ ,  $p = 0.403$ ). Left ventricular internal diameter LVID ( $65 \pm 7$  mm vs.  $74 \pm 12$  mm,  $p = 0.024$ ), end diastolic volume EDV ( $238 \pm 65$  ml vs.  $337 \pm 142$  ml,  $p = 0.022$ ), and end systolic volume ESV ( $158 \pm 62$  ml vs.  $228 \pm 110$  ml,  $p = 0.049$ ) were significantly different in the two groups, (Table 2). There was no significant correlation between the age, QRS duration and IVMD ( $r = 0.29$ ,  $p = 0.146$ ), (Table 3). There was a trend toward a greater prolongation of QRS duration with increasing IVMD seen in the

scatter-plot, (Figure 2a). The correlation analysis showed that there was a positive correlation between the ESV and IVMD ( $r = 0.40$ ,  $p = 0.043$ ), (Figure 2b), and a negative correlation between the ejection fraction (EF) and IVMD ( $r = 0.45$ ,  $p = 0.021$ ), (Figure 2c).

## Discussions

The present study shows IVMD commonly occurs in HF patients with narrow QRS duration Gr1 (13/18, 72.2%) and wide QRS Gr2 (7/8, 87.5%),  $\chi^2 = 0.70$ ,  $p = 0.403$ . The statistical analyses found that the degree of LV dyssynchrony or IVMD did not correlate with the duration of QRS complexes, although there was a trend of increasing LV asynchrony as the QRS duration increased, (Figure 2a).

**Table 1. Clinical characteristic of heart failure patients (n=26) with narrow and wide QRS complexes**

	Narrow QRS Gr1 (n=18)	Wide QRS Gr2 (n=8)	$\chi^2$	T	p
Age (years)	56±14.1	67.3±13.9		1.84	NS
Male: female (%)	67: 33	75: 25	0.17		NS
QRS Duration (ms)	94.3±13.5	144.5±16.3		8.21	0.000
Heart Failure Causes (%)					
ICM	56	75	0.85		NS
DCM	44	25			
Medications (%)					
Diuretic	61	75	0.45		NS
ACEI	61	63	0.00		NS
β- blocker	56	63	0.11		NS
ARB	17	25	0.24		NS
Spironolactone	67	88	1.18		NS
Digitalis	50	75	1.36		NS

HF- heart failure, ICM- Ischemic Cardiomyopathy, DCM- Dilated Cardiomyopathy, ACEI- angiotensin converting enzyme inhibitors, ARB- angiotensin II receptor blockers

**Table 2. Echocardiographic characteristics of patients with HF (n=26) with narrow and wide QRS complexes**

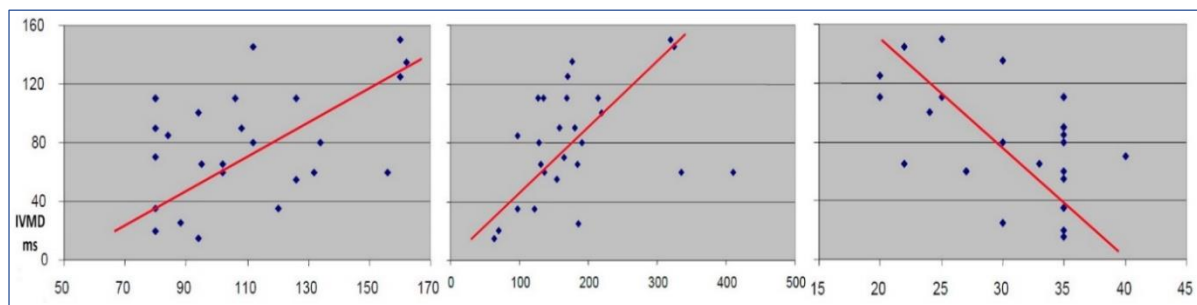
	Narrow QRS (n=18)	Wide QRS (n=8)	T	p
Echocardiography				
LVEF (%)	30.7±5.9	30.3±5.8	0.19	NS
LVIDd (mm)	65±7	74±12	2.40	0.024
IVMD (ms)	73±36	97±38	1.54	NS
EDV (ml)	238±65	337±142	2.46	0.022
ESV (ml)	158±62	228±110	2.08	0.049
Systolic Dyssynchrony	13 (72.2%)	7 (87.5%)	0.70	0.403

LVEF, left ventricular ejection fraction. LVIDd, left ventricular internal diameter in end-diastole. IVMD, intraventricular mechanical dyssynchrony (maximal difference in time to peak myocardial sustained systolic velocity among all 12 left ventricular segments)

**Table 3. Correlation between intraventricular mechanical delay and clinical and echocardiographic parameters**

	Maximal Difference in T <sub>s</sub> (Intraventricular Conduction Delay)	
	R	p
Age	0.156	NS
QRS Duration	0.293	NS
Ejection Fraction	0.449	0.021
End Systolic Volume	0.400	0.043
LVEDd	0.191	NS

LVEDd, left ventricular end diastolic diameter



**Figure 2a. QRS Duration (ms)**  
(n=26, r = 0.29, p = 0.146)

**Figure 2b. End Systolic Volume (ml)**  
(n = 26, r = 0.40, p = 0.043)

**Figure 2c. Ejection Fraction (%)**  
(n = 26, r = 0.45, p = 0.021)

The ESV increased in proportion to IVMD, and IVMD increased as the left ventricular ejection fraction (LVEF) decreased. Correlation analysis showed that ESV was positively correlated with IVMD ( $r=0.40$ ,  $p=0.043$ ) and IVMD was negatively correlated with LVEF ( $r=0.45$ ,  $p=0.021$ ). This shows that IVMD correlates more with the systolic function of the myocardium rather than the QRS duration. Therefore, it appears that more severe systolic dysfunction and LV dilatation were associated with more severe systolic dyssynchrony, independent of QRS duration. These findings support some of the studies in which patients undergoing CRT, the IVMD and not QRS duration is a better predictor of acute hemodynamic, echocardiographic, and clinical response.<sup>5,6</sup>

Recent data have demonstrated that mechanical dyssynchrony is not necessarily related to electrical dyssynchrony.<sup>7,8</sup> Indeed, some patients with a wide QRS complex do not exhibit LV dyssynchrony, whereas some patients with a narrow QRS complex may demonstrate LV dyssynchrony.<sup>9-11</sup> These considerations suggest that the surface electrocardiogram may not be the optimal marker to select candidates for CRT. New imaging techniques, in particular various echocardiographic approaches, may be superior to select potential responders to CRT.

Our findings suggest that in HF patients with narrow QRS complexes also coexists with mechanical dyssynchrony. Studies report that CRT improved the functional status of HF patients with normal QRS duration who had echocardiographic evidence of LV systolic asynchrony.<sup>12,13</sup>

The limitation of this study is the small sample size and a short duration of time. For more generalized inference of our findings, a large sample size, possibly multicentric design with a longer period of time is warranted to provide evidence to modify the existing guideline to go for CRT based on wide QRS complex.

In this study the HF patients with a slightly prolonged QRS or even with normal QRS also exhibited ventricular dyssynchrony and so the assessment of IVMD by TDI may add value before selecting patients for CRT and not on the basis of wide QRS alone.

## Conclusions

The heart failure (HF) patients with a slightly prolonged QRS or even with normal QRS also exhibited ventricular dyssynchrony assessed by the intraventricular mechanical dyssynchrony (IVMD) on Tissue Doppler Imaging (TDI) echocardiography.

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## Conflict of Interests

None

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