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Khidir, M.J.H.; Delgado, V.; Marsan, N.A.; Schalij, M.J.; Bax, J.J.

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QRS duration versus morphology and survival after cardiac resynchronization therapy

Mand J.H. Khidir, Victoria Delgado*, Nina Ajmone Marsan, Martin J. Schalij and Jeroen J. Bax

Heart Lung Center, Leiden University Medical Center, Leiden, The Netherlands

Abstract

Aims The prognostic implications of QRS duration and morphology in heart failure patients treated with cardiac resynchronization therapy (CRT) remains debated. The present evaluation investigated the association between QRS duration (<150 vs. \geq 150 ms) and QRS morphology (left bundle branch block [LBBB] vs. non-LBBB) and long-term prognosis of a large cohort of unselected heart failure patients treated with CRT according to contemporary guidelines.

Methods and results Of 973 heart failure patients treated with CRT (mean age 66.1 ± 9.8 years, 76% male), 658 patients (68%) showed QRS duration \geq 150 ms, and 772 patients (79%) had LBBB configuration. Compared with patients with QRS duration <150 ms, patients with QRS duration \geq 150 ms had less frequently ischaemic cardiomyopathy and atrial fibrillation and showed larger left ventricular volumes and lower left ventricular ejection fraction. Compared with patients with non-LBBB configuration, patients with LBBB morphology were younger, less often males and less often had ischaemic cardiomyopathy and atrial fibrillation. On multivariable analysis, after correcting for relevant clinical and echocardiographic variables, LBBB morphology was significantly associated with better survival [hazard ratio (HR) 0.737; 95% confidence interval (CI) 0.584–0.931; $P = 0.010$], whereas there was no statistically significant association between QRS duration \geq 150 ms and survival (HR 0.889; 95% CI 0.726–1.088; $P = 0.252$).

Conclusions In this large population of heart failure patients treated with CRT, QRS morphology was independently associated with long-term survival. The association between QRS duration and long-term survival was not statistically significant.

Keywords Cardiac resynchronization therapy; Left bundle branch block; Prognosis; QRS duration

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*Correspondence to: Victoria Delgado, Department of Cardiology, Heart Lung Center, Leiden University Medical Center, Albinusdreef 2, 2300 RC Leiden, The Netherlands. Tel: +31 71 5262020; Fax: +31 71 5266809. Email: v.delgado@lumc.nl

Introduction

Cardiac resynchronization therapy (CRT) is an established therapy for heart failure patients with reduced left ventricular ejection fraction (LVEF \leq 35%) and prolonged QRS duration (\geq 120 ms) leading to important improvements in left ventricular (LV) function and prognosis.^{1–4} However, the individual prognostic benefit is not consistent, and selection of patients who will benefit from CRT remains challenging. Sub-analyses from randomized controlled trials and meta-analyses pointed out that QRS duration and morphology are relevant for prognosis of patients treated with CRT.^{5–9} Patients with shorter QRS duration and/or non-left bundle branch block (LBBB) morphology appear to benefit less than patients with longer QRS duration and/or LBBB morphology.^{5–9} However, the

patients included in randomized trials with non-LBBB configuration represent a minority (5–30%), and approximately one third has a QRS duration between 120–150 ms.^{1–4} In addition, the impact of QRS duration and morphology on CRT outcomes of selected patients included in randomized trials (frequently excluding patients with atrial fibrillation or associated comorbidities) may differ from unselected populations. A large registry has demonstrated that patients with QRS duration $>$ 150 ms, and LBBB morphology had the most benefit from CRT, while the prognostic benefit of patients with shorter QRS duration or non-LBBB configuration remained controversial.¹⁰ To provide further evidence in this important domain, the current evaluation investigated the association between QRS duration (<150 vs. \geq 150 ms) and QRS morphology (LBBB vs. non-LBBB) and long-term prognosis of a large cohort of

unselected heart failure patients treated with CRT according to contemporary guidelines.

