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Significance of QRS Complex Duration in Patients With Heart Failure

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Prolongation of QRS (≥120 ms) occurs in 14% to 47% of heart failure (HF) patients. Left bundle branch block is far more common than right bundle branch block. Left-sided intraventricular conduction delay is associated with more advanced myocardial disease, worse left ventricular (LV) function, poorer prognosis, and a higher all-cause mortality rate compared with narrow QRS complex. It also predisposes heart failure patients to an increased risk of ventricular tachyarrhythmias, but the incidence of cardiac or sudden death remains unclear because of limited observations. A progressive increase in QRS duration worsens the prognosis. No electrocardiographic measure is specific enough to provide subgroup risk categorization for excluding or selecting HF patients for prophylactic implantable cardioverter-defibrillator (ICD) therapy. In ICD patients with HF, a wide underlying QRS complex more than doubles the cardiac mortality compared with a narrow QRS complex. There is a high incidence of an elevated defibrillation threshold at the time of ICD implantation in patients with QRS ≥200 ms. Mechanical LV dyssynchrony potentially treatable by ventricular resynchronization occurs in about 70% of HF patients with left-sided intraventricular conduction delay, a fact that would explain the lack of therapeutic response in about 30% of patients subjected to ventricular resynchronization according to standard criteria relying on QRS duration. The duration of the basal QRS complex does not reliably predict the clinical response to ventricular resynchronization, and QRS narrowing after cardiac resynchronization therapy does not correlate with hemodynamic and clinical improvement. Mechanical LV dyssynchrony is best shown by evolving echocardiographic techniques (predominantly tissue Doppler imaging) currently in the process of standardization. (J Am Coll Cardiol 2005;46:2183–92) © 2005 by the American College of Cardiology Foundation

As long ago as 1962, there was speculation regarding the prognosis of QRS prolongation in patients with heart failure (HF) (1). Thereafter, a few studies reported mortality rates of 50% to 70% (over 50 to 60 months of follow-up) in patients with HF with left ventricular (LV) conduction delay (2–4) but others could not corroborate these findings (5). The conflicting results of these older studies may have been related to the prevailing unstandardized diagnosis and management of HF. Since then, important therapeutic advances have generated new questions about the significance of QRS prolongation in patients with HF.

INCIDENCE

Prolongation of QRS (≥120 ms) occurs in 14% to 47% of patients with HF (Table 1) and is generally accepted as occurring in approximately 30% (4,6–19). Left bundle branch block (LBBB) occurs more commonly than right bundle branch block (RBBB) (25% to 36% vs. 4% to 6%, respectively) (13,20,21). There are a number of possible causes for the varying reported incidence of QRS prolongation in the HF population. The definition of QRS prolongation is not uniform; some studies set the limit at 120 ms and others at 150 ms. No two studies used the same methodology to measure QRS duration (Table 1) (4,6–11,13,14,17). Indeed, a variety of methodologies were applied to measure QRS duration: computer-reported measurements, average of several complexes, or widest complex on electrocardiogram (ECG). Some reports either were vague or simply did not state how QRS durations were measured.

Although all of the studies in Table 1 were conducted in patients with HF, there is obviously some heterogeneity among studied populations. Some patients with HF may not have had true LV systolic dysfunction, particularly in studies in which the LV ejection fraction (LVEF) was not determined. Some study populations consisted of patients with advanced HF (11,15), others involved HF patients with implanted defibrillators (a group that generally has more severe disease than the populations in most other reports) (14), whereas others focused on clinically stable outpatients (13).

LV FUNCTION AND CLINICAL STATUS

Prolongation of QRS (≥120 ms) is a significant predictor of LV systolic dysfunction in patients with HF (4,8,10,11,22). In contrast, the significance of QRS prolongation has not yet been evaluated in HF with a normal LVEF and diastolic

