Europace (2007) 9, 1171–1176
doi:10.1093/europace/eum234

EUROPEAN SOCIETY OF CARDIOLOGY®

Frequency of inter- and intraventricular dyssynchrony in patients with heart failure according to QRS width

Zahra Emkanjoo[1]*, M. Esmaeilzadeh[2], N. Mohammad Hadi[1], A. Alizadeh[1], M. Tayyebi[1], and M.A. Sadr-ameli[1]

[1] *Department of Pacemaker and Electrophysiology, Rajaie Cardiovascular Research and Medical Centre, PO Box 1996911151, Tehran, Iran; and* [2] *Department of Echocardiography, Rajaie Cardiovascular Research and Medical Centre, Tehran, Iran*

Received 12 June 2007; accepted after revision 26 September 2007; online publish-ahead-of-print 19 October 2007

KEYWORDS
Cardiac resynchronization therapy;
Tissue Doppler imaging

Aims Cardiac resynchronization therapy (CRT) is an effective treatment for heart failure patients with prolongation of QRS duration. Despite careful patient selection, some do not respond to CRT based on QRS complex duration. We sought to evaluate the presence of left ventricular dyssynchrony using tissue Doppler imaging (TDI) according to QRS duration in heart failure patients.
Methods and results Ninety-nine patients (mean age 52.6 ± 15.3 years) with severe heart failure [left ventricular (LV) ejection fraction, <35%] were prospectively evaluated. On the basis of QRS width, the patients were divided into two groups. Forty-eight patients (48.5%) had a normal QRS duration (<120 ms), Group I, and 51 (51.5%) had a prolonged QRS duration, Group II. All patients underwent echocardiography coupled with TDI. Spectral displays of six basal and six middle LV segments with pulsed-wave TDI were obtained to assess the time to peak systolic point from R-wave on electrocardiogram (Ts). The standard deviation of Ts (Ts-SD) and the maximal temporal difference of Ts (Ts-diff) were measured. Interventricular dyssynchrony [defined as the presence of an interventricular mechanical delay (IVMD) >40 ms] and intra-LV mechanical delays (defined as Ts-SD >33.4 ms and Ts-diff >100 ms) were correlated with the QRS width and morphology. We found a greater IVMD in Group II patients, compared with patients in Group I (42.5 ± 22.3 vs. 26.8 ± 21, respectively, $P < 0.001$). Intraventricular dyssynchrony defined as Ts-SD ≥33.4 ms was found in 45.1% of patients in Group II compared with 23% of patients in Group I ($P = 0.03$). Similarly, the Ts-diff was prolonged in Group II patients compared with Group I ($P = 0.02$). By linear regression analysis, a weak relation was found between Ts-SD and QRS duration ($P = 0.055$). A substantial portion of patients with prolonged QRS did not exhibit ventricular dyssynchrony defined either as total asynchrony index ≥33.4 ms or as IVMD >40 ms.
Conclusion A substantial proportion of patients with prolonged QRS (32.1%) did not exhibit inter- or intraventricular dyssynchrony, which may represent a limitation in identifying the ideal QRS interval for the selection of patients for CRT.

Introduction

Cardiac resynchronization therapy (CRT) has been shown to be an effective treatment for advanced drug-refractory heart failure in selected patients. Nevertheless, ~20–30% of patients in multicenter trials do not respond clinically.[1–4] A long QRS duration (>120 ms) with complete left bundle branch block (LBBB) has been proposed as a determinant criterion for the selection of patients to CRT because it may be associated with marked intra-left ventricular (intra-LV) dyssynchrony.[1,2] Even though QRS duration has been used as an inclusion criteria in all major trials, baseline or shortening of QRS complex duration did not predict haemodynamic, clinical, or echocardiographic improvement. Furthermore, it has been shown that there is no association between electrical dyssynchrony with mechanical dyssynchrony and vice versa. Tissue Doppler imaging (TDI) has been shown to be useful to assess the severity of LV systolic asynchrony.[5,6]

Widening of the QRS complex on the surface electrocardiogram (ECG) usually indicates an impaired or slowed propagation of the electrical input, a finding frequently associated with increased morbidity and mortality in heart failure patients.[7] More so than the electrical activation sequence, the mechanical one during ventricular systole

* Corresponding author. Tel: +98 21 2391; fax: +98 21 22055594.
E-mail address: emkanjoo@rhc.ac.ir

predominates in terms of haemodynamic variations and clinical consequences. Recent studies have revealed that intraventricular conduction block with or without prolonged atrioventricular conduction adversely influences ventricular function due to discoordinate contraction.[8,9] On the basis of the same apparent intraventricular conduction block visible on the surface ECG, it has been suggested that some heart failure patients present with interventricular mechanical asynchrony whereas others have intra-LV asynchrony.[10,11] Accordingly, it is likely that these two ventricular mechanical dyssynchronizations may have different consequences in terms of clinical and haemodynamic outcome, especially in heart failure patients.