Methods

Patients and data collection

From an ongoing registry of heart failure recipients of a CRT with/without defibrillator function between 1999 and 2013, 973 patients were included in this analysis.¹¹ All patients had drug-refractory heart failure symptoms, LVEF $\leq 35\%$ and prolonged QRS duration (≥ 120 ms) according to recommendations.^{12,13} Patients with right ventricular pacing who received an upgrade of the device were excluded from this analysis. Twelve-lead electrocardiograms (ECGs), together with clinical and echocardiographic evaluation, were routinely performed before device implantation and after 6-month follow-up. Patients were followed-up regularly at the heart failure outpatient clinic of the Leiden University Medical Center. All-cause mortality together with heart transplantation and LV assist device (LVAD) implantation was the composite primary endpoint. Survival follow-up data were retrieved from municipality registries. Data of patients lost at follow-up were considered up to the last date of follow-up. The association between QRS duration and morphology and the primary endpoint was assessed. The Dutch Central Committee on Human-related Research (CCMO) allows the use of anonymous data without prior approval of an institutional review board provided that the data are acquired for routine patient care. All data used for this study were acquired for clinical purposes and handled anonymously.

QRS duration and morphology

Standard 12-lead ECGs were acquired with calibration at 0.1 mV/mm at a paper speed of 25 mm/s. QRS duration was automatically detected and visually controlled. QRS morphology was defined according to current definitions.¹⁴ QRS duration and morphology were both categorized into <150 vs. ≥ 150 ms and LBBB vs. non-LBBB, respectively.

Clinical and echocardiographic evaluation

Clinical evaluation included assessment of the New York Heart Association (NYHA) functional class, 6 min walk test¹⁵ and quality of life according to the Minnesota Living with Heart Failure questionnaire.¹⁶

Transthoracic echocardiography was performed with the patients in left lateral decubitus position. Commercially available equipment (Vingmed Vivid 7 or 9, General Electric Vingmed, Milwaukee, USA) was used for data acquisition. Standard parasternal and apical views were acquired to

assess LV dimensions and function. In addition, colour, continuous, and pulsed wave Doppler data were obtained to evaluate LV diastolic function, valvular heart disease, and to estimate pulmonary pressures. LV end-diastolic and end-systolic volumes were measured from the apical two and four-chamber views, and LVEF was calculated using the Simpson's method.¹⁷ Mitral regurgitation severity was graded semi-quantitatively using an integrative approach including vena contracta width and measurement of regurgitant volume and effective regurgitant orifice area with the proximal isovelocity surface method when possible.^{18,19}

Definition of response to cardiac resynchronization therapy

Response to CRT was defined as a reduction of $\geq 15\%$ in LV end-systolic volume at 6 month follow-up. Patients who died or underwent heart transplantation or LV reconstructive surgery within 6 months after CRT implantation were considered non-responders.²⁰

Device implantation

Through a subclavian or cephalic vein access, the right atrial and ventricular leads were positioned traditionally. The coronary sinus was cannulized with the use of a guiding catheter, and a venogram was obtained. Afterwards, the LV lead was inserted in the coronary sinus and positioned in the lateral or posterolateral vein when possible. All leads were connected to a dual chamber biventricular CRT device. Evaluation of the device function was commonly combined with the regular controls at the heart failure outpatient clinic. The atrioventricular (AV) and inter-ventricular delays were set empirically at 120–140 and 0 ms, respectively, and CRT optimization was performed at follow-up at the discretion of the treating physician.

Statistical analysis

Continuous data are presented as mean \pm standard deviation (if normally distributed) and dichotomous data are presented as frequencies and percentages. Comparisons of continuous and dichotomous data between patient groups were performed using the Student's *t*-test and χ^2 test, respectively. Two-sided *P*-values < 0.05 were considered significant. Cox proportional hazards model was used to identify the variables associated with the primary endpoint. Variables with a significant *P*-value on univariable analysis were entered in the multivariable model using the enter method. In addition, AV node ablation performed in patients with atrial fibrillation

and low biventricular pacing rate was included as time-dependent co-variate. The hazard ratios (HR) and 95% confidence intervals (CI) are reported. All analyses were performed with SPSS for Windows, version 23.0 (SPSS, Chicago, IL).

Results

Baseline characteristics

Table 1 summarizes the baseline characteristics. The mean age was 66.1 ± 9.8 years, the majority of the population was male (76%), and ischaemic cardiomyopathy was the underlying cause of heart failure in 59% of the patients. NYHA functional class III or IV was reported by 697 patients (74%), and mean LVEF was $26 \pm 8\%$. The majority of patients ($n = 924$; 95%) received a CRT device with defibrillator capabilities.