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Abbreviations and Acronyms

CI	= confidence interval
CRT	= cardiac resynchronization therapy
ECG	= electrocardiogram
HF	= heart failure
HR	= hazard ratio
ICD	= implantable cardioverter-defibrillator
LBBB	= left bundle branch block
LV	= left ventricle/ventricular
LVEF	= left ventricular ejection fraction
NYHA	= New York Heart Association
RBBB	= right bundle branch block
VT	= ventricular tachycardia

dysfunction. In patients with HF, an inverse correlation exists between QRS prolongation and LVEF (Table 1) (4,8,10,11,13,18). In a study of nearly 3,500 patients with HF, Shenkman et al. (7) found a stepwise increase in the prevalence of systolic LV dysfunction as QRS complex duration increased progressively above 120 ms. A more recent study conducted in 343 patients with HF reported LVEF of 41%, 36%, 29%, and 25% in patients with QRS durations of <100 ms, 100 to 119 ms, 120 to 149 ms, and ≥150 ms, respectively (10). These observations in patients with HF are in keeping with the findings of Murkofsky et al. (23), who analyzed 226 patients (without typical bundle branch block, pacemaker, or stated HF) referred for radionuclide exercise ventriculography. The study indicated a high likelihood of an abnormal LVEF <45% with a QRS >0.10 s. The specificity increased for each 0.01-s increase in QRS duration so that it increased to over 99% with a QRS increment from >0.10 s to >0.12 s (23).

Moderate or severe mitral regurgitation was seen in 8% and 20% of patients with HF with QRS <120 ms and ≥120 ms, respectively. Increasing QRS duration was also associated with more severe tricuspid regurgitation (10).

PROGRESSION OF QRS DURATION

As a rule, QRS duration increases as LV function worsens (4,8,10,13,24). One HF study indicated that the incidence of QRS prolongation (>120 ms) increased from 10% to 32% and 53% when patients moved from New York Heart Association (NYHA) functional class I to class II and III, respectively (24). In a study of 5,517 outpatients with HF, QRS prolongation was seen more frequently in patients with advanced NYHA functional class (32.8% of patients with complete LBBB vs. 26.4% without complete LBBB were in NYHA class III to IV) (21). Gasparini et al. (25) reported similar findings in a study of 158 patients with severe HF undergoing biventricular pacemaker implantation: 86% of patients with QRS >150 ms were in NYHA functional class III or IV versus 60% of patients with QRS <150 ms ($p = 0.002$). According to Xiao et al. (26), who analyzed a series of patients with dilated cardiomyopathy of mixed etiology admitted to a tertiary center (not necessarily for a procedure), QRS prolongation progresses at an annual rate of 5 ms in a population presumed to have HF and who received appropriate therapy for it, although HF diagnosis was not specifically indicated by the investigators. Larger increases in QRS duration occur in patients with early mortality. In the study by Xiao et al. (26), the time from reaching a QRS of 160 ms to death was 9.8 ± 18 months in patients without an implanted pacemaker versus 31 ± 16 months in patients with a pacemaker (26). The significance of these observations is unclear unless one postulates that ventricular pacing was intermittent because impaired LV dysfunction is related to the cumulative percent of ventricular pacing (27–30).

One study of 56 patients with symptomatic HF (followed up from 180 to 7,660 days; mean, 1,755 days) and necropsy-proven idiopathic dilated cardiomyopathy documented an increase in QRS duration from an average of 0.10 s to an average of 0.13 s in 76% of patients before death (20). These results are consistent with those of other reports in cardiomyopathy (ischemic or non-ischemic) and patients with HF identifying QRS prolongation as a poor prognostic indicator (4,26).

MORTALITY

Patients with HF with QRS prolongation have higher all-cause mortality and possibly a higher incidence of sudden death (or cardiac death) than those with narrow QRS complexes (4,9,11,13,31,32) (Table 2). In fact, mortality rates progressively increase as intraventricular conduction delay increases. In one study, QRS <0.12 s, QRS 0.12 to 0.16 s, and QRS >0.16 s correlated with 20%, 36%, and 58% mortality at 36 months, respectively (9).

Kalra et al. (8) investigated the optimal QRS duration that separates patients with HF into those with a relatively benign versus a poor prognosis (i.e., increased mortality or heart transplantation). Patients with a QRS ≥0.12 s had a three-fold increased risk for the combined end point of death or transplantation. Also, five-year survival was significantly lower in this patient population when compared with patients with HF with QRS <0.12 s (47% vs. 84%; $p < 0.0001$) (8).

In patients with B-type natriuretic peptide levels >400 pg/ml, QRS prolongation was found to be a significant univariate and multivariate predictor of all-cause death, cardiac death, and pump failure death (33). In a study of 82 patients with HF and dilated cardiomyopathy, change in QRS duration over time (≥0.5 ms/month) was a multivariate predictor of cardiac death or need for heart transplant at one year (34). In another study, QRS duration was the only electrocardiographic parameter with independent prognostic value for adverse outcomes (22). In 100 patients with HF referred for cardiac transplantation, 55% of patients with QRS duration ≥0.12 s (vs. 24% with QRS <0.12 s) went on to transplantation or death (11). The time course of the transplantation patients was not stated.