This study aimed at (i) determining the prevalence of inter- and intraventricular dyssynchrony using standard echocardiography and TDI in patients with heart failure in terms of QRS duration and (ii) assessing the relation between inter- and intraventricular dyssynchrony.

Methods

We studied 99 patients with severe heart failure [left ventricular ejection fraction (LVEF), <35%]. We excluded patients with non-sinus rhythm and previous pacemaker implantation. The patients were included between November 2005 and December 2006: 68 (69%) were males and 31 (31%) females (mean age, 52.6 ± 15.3; range, 18–79 years). Forty-eight (48.5%) patients had a QRS duration of <120 ms (Group I) and 51 (51.5%) had a QRS duration of >120 ms (Group II). Heart failure aetiology was ischaemic cardiomyopathy in 54 (54.5%), dilated cardiomyopathy in 43 (43.4%), and valvular heart disease in 2 (2%) patients; 58.6% had NYHA class III, 24.2% had class VI, and 17% had class II symptoms. All patients were treated with β-receptor blockers, angiotensin-converting enzyme inhibitors, or angiotensin-receptor blockers and diuretics. Standard surface 12-lead electrograms (ECGs) were recorded at a paper speed of 50 mm/s. The QRS duration was measured with a calliper and the longest QRS duration was obtained. The study protocol was approved by the local Ethics Committee, and an informed consent was obtained from all patients.

Standard echocardiographic studies

A complete study of M-mode and Doppler blood flow measurements was performed using a Vivid 7 digital ultrasound scanner (GE, Milwaukee, WI, USA) equipped with an ergonomically designed M3S with a 3.5 MHz phase array matrix transducer. Left ventricular ejection fraction was evaluated eyeball and with Simpson's method if accurate endocardial border detection was possible. Mitral valve opening and closing times were measured using diastolic blood flow recording with sample volume place at the level of mitral valve tip. Mitral regurgitation was graded according to the jet area method in an apical four-chamber view.

Aortic and pulmonic valves' opening and closing times were also measured using systolic blood flow by pulsed Doppler with sample volume placed at the level of the aortic and pulmonic annulus. The aortic pre-ejection time was measured from the beginning of QRS complex to the beginning of the aortic flow velocity curve recorded by pulsed-wave Doppler in apical view. The pulmonary pre-ejection time was measured from the beginning of QRS complex to the beginning of the pulmonary flow velocity curve recorded in the left parasternal view. The difference between the two values determined the interventricular mechanical delay (IVMD); an IVMD > 40 was considered as the cut-off value for interventricular dyssynchrony. Using M-mode recording from the parasternal short-axis view (at the papillary muscle level), the septal-to-posterior wall motion delay (SPWMD) was obtained and a cut-off value ≥130 ms was proposed as a marker of intraventricular dyssynchrony. All echocardiographic measurements were obtained by two independent observers without knowledge of the clinical status of the patients. Intraobserver agreement was calculated by repeated measurement of the same recording in 10 patients. The correlation coefficient for Ts-SD, Ts-diff, septal-to-lateral delay, and SPMMD were 0.92, 0.92, 0.90, and 0.87, respectively.

Tissue Doppler echocardiography

Spectral displays of six basal and six middle LV segments with pulsed-wave TDI were obtained in the four-, three-, and two-chamber apical views, and stored digitally. Gain and filter settings were adjusted as needed to eliminate background noise and to allow for a clear spectral display. The measurements were performed with a sweep of 100 mm/s. Offline analysis of three end-expiratory beats was performed and the results were averaged.