Table 1. Incidence of QRS Prolongation in Heart Failure Patients: Correlation With Left Ventricular Function

Study	Year	No. of Patients	LVEF (%)	QRS ≥120 ms (%)	QRS ≥150 ms (%)	QRS Measurement	LVEF and QRS Correlation (p Value)
Bader et al. (6)	2004	104	31 ± 9*	47 34 with QRS >140 ms	NS	Interpreted by two independent blinded observers	NS
Sandhu et al. (10)	2004	343	25 ± 18†	24	12	MUSE electrocardiographic system analysis of intervals	Yes (<0.0001)
Freudenberger et al. (11)	2004	100	19 ± 7‡	34	NS	Interpreted by two blinded cardiologists	Yes (0.04)
Shen et al. (12)	2004	1,129	38 ± 14	20 with QRS >130 ms	6	NS 58% LBBB 22% RBBB 20% IVCD	Only patients with LVEF ≤35% were analyzed. Yes with QRS ≥130 ms (0.02)
Baldasseroni et al. (13)	2003	5,517	NS	38	NS	Measured by a single cardiologist at each participating center using a standardized format	Yes (0.001)
Bode-Schnurbus et al. (14)	2003	165	33 ± 14*	NS	16	Mean of three complexes in leads V_3 to V_6	Trend only
Galizio et al. (15)	2003	200	NS	54	34	NS	NS
Grimm et al. (16)	2003	566	31 ± 10*	39	24	NS	NS
Kearney et al. (17)	2003	184	24 ± 1†	NS	29	Reynolds Medical Pathfinder system by independent blinded staff	– No difference in groups QRS ≤150 vs. >150 ms (0.08)
Yu et al. (18)	2003	112	38 ± 10*	40	NS	NS	Yes (<0.001)
Iuliano et al. (4)	2002	669	24 ± 8‡	43	NS	ECG read by computer and cardiologist	Yes (<0.001)
Kalra et al. (8)	2002	155	23 ± 9*	47	19	Average of three readings from lead V_2 with electronic calipers	Yes (<0.001)
Shenkman et al. (7)	2002	3,471	NS	21	8	Mean duration in all 12 leads as measured by computer	NS
Farwell et al. (19)	2000	721	37 ± 14*	25	NS	NS	NS
Shamim et al. (9)	1999	241	28*	38	NS	Average of three readings from lead V_2 with electronic calipers	Trend only

Several articles included in the table did not provide standard deviations of data. LVEF and QRS correlation indicates the presence of a statistically significant lower LVEF with wide QRS duration compared with LVEF in patients with narrow QRS duration. *Mean LVEF of all patients regardless of QRS duration; some studies provided LVEF of subgroups but not from the entire group; †only patients with QRS ≥150 ms; ‡only patients with QRS >120 ms.

ECG = electrocardiogram; HF = heart failure; IVCD = intraventricular conduction delay; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NS = not stated; QRS measurement = method used to determine QRS duration; RBBB = right bundle branch block; Year = year of publication.

In a substudy of the Multicenter Unsustained Tachycardia Trial (MUSTT) (35), Zimetbaum et al. (36) analyzed ECGs from 1,638 patients (approximately 70% had HF) who did not receive antiarrhythmic drugs or implantable cardioverter-defibrillators (ICDs). Seventy-five percent of the patients with LV hypertrophy had clinical congestive HF, and so did 62% of those without LV hypertrophy. The primary end point was cardiac arrest or arrhythmic death. Multivariate analyses identified nonspecific intraventricular conduction delay (defined as QRS ≥0.11 s but morphologically different from LBBB or RBBB) as a predictor of arrhythmic or cardiac arrest (hazard ratio [HR], 1.44; 95% confidence interval [CI], 1.11 to 1.88) and total (HR, 1.47; CI, 1.22 to 1.78) mortality. The LBBB was also a significant predictor of arrhythmic (HR, 1.49; CI, 1.02 to 2.17) and total (HR, 1.61; CI, 1.26 to 2.08) mortality. The RBBB, however, was not associated with increased arrhythmic or total mortality (36).

Prolongation of QRS and severe cardiomyopathy (defined as LVEF <30%) have an additive effect on mortality. The highest mortality rates are seen in patients with HF with QRS prolongation and LVEF <35% secondary to both ischemic and non-ischemic etiologies (4,7).

In 1995, Silverman et al. (32) reported that QRS prolongation had a different prognostic value in patients with chronic HF with non-ischemic versus ischemic cardiomyopathy. They found that a prolonged QRS carried a significantly worse prognosis only in patients with non-ischemic cardiomyopathy. These results are at variance from the observations of Iuliano et al. (4), who found no significant difference (median follow-up, 45 months) in

Table 2. Relationship of QRS Duration and Mortality in Heart Failure Patients

Study	Year	No. of Patients	Etiology	Mean Follow-Up (months)	QRS Limit (s)	Patients With Wide QRS (%)	Mean LVEF (%)	Significantly Increased All-Cause Mortality*	Significantly Increased Sudden Death*	Significantly Increased Cardiac Death*
Freudenberger et al. (11)	2004	100	Isch 42%	35	≥0.12	34	19 ± 7†	Yes	NS	NS
Baldasseroni et al. (13)	2003	5,517	Isch 46%	12	>0.12	38	NS	Yes	NS	NS
Bode-Schnurbus et al. (14)	2003	165	NS	24	≥0.15	16	33 ± 14‡	No	NS	Yes
Kearney et al. (17)	2003	184	Isch 86%	60	>0.15	29	24 ± 1§	Yes	No	Yes
Iuliano et al. (4)	2002	669	Isch 71% Nonisch 29%	Median = 45	≥0.12	43	24 ± 8†	Yes Yes No	Yes Yes No	NS NS NS
Kalra et al. (8)	2002	155	NS	28 ± 25	≥0.12	47	23 ± 9‡	Yes	NS	NS
Shamim et al. (22)	2002	112	Isch 62% Nonisch 38%	12	Mean = 0.13	NS	38‡	Yes	NS	NS
Shenkman et al. (7)	2002	3,471	NS	32 ± 30	≥0.12	21	NS	No	NS	NS
Farwell et al. (19)	2000	721	Isch 61%	12	≥0.12	25	37 ± 14‡	No	NS	NS
Shamim et al. (9)	1999	241	NS	31 ± 18	≥0.12	38	28‡	Yes	NS	NS
Huang et al. (31)	1995	64	NS	18 ± 12	>0.12	20	NS	Yes	NS	NS
Silverman et al. (32)	1995	200		19 ± 14	≥0.12	33	22 ± 8‡	No	NS	NS
Isch			44%		≥0.12		24 ± 8‡	No	NS	NS
Nonisch			56%		≥0.12		21 ± 8‡	Yes	NS	NS

Several articles included in the table did not provide standard deviations of data. *Compared with patients with a narrow QRS complex; †only patients with QRS >120 ms; ‡mean LVEF of all patients regardless of QRS duration; some studies provided LVEF of subgroups but not from the entire group; §only patients with QRS ≥150 ms.
Isch = ischemic; LVEF = left ventricular ejection fraction; Nonisch = nonischemic; NS = not stated; Year = year of publication.

mortality or sudden death in patients with non-ischemic cardiomyopathy and QRS >0.12 s versus QRS <0.12 s. However, Iuliano et al. (4) reported a significantly higher all-cause and sudden-death mortality rate in patients with HF with ischemic cardiomyopathy and a longer QRS duration. Comparing the groups with QRS ≥0.12 s versus QRS ≤0.12 s (median follow-up, 45 months), the mortality was 51% vs. 34% and the sudden death rate was 25% vs. 17%, respectively (4).

VENTRICULAR TACHYCARDIA

The aforementioned data raise the question of whether ventricular tachycardia (VT) accounts for the increased mortality in patients with HF with QRS prolongation. A wide QRS complex predisposes patients with HF to bundle branch re-entrant VT (bundle branch to bundle branch), a relatively rare arrhythmia that occurs predominantly in patients with dilated cardiomyopathy and a wide QRS complex in the form of LBBB or a nonspecific intraventricular conduction delay resembling LBBB (37–39). Although many patients with this form of VT receive ICDs because of the risk of other types of VT, the diagnosis of bundle branch re-entry VT is important because it can be easily eliminated by ablation of the right bundle branch.