Myocardial regional velocity curves were constructed from the digitized images.[12] For detailed assessment of regional myocardial function, the sampling windows were placed at the myocardial segment of interest. In each view, both the basal and mid-segments were assessed. In this way, the following segments were interrogated: septal, anteroseptal, anterior, lateral, inferior, and posterior segments at both basal and middle levels. For the measurement of time intervals, the R-wave of QRS complex was used as the reference point, from which the time to peak myocardial systolic velocities (Ts) during ejection phase was measured.[5] For the assessment of synchronity, the standard deviation of Ts (Ts-SD) of all the LV segments and the maximal difference in Ts (Ts-diff) between any two the LV segments were calculated (intraventricular dyssynchrony defined as a standard deviation of 33.4 ms referred to as dyssynchrony index).

We also assessed another echocardiographic determinant of baseline ventricular dyssynchrony as an electromechannical delay on TDI between the septum and lateral wall, the so-called septal-to-lateral delay, of >60 ms.

Statistical analysis

The data were analysed using the SPSS software (version 13, SPCC Inc., Chicago, IL, USA). Summary data are expressed as mean ± SD or percentage of patients. The comparison of the baseline characteristics between the groups were done with independent sample *t*-test and with the χ^2 test for categorical variables. Linear regression analysis was used to evaluate the association between inter- and intraventricular dyssynchrony and ARS duration. A *P*-value of <0.05 was considered statistically significant.

Results

A total of 99 patients, mean age 52.6 ± 15.3 years, were included in this study. According to QRS duration, the patients were divided into two groups: 48 patient with a QRS duration <120 ms (Group I) and 51patients with a QRS duration >120 ms (Group II). In 51 patients with prolonged QRS duration, 39 (76.5%) had LBBB, 6 (11.8%) had right bundle branch block (RBBB), and 5 (9.8%) had undetermined pattern. Clinical characteristics of patients according to QRS duration are shown in *Table 1*.

Mean age was similar between the two groups. There was no relation between the aetiology of heart failure and QRS duration. Group II patients had a more advanced LV systolic dysfunction than Group I patients ($\text{LVEF} = 16.96 \pm 6$ vs. 20.53 ± 7.5, respectively, $P = 0.006$). Left ventricular volumes increased in parallel to QRS duration (*Table 2*).

Thirty (65.2%) Group I and 22 (43.1%) Group II patients had moderate to severe MR. There was no difference in degree of MR between the two groups.

Table 1 Clinical characteristics of patients

Characteristics	Group I ($n = 48$)	Group II ($n = 51$)	*P*-value
Age (years)	50.3 ± 15.2	54.75 ± 15	0.1
Gender (male, %)	47.1	52.9	0.9
NYHA class	3.1 ± 0.7	2.9 ± 0.7	0.5
Heart failure aetiology			
Ischemic cardiomyopathy (%)	60.4	49.1	
Dilated cardiomyopathy (%)	39 0.6	47.2	0.7
Dilated cardiomyopathy and valvular disease (%)	–	3.8	
Electrocardiographic data			
Complete LBBB (%)	–	75.5	
Incomplete LBBB (%)	4.2	–	0.0001
Complete RBBB (%)	–	13.2	
Undetermined pattern (%)	18.8	11.3	

Data are presented as the mean ± SD, or percentage of patients.

Table 2 Echocardiographic characteristics

Variable	Group I	Group II	*P*-value
End-diastolic LV volume	179.2 ± 58	214.4 ± 93	0.001
End-systolic LV volume	143.1 ± 40	170.7 ± 84	0.004
LVEF (%)	20.5 ± 7.5	16.9 ± 6.1	0.01
Aortic pre-ejection interval (ms)	112.04 ± 51.5	126.45 ± 30.4	NS
Pulmonic pre-ejection interval (ms)	91.38 ± 46.2	104.7 ± 30	NS
Interventricular electromechanical delay (ms)	26.8 ± 21	42.5 ± 22	0.001
IVMD >40 ms			
SPWMD > 130 ms (%)	14	31	0.047
SLWMD >60 ms (%)	35.4	35.8	NS
Ts-SD ≥33.4 ms (%)	23	45.1	0.03
Ts-diff ≥100 ms (%)	25.0	42.75	0.017
No ventricular dyssynchrony (%)	64.4	32.1	0.002

SPWMD, septal-to-posterior wall motion delay; SLWMD, septal-to-lateral wall delay; Ts, time to peak systolic point from R wave on electrocardiogram;Ts-SD, standard deviation of Ts; Ts-diff, maximal temporal difference of Ts.

Interventricular dyssynchrony

There was no difference in pulmonary pre-ejection period between Group I and II (85 ± 47 vs. 104 ± 30, respectively). It was the same for aortic pre-ejection period (112.5 ± 52 vs. 127.2 ± 30.5, respectively). Nevertheless, we found a greater IVMD in Group II patients, compared with patients in Group I (42.5 ± 22.3 vs. 26.8 ± 21, respectively, $P = 0.001$). Linear regression demonstrated significant relation between QRS duration and IVMD, although in a context of wide scattering of the data ($n = 99$, $r = 0.26$, $P < 0.0001$) (*Figure 1*). Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and LVEF were not different in patients with interventricular dyssynchrony and in those without dyssynchrony.

There was not relation between aetiologies of heart failure (ischemic vs. dilated) and IVMD. NYHA class was not different in patients with interventricular dyssynchrony and in those without dyssynchrony (82.6% NYHA class III and VI and 17.5% NYHA class II in patients with IVMD < 40 vs. 85.7% NYHA class III and VI and 14.3% NYHA class II in patients with IVMD > 40, respectively). A significant association was shown between LBBB morphology and IVMD ($P < 0.0001$).

Intraventricular dyssynchrony

Intraventricular dyssynchrony, defined as total asynchrony index (Ts-SD) ≥ 33.4 ms, was found in 44% of patients in Group II compared with 25% of patients in Group I ($P = 0.03$). Similarly, the maximum difference in Ts (Ts-diff) was prolonged in the Group II compared with Group I ($P = 0.02$). Linear regression demonstrated a weak relation between Ts-SD and QRS duration ($n = 99$, $r = 0.22$, $P = 0.055$; *Figure 2*).

Septal-to-posterior wall motion delay was significantly longer in Group II patients compared with patients in Group I (>130 ms in 32.7% of Group II patients vs. 14% of patients in Group I, $P = 0.03$). Linear regression demonstrated a relation between QRS duration and SPWMD (confidence interval, 1.05–8.5; $P = 0.033$). Septal-to-lateral delay >60 ms was found in 19 (37.3%) of patients in Group II and in 17 (35.4%) of patients in Group I ($P = 0.5$). No association existed between QRS duration and septal-to-lateral delay.

Left ventricular ejection fraction, LVESV, and LVEDV were similar in patients with and without intraventricular dyssynchrony. No significant relation was found between aetiology of heart failure, severity of MR, and intraventricular dyssynchrony. Echocardiographic characteristics of patients according to QRS duration are shown in *Table 3*. It is worthy to note that a substantial portion of patients (32.1%) with prolonged QRS did not exhibit ventricular dyssynchrony defined either as total asynchrony index ≥33.4 ms or IVMD >40 ms. No correlation was found between intraventricular dyssynchrony and QRS morphology (*Table 4*).

Correlation between interventricular mechanical delay and total asynchrony index

In patients with intraventricular dyssynchrony (total asynchrony index, ≥33.4), 51% also had interventricular dyssynchrony, in patients without intraventricular dyssynchrony, 27.3% had interventricular dyssynchrony ($P = 0.03$) (*Table 5*).

Discussion

Recent studies have shown that surface ECG is not sensitive enough to detect the presence and severity of electromechanical delay resulting in asynchronous contraction. The mechanical abnormalities determined by the conduction