Horwich et al. (40) studied 777 patients using electrophysiologic studies for assessment of VT inducibility. The percentage of patients with HF was not specified. Sustained monomorphic VT was induced in 49% and 23% ($p < 0.0001$) of patients with QRS ≥120 ms and <120 ms, respectively, with bundle branch re-entrant VT in a minority, and multivariate analysis showed that QRS duration was an independent risk factor for VT inducibility. In fact, the risk of inducible sustained monomorphic VT increased by 2.4% for each 1 ms increase in QRS duration. This suggests that intraventricular conduction delay with or without a scarred myocardium can act as a substrate for re-entrant VT.

ICD TRIALS

Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II). In MADIT-II, Moss et al. (41,42) studied the effect of prophylactic cardioverter-defibrillator implantation in patients with NYHA functional class I to III, LVEF ≤30%, and a myocardial infarction one or more months before enrollment in the study. The patients were characterized as having substantial LV dysfunction (mean baseline LVEF was about 23%), and 70% were in NYHA functional class I or II HF. The actual incidence of clinical HF was not mentioned, but it was probably common in this highly selected patient population. We believe that the MADIT-II observations can be extrapolated to the general HF patient population. Three clinically relevant categories of QRS duration (<0.12 s, 0.12 to 0.15 s, >0.15 s) were analyzed. There was a trend toward better reduction in mortality with ICD therapy in patients with the wider QRS complexes, but it was not statistically significant. Moss et al.

(42) then extended their analysis of the MADIT II data to include each of six QRS durations (<0.09 s, 0.09 to 0.10 s, 0.11 to 0.12 s, 0.13 to 0.14 s, 0.15 to 0.16 s, >0.16 s). Similar HRs (mortality reduction) were found across all six QRS durations, suggesting that QRS duration is not an effective risk stratification factor for ICD therapy in the MADIT II population.

In addition to the reduction in mortality results, the MADIT II investigators also noted a slightly higher rate of hospitalization for HF in the ICD group compared with control patients (19.8% vs. 14.9%, respectively) (41). The higher hospitalization rate might have been attributable to mechanical LV dyssynchrony induced by chronic right ventricular pacing (27,28,30). Indeed, preliminary data from the MADIT II trial suggested that HF is related to the percentage of ventricular pacing (43), hence the importance of minimizing right ventricular pacing, especially in patients who do not need it.

Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). The SCD-HeFT was a randomized, placebo-controlled study designed to determine whether amiodarone or a single-chamber ICD programmed to shock only (no back-up pacing) would reduce all-cause mortality when compared with placebo (double-blind to drug therapy) in patients with dilated cardiomyopathy (ischemic or nonischemic), NYHA functional class II and III HF, and LV dysfunction (LVEF ≤35%) (44–46). A total of 2,521 patients were enrolled with randomization to ICD (n = 829), amiodarone therapy (n = 845), or placebo (n = 847). The median age of patients was 60 years (range, 19 to 90 years). Unlike the MADIT II trial, the SCD-HeFT study incorporated patients with nonischemic cardiomyopathy as well as those with ischemic HF. Most importantly, both patient groups were found to benefit from ICD therapy. When stratifying the ECG data in the ICD versus placebo groups, ICD therapy was associated with a significant reduction in the risk of mortality compared with placebo, regardless of the ECG measure, including QRS duration <120 ms or ≥120 ms. Another analysis found that although ICD shock rates were highest in patients with a longer QRS duration, patients with a narrow QRS also experienced a significant number of shocks, suggesting that treatment is warranted for this group also at higher risk.

A subset of MADIT II-like patients enrolled in SCD-HeFT (approximately 80% of the ischemic patients in SCD-HeFT met MADIT II criteria) showed the same reduction in mortality with ICD therapy regardless of QRS duration. Thus, for the SCD-HeFT population, no ECG measure seems to be specific enough to provide subgroup risk categorization for either excluding or selecting patients for ICD therapy.

On the basis of the MADIT II and SCD-HeFT data, the Centers for Medicare and Medicaid recently abandoned their restrictions on Medicare reimbursement for ICDs in patients with a prior myocardial infarction and LVEF of 30% or less and QRS duration ≤120 ms (47).