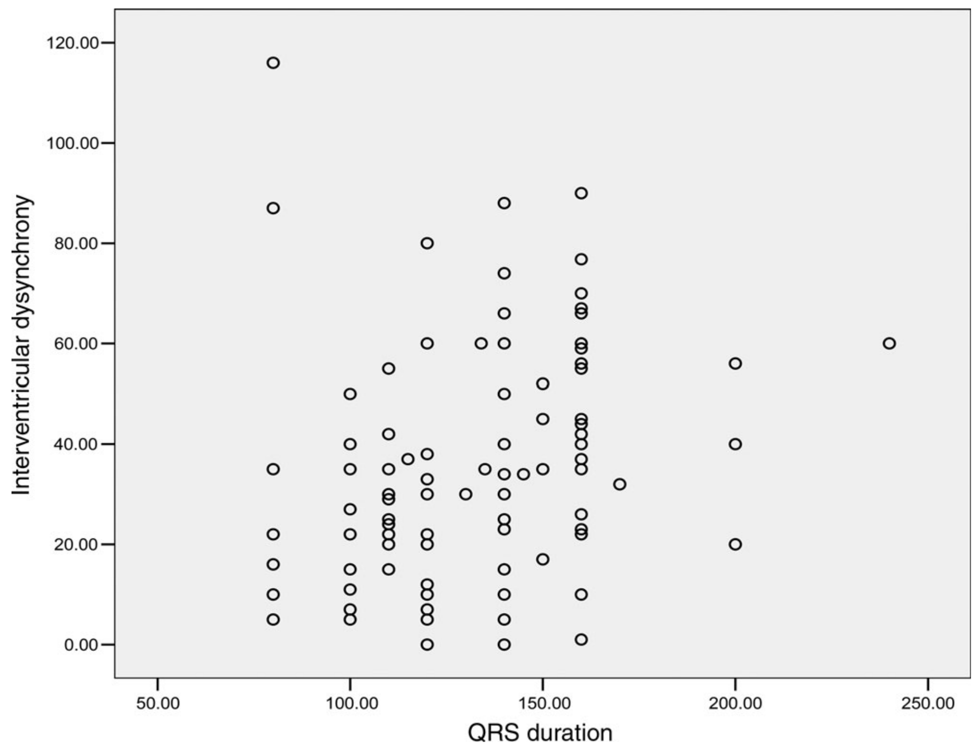

Figure 1 Relations between interventricular mechanical delay and QRS duration. $Y = 0.198 + 9.013n$, $n = 99$, $r = 0.26$, and $P < 0.0001$.

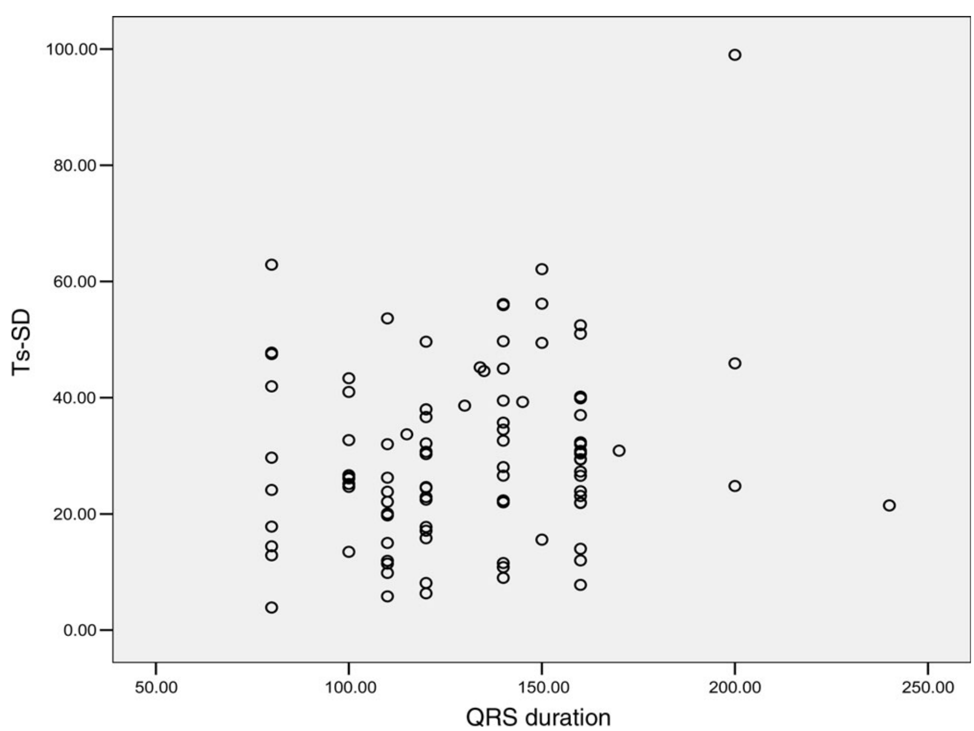

Figure 2 Relationship between intraventricular mechanical delay (Ts-SD) and QRS duration. $Y = 0.112 + 15.8n$, $n = 99$, $r = 0.22$, and $P = 0.055$.

disturbances in heart failure patients with either normal or slightly prolonged QRS duration have not been fully characterized. In patients with impaired LV function, mechanical dyssynchrony of the left ventricle may be absent in ~30% of patients with congestive heart failure and intraventricular conduction delay and present in ~40–50% of patients with QRS duration of ≤120 ms.[13–16]

The study by Yu *et al*.[17] has illustrated for the first time that there is a mechanical delay in the LV free wall in patients with cardiac diseases even with a normal surface ECG. Bader *et al*.[15] have showed that more than half of heart failure patients without complete BBB have major intra-LV electromechanical asynchrony and the QRS width and morphology are therefore not predictive of

Table 3 Identifying patients with intra- and interventricular dyssynchrony defined as TS-SD and IVMD

Variable	Group I	Group II
Presence of intra-LV dyssynchrony alone (%)	20.8	13.2
Presence of interventricular dyssynchrony alone (%)	10.4	24.5
Presence of interventricular and intra-LV dyssynchrony (%)	4.2	30.2
No ventricular dyssynchrony (%)	64.6	32.1

Ts-SD, standard deviation of Ts; IVMD, interventricular electromechanical delay.

Table 4 Distribution of conduction disorders according to different types of ventricular dyssynchrony

Conduction disorder	Intra-LV dyssynchrony, *n*(%)	Interventricular dyssynchrony, *n*(%)
LBBB	19 (45.2)	26 (62)
RBBB	1 (14.3)	1 (14.3)
Undetermined	6 (14.3)	2 (42.9)

Table 5 Correlation between interventricular electromechannical delay and total asynchrony index

	No. of patients	
	Ts-SD $\geq$ 33.4 ms	Ts-SD $<$ 33.4 ms
Interventricular mechanical delay $\geq$40 ms	18	18
Interventricular mechanical delay $<$40 ms	17	47

Ts-SD, standard deviation of Ts (time to peak systolic point from R wave on electrocardiogram).

loco-regional asynchronous contraction abnormalities, unless superior to 140 ms.

In another study, it has been shown that LV asynchrony is not uncommon in patients with systolic heart failure with normal QRS duration, although it is less prevalent than in those with wide QRS complexes.[14]

In the present study, we found a greater prevalence of interventricular dyssynchrony (IVMD $>$ 40) in patients with a QRS duration $>$120 ms, compared with patients with a QRS duration $<$120 ms (42.5 ± 22.3 vs. 26.8 ± 21, respectively, $P < 0.001$). A small percentage of patients with a normal QRS duration (14.9%) were found to have interventricular dyssynchrony. The data are consistent with those obtained by Ghio *et al.*[18]

Despite the greater prevalence of intraventricular dyssynchrony (defined as total asynchrony index $\geq$33.4 ms) in the group with QRS duration $>$120 ms, a weak relation was found between total asynchrony index $\geq$33.4 ms and QRS duration ($P = 0.055$).

A substantial proportion of patients with narrow QRS duration (25%) exhibit intraventricular dyssynchrony (defined as total asynchrony index $\geq$33.4 ms).

In this study, we assessed multiple potential echocardiographic determinant of baseline ventricular dyssynchrony such as SPWMD and septal-to-lateral wall. SPWMD was significantly longer in the patients with QRS duration $>$120 ms compared with patients with a normal QRS duration ($P = 0.03$). However, frequently, SPWMD cannot be obtained, either because the septum is akinetic after extensive anterior infarction or because the maximum posterior motion is ill-defined. In addition, it is often not possible to obtain perpendicular M-mode sections of the proximal LV. The present study has also shown a significant relation between inter- and intraventricular dyssynchrony.

But the fact remains that a substantial portion of patients (32%) with prolonged QRS do not exhibit inter- or intraventricular dyssynchrony. A wide QRS may be helpful in identifying the presence of interventricular dyssynchrony, but it may not be related to intraventricular dyssynchrony. Echocardiography plays an increasing role in the selection of patients for CRT. However, there currently is no gold standard for diagnosis dyssynchrony, so comparing the accuracy of the different echocardiographic parameters is not possible. TDI results should be interpreted with caution as far as the patient selection for CRT is concerned. Predictive values of the proposed indices for identifying responders to CRT are still to be clarified. In the meantime, it is probably inappropriate to deny CRT to patients who fulfil currently accepted criteria (i.e. drug refractory NYHA FC III or IV, LVEF $\leq$35%, and QRS $>$120 ms) simply because dyssynchrony may not be demonstrated by echocardiography.