Despite the above considerations, a wide QRS complex remains an important prognostic marker in ICD patients with HF. In a recent study over 24 months in ICD patients with HF, those with a wide underlying QRS complex showed more than double the cardiac mortality than those with a narrow QRS complex (14). In view of two recent meta-analyses suggesting that resynchronization decreases mortality (48,49), it is tempting to postulate that the mortality in ICD patients with a wide QRS complex might have been reduced by upgrading their devices to biventricular ICDs. The association of a wide QRS complex with more advanced disease in ICD patients is also reflected in the high incidence of an elevated defibrillation threshold at the time of ICD implantation in patients with QRS ≥200 ms, requiring the use of high-output ICDs (50).

CARDIAC RESYNCHRONIZATION

Growing experience with cardiac resynchronization therapy (CRT) has highlighted the limitations of a wide QRS complex as a surrogate for mechanical LV dyssynchrony (51–83). Widening of the QRS complex was a major entry criterion in the recent trials and other studies of biventricular pacing in patients with HF with LVEF ≤35% (Table 3). The QRS duration in the major trials ranged from >120 to >150 ms (63,67,77,84).

Electrocardiographic parameters. QRS DURATION AND MECHANICAL DYSSYNCHRONY. Barring a very wide spontaneous QRS complex, which probably increases the likelihood of associated mechanical LV dyssynchrony (54), the latter is not necessarily related to electrical dyssynchrony judged by QRS duration (Table 3). Indeed, the correlation is weak. Some patients with a wide QRS and a severely depressed LVEF may show no area of substantial mechanical delay (85). Thus, the predictive value of the basal QRS complex is poor for responders and nonresponders. (Table 3: responders consist of patients who had a statistically significant decrease in NYHA functional class (or equivalent) and/or increase in LVEF (or equivalent), and nonresponders consist of those who showed no change in these two indexes). This may explain why 20% to 30% of the patients in the major trials did not have a response to CRT (86–89). In this respect, Bleeker et al. (85) evaluated the role of the QRS complex as a marker of mechanical LV dyssynchrony (based on septal-to-lateral conduction delay) in 90 patients with severe HF (LVEF <35%, NYHA functional class III to IV). Severe mechanical LV dyssynchrony was defined as an electromechanical delay >60 ms between the septum and the lateral wall based on tissue Doppler imaging, the technique that has thus far been used the most frequently to determine LV mechanical dyssynchrony. The >60 ms value was based on previous observations that a delay >60 ms between the peak systolic velocity of the septum and lateral wall was highly predictive of response to CRT. Severe mechanical LV dyssynchrony was observed in 27% of the patients with a narrow QRS complex