Conclusion

A substantial proportion of patients with prolonged QRS (32.1%) did not exhibit inter- or intraventricular dyssynchrony that may represent a limitation in identifying the ideal QRS interval for the selection of patients for CRT. Alternatively, 25 and 15% of patients with a narrow QRS complex showed intra- and interventricular dyssynchrony, respectively. The present study emphasized the concept that the selection of candidates for CRT should be performed using more sophisticated imaging techniques.

Conflict of interest: none declared.

References

1. Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Linde C *et al*. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001;**344**:837–80.
2. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E *et al*. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002; **346**:1845–53.
3. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T *et al*. Cardiac resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Eng J Med* 2004;**350**: 2140–50.
4. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L *et al*. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;**352**:1539–49.
5. Yu CM, Chau E, Sanderson JE, Fan K, Tang MO, Fung WH *et al*. Tissue Doppler echocardiographic evidence of reverse remodeling and improved synchrony by simultaneously delaying regional contraction after biventricular pacing therapy in heart failure. *Circulation* 2002;**105**:438–45.

6. Sogaard P, Kim WY, Jensen HK, Mortensen P, Pedersen AK, Kristensen BO *et al*. Impact of acute biventricular pacing in patients with heart failure. A tissue doppler and three-dimensional echocardiographic study. *Cardiology* 2001;**95**:173–82.
7. Silvet H, Padamanabham S, Pai R. Increased QRS duration reduces survival in patients with left ventricular dysfunction: results from a cohort of 2263 patients (abstr). *J Am Coll Cardiol* 1999;**33**:146.
8. Xiao HB, Roy C, Fujimoto S, Gibson DG *et al*. Natural history of abnormal conduction and its relation to prognosis in patients with dilated cardiomyopathy. *Int J Cardiol* 1996;**53**:163–70.
9. Murkofsky RL, Dangas G, Diamond JA, Mehta D, Schaffer A, Ambrose JA *et al*. A prolonged QRS duration on surface electrocardiogram in a specific indicator of left ventricular dysfunction. *J Am Coll Cardiol* 1998;**32**:476–82.
10. Garrigue S, Reuter S, Labeque JN, Jais P, Hocini M, Haisagurre M *et al*. Usefulness of biventricular pacing in patients with congestive heart failure and right bundle branch block. *Am J Cardiol* 2001;**88**:1436–41.
11. Kerwin WF, Botvinick EH, ÓConnell JW, Merrick SH, De Marco T, Chatterjee K *et al*. Ventricular contraction abnormalities in dilated cardiomyopathy: effects of biventricular pacing to correct interventricular dyssynchrony. *J Am Coll Cardiol* 2000;**35**:1221–7.
12. Gorcsan J, Strum DP, Mandarino WA, Gulati VK, Pinsky MR. Quantitative assessment of alterations in regional left ventricular contractility with colour-coded tissue Doppler echocardiography; comparison with sonomicrometry and pressure-volume relations. *Circulation* 1997;**95**:2413–33.
13. Fauchier L, marie O, Casset-Senon D, Babuty D, Cosnay P, Fauchier JP. Reliability of QRS duration and morphology on surface electrocardiogram to identify ventricular dyssynchrony in patients with idiopathic dilated cardiomyopathy. *Am J Cardiol* 2003;**92**:341–4.
14. Yu CM, Lin H, Zhang Q, Sanderson JE. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. *Heart* 2003;**89**:54–60.
15. Bader H, Garrigue S, Lafitte S, Reuter S, Jais P, Haissaguerre M *et al*. Intra-left ventricular electromechanical asynchrony. A new independent predictor of severe cardiac events in heart failure patients. *J Am Coll Cardiol* 2004;**43**:248–56.
16. Achilli A, Sassara M, Ficili S, Pontillo D, Achilli P, Alessi C *et al*. Long term effectiveness of cardiac resynchronisation therapy in patients with refractory heart failure and narrow QRS. *J Am Coll Cardiol* 2003;**42**:2117–24.
17. Yu CM, Yang H, Lau CP, Wang Q, Wang S, Lam L *et al*. Regional left ventricular mechanical asynchrony in patients with heart disease and normal QRS duration: implication for biventricular pacing therapy. *Pacing Clin Electrophysiol* 2003;**26**(2 pt 1):562–70.
18. Ghio S, Constantin C, Klersy C, Serio A, Fontana A, Campana C *et al*. Interventricular and intraventricular dyssynchrony are common in heart failure patients, regardless of QRS duration. *Eur Heart J* 2004;**25**:571–8.