Table 3. Biventricular Pacing and QRS Duration

Study	Year	No. of Patients*	Form of Prolonged QRS	Mean Follow-Up (months)	Mean QRS Before CRT (ms)	Mean QRS After CRT (ms)	Previous QRS vs. QRS After CRT† p Value	Clinical and Hemodynamic Improvement	Relationship Between QRS Shortening and Clinical Improvement	Correlation of Spontaneous QRS Duration and Clinical Response
Bonanno et al. (51)	2004	37	NS	8 ± 8	189 ± 35	162 ± 13	<0.001	NYHA ↓, LVEF ↑	NS	NS
Molhoek et al. (52)	2004	61	100% LBBB	6	177 ± 30	161 ± 24	<0.01	NYHA ↓, LVEF NS	No	No
Penicka et al. (53)	2004	49	100% "LBBB-like"	6				NYHA ↓, LVEF ↑	No	Yes
Responders		27			190 ± 30	152 ± 37	<0.01	Yes	No	—
Non-responders		22			171 ± 27	154 ± 30	<0.01	No	No	—
Yu et al. (54)	2004	58							No	No
QRS 120 to 150 ms		27	15% LBBB 85% IVCD	3	134 ± 14	NS	NS	NYHA ↓, LVEF ↑		
QRS >150 ms		31	87% LBBB 13% IVCD	3	172 ± 22	NS	NS	NYHA ↓, LVEF ↑		
Achilli et al. (55)	2003	52	NS	18 ± 9	151 ± 31	124 ± 10	<0.001	NYHA ↓, LVEF ↑	NS	NS
Bax et al. (56)	2003	22	100% LBBB	3	172 ± 33	158 ± 26	<0.05	NYHA ↓, LVEF ↑	NS	NS
Chan et al. (57)	2003	63	NS	3	182 ± 31	151 ± 25	<0.001	NYHA ↓, LVEF ↑	Yes	NS
Duncan et al. (58)	2003	34	IVCD	12	172 ± 19	159 ± 33	0.04	NYHA ↓, LVESD ↓, LVEDD ↓, LVEF NS	NS	NS
Gasparini et al. (59)	2003	104	85% LBBB 8% RBBB 7% Other	9	165 ± 37	143 ± 38	0.013	NYHA and LVEF improved but statistical data ns	NS	NS
Gasparini et al. (25)	2003	158	NS	11					NS	No
QRS 110 to 150 ms		30	NS		130 ± 15	133 ± 15	NS	NYHA ↓, LVEF ↑	NS	—
QRS ≥150 ms		128	NS		184 ± 22	152 ± 17	<0.0001	NYHA ↓, LVEF ↑	NS	—
Toussaint et al. (60)	2003	34	100% LBBB	20 ± 7	179 ± 18	159 ± 16	<0.0001	NYHA ↓, LVEF ↑	No	No
Young et al. (61)	2003	187	13% RBBB Rest NS	6	165 ± 22	−20	<0.001	NYHA ↓ Trend ↓LV Vols, LVEF NS	NS	No
Yu et al. (62)	2003	30	57% LBBB 43% IVCD	3	167 ± 33	145 ± 25	0.001	NYHA ↓, LVEF ↑	No	No
Abraham et al. (63)	2002	228	NS	6	167 ± 21	Median decrease of 20 ms	<0.001	NYHA ↓, LVEF ↑	NS	No
Ansalone et al. (64)	2002	31	100% LBBB	>1 week and <1 month	160 ± 27	123 ± 24	<0.001	NYHA ↓, LVEF ↑	No	NS
Martinelli-Filho et al. (65)	2002	24	100% LBBB	24.5	180.7	177.4	ns	NYHA ↓, LVEF ↑	NS	NS
Gras et al. (66)	2002	103	NS	12	178 ± 28	152 ± 24	<0.001	NYHA ↓, LVEF ↑	NS	NS
Linde et al. (67)	2002	48	87% LBBB Rest NS	12	176 ± 19	156 (from figure only)	<0.05	NYHA ↓, LVEF ↑	NS	NS
Lunati et al. (68)	2002	52	"Majority LBBB"	12 ± 5	194 ± 33	159 ± 19	<0.0001	NYHA ↓, LVEF ↑	NS	No
Pitzalis et al. (69)	2002	20	100% LBBB	1	169 ± 16	132 ± 12	<0.0001	LVEF ↑, NYHA NS	NS	No
Reuter et al. (70)	2002	102	0% RBBB	12	184 ± 38	168 ± 25	<0.01	NYHA ↓, LVEF ↑	No	No
Ricci et al. (71)	2002	48	NS	9 ± 4	154 ± 29	120 ± 18	<0.001	NYHA ↓, LVEF ↑	NS	NS

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Table 3 Continued

Study	Year	No. of Patients*	Form of Prolonged QRS	Mean Follow-Up (months)	Mean QRS Before CRT (ms)	Mean QRS After CRT (ms)	Previous QRS vs. QRS After CRT† p Value	Clinical and Hemodynamic Improvement	Relationship Between QRS Shortening and Clinical Improvement	Correlation of Spontaneous QRS Duration and Clinical Response
Saxon et al. (72)	2002	53	63% LBBB 3% RBBB 34% Other	4	177 ± 34	157 ± 32	0.12 ns	LVEF not ↑, LVEDD ↓, LVEDD ↓, LVESV ↓, NYHA NS	No	No
Sogaard et al. (73)	2002	20	90% LBBB 10% RBBB	12.6	189 ± 23	NS	NS	NYHA ↓, LVEF ↑	NS	No
Yu et al. (74)	2002	25	NS	3	162 ± 30	142 ± 20	0.001	NYHA ↓, LVEF ↑	NS	NS
Alonso et al. (75)	2001	102	NS	15 ± 13	185 ± 26	158 ± 19	<0.001	NYHA ↓, LVEF ↑	NS	NS
Ansalone et al. (76)	2001	21	100% LBBB	>1 week and <1 month	158 ± 31	122 ± 27	0.00006	NYHA ↓, LVEF ↑	NS	NS
Cazeau et al. (77)	2001	48	NS	3	174 ± 20	157 ± 30	<0.002	NYHA NS, LVEF NS QOL ↑, 6WD ↑	NS	NS
Leclercq et al. (78)	2000	37 22, SR 15, AF	80% "LBBB aspect" 20% PM	14 ± 9	181 ± 23	About 10% reduction	NS	NYHA ↓, LVEF ↑ only in the AF group	NS	NS
Leclercq et al. (79)	2000	50	40% PM Rest "LBBB aspect"	15 ± 10	197 ± 32	162 ± 29	<0.001	NYHA ↓ LVEF ↑	NS	NS
Reuter et al. (80)	2000	47	NS	8	193 ± 40	168 ± 29	<0.01	NYHA ↓, LVEF not ↑	No	NS
Toussaint et al. (81)	2000	21	NS	12	180	164	0.001	LVEF ↓, NYHA NS	NS	NS
Alonso et al. (82)	1999	26	88% LBBB 4% RBBB 8% IVCD	8 ± 4	179 ± 22‡	154 ± 17‡	0.0004‡	NYHA ↓, LVEF NS	Yes	NS
Gras et al. (83)	1998	68	NS	3	179	143	<0.001	NYHA ↓, LVEF not ↑	No	NS

*Studies with ≥20 patients; †p value comparing QRS duration before and after CRT; ‡p value is for the responder group (19 of 26 patients). There was no difference in QRS duration after CRT in the non-responder group (7 of 26 patients). Patients were not evaluated a single group. Acute studies are not included. Several articles in the Table provided no standard deviations on data.

AF = atrial fibrillation; CRT = cardiac resynchronization therapy; IVCD = intraventricular conduction delay; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; ms = milliseconds; No. = number; NS = not stated; ns = not statistically significant; NYHA = New York Heart Association; PM = previously implanted conventional pacemaker; pts = patients; RBBB = right bundle branch block; Vols = volumes; Year = year of publication.

(>120 ms), in 60% of patients with a QRS duration 120 to 150 ms, and in 70% of patients with QRS >150 ms. Thus, 30% to 40% of patients with a wide QRS (predominantly reflecting left-sided conduction delay) complex did not show mechanical LV dyssynchrony, a figure that correlates with the reported percentage of nonresponders to CRT selected on the basis of QRS duration. For this reason, echocardiographic assessment with quantification of LV dyssynchrony is emerging as a superior predictor of CRT outcome than the widened QRS complex (53–55,62,69,73,85,86,89–91).

RBBB. So far, the experience of CRT in a small number of patients with RBBB and systolic HF is mixed, and it is likely that benefit may be restricted to patients with demonstrable mechanical LV dyssynchrony by echocardiography (92).

NARROW QRS COMPLEX <120 MS. It is possible that patients with HF with a narrow QRS complex (<120 ms) may benefit from CRT if they have echocardiographic mechanical LV dyssynchrony. This question is presently under intensive clinical investigation (55,93).

QRS NARROWING AFTER CARDIAC RESYNCHRONIZATION. The paced QRS complex often narrows after resynchronization, but there is no correlation between QRS narrowing and the clinical response (Table 3). In some cases the QRS complex after CRT may actually lengthen or remain unchanged despite substantial improvement in mechanical LV dyssynchrony. Increased QRS duration with CRT does not necessarily reflect the presence of ventricular areas with slow conduction resulting in more heterogeneous myocardial activation. With mono-chamber LV pacing, there is an obvious discrepancy between QRS duration (compared with baseline) and hemodynamic and clinical improvement (94). Thus, in patients with HF, the paced QRS duration cannot be assumed to reflect a more heterogeneous propagation pattern of LV activation and prolonged duration of mechanical activation.

CONCLUSIONS

A wide QRS complex reflecting left-sided intraventricular conduction delay in patients with HF is associated with more advanced myocardial disease, worse LV function, poorer prognosis, and a higher all-cause mortality rate compared with patients with a narrow QRS complex. The influence of a wide QRS complex on the incidence of cardiac or sudden death is unclear because of limited observations. A progressive increase in QRS duration worsens the prognosis. In patients with systolic HF, the presence of a left-sided conduction delay alone can no longer be automatically equated with the presence of mechanical LV dyssynchrony, which is actually present in only about 70% of cases. Mechanical LV dyssynchrony is best shown by evolving echocardiographic techniques (predominantly tissue Doppler imaging) currently in the process of standardization. Echocardiographic parameters will complement or even replace QRS complex duration as a criterion for CRT patient selection. The duration of the basal QRS complex does not reliably predict the clinical response to ventricular resynchronization, and QRS narrowing after CRT does not correlate with hemodynamic and clinical improvement.

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