QRS duration and morphology

A total of 315 patients (32%) showed a QRS duration <150 ms while the remaining 658 patients (68%) showed a

QRS duration ≥ 150 ms group. Patients in the latter group were less often affected by ischaemic cardiomyopathy and had less frequently atrial fibrillation as baseline rhythm compared with patients with a QRS duration <150 ms (Table 1). Furthermore, patients with a QRS duration ≥ 150 ms had larger LV volumes and lower LVEF than their counterparts. The distribution of CRT with defibrillator capabilities was similar between the groups QRS duration <150 vs. ≥ 150 ms (96 vs. 94%, $P = 0.292$).

Based on QRS morphology, 772 patients (79%) were categorized in the LBBB group and 201 (21%) patients in the non-LBBB group. The latter group comprised 114 patients with right bundle branch block and 87 with inter-ventricular conduction delay. Compared with patients in the non-LBBB group, patients with LBBB were younger, less often males, and less often had ischaemic cardiomyopathy. Additionally, atrial fibrillation was less frequent in patients with LBBB, the functional capacity was higher (as demonstrated by significantly longer walked distances during the 6 min walk test), and the renal function was better compared with patients with non-LBBB. Finally, the mean QRS duration in patients with LBBB was significantly longer than the QRS duration in patients with non-LBBB. There were no differences in the distribution of CRT with defibrillator

Table 1 Baseline characteristics

	Overall population ($n = 973$)	QRS duration		P-value	QRS morphology		P-value
		<150 ms ($n = 315$)	≥ 150 ms ($n = 658$)		Non-LBBB ($n = 201$)	LBBB ($n = 772$)	
Age (year)	66.1 ± 9.8	65.2 ± 10.2	66.5 ± 9.6	0.054	67.4 ± 9.7	65.8 ± 9.8	0.037
Gender (male)	738 (76%)	251 (80%)	487 (74%)	0.064	166 (83%)	572 (74%)	0.016
Aetiology (ischaemic)	570 (59%)	207 (66%)	363 (55%)	0.002	150 (75%)	420 (54%)	<0.001
NYHA III-IV	697 (74%)	223 (73%)	474 (74%)	0.816	146 (76%)	551 (73%)	0.427
Atrial fibrillation	158 (16%)	65 (21%)	93 (14%)	0.013	50 (25%)	108 (14%)	<0.001
6MWT (m)	319 ± 122	317 ± 120	320 ± 123	0.724	291 ± 120	327 ± 122	0.001
QoL	33 ± 19	35 ± 20	33 ± 18	0.206	36 ± 21	33 ± 18	0.097
Body mass index	26.4 ± 4.3	26.6 ± 4.3	26.3 ± 4.3	0.491	26.2 ± 3.7	26.5 ± 4.4	0.357
Diabetes mellitus	213 (22%)	78 (25%)	135 (21%)	0.157	53 (26%)	160 (21%)	0.104
eGFR (mL/min/1.73 m ²)	65 ± 24	66 ± 25	64 ± 23	0.217	61 ± 23	66 ± 24	0.024
Echocardiography							
LVEDV (mL)	218 ± 79	198 ± 70	227 ± 81	<0.001	208 ± 73	220 ± 80	0.058
LVESV (mL)	164 ± 70	147 ± 59	172 ± 73	<0.001	154 ± 62	167 ± 71	0.018
LVEF (%)	26 ± 8	27 ± 8	25 ± 8	0.008	27 ± 8	26 ± 8	0.059
Mitral regurgitation grade 3–4+	156 (16%)	43 (15%)	113 (18%)	0.213	32 (17%)	124 (17%)	1.000
Electrocardiogram							
QRS duration (ms)	161 ± 23	136 ± 8	173 ± 16	$<0.001^a$	158 ± 21	162 ± 23	0.019
QRS morphology (LBBB)	772 (79%)	241 (77%)	531 (81%)	0.154	0 (0%)	772 (100%)	$<0.001^a$
Medication							
Diuretic	805 (83%)	261 (83%)	544 (83%)	1.000	175 (87%)	630 (82%)	0.086
Spironolactone	442 (45%)	160 (51%)	282 (43%)	0.024	94 (47%)	348 (45%)	0.727
ACE-inhibitor	857 (88%)	272 (86%)	585 (89%)	0.296	172 (86%)	685 (89%)	0.268
β -blocker	706 (73%)	242 (77%)	464 (71%)	0.047	132 (66%)	574 (74%)	0.018
Anticoagulation/	798 (82%)	267 (85%)	531 (81%)	0.146	175 (87%)	623 (81%)	0.047
Antiplatelet drugs							
Statin	570 (59%)	196 (62%)	374 (57%)	0.127	137 (68%)	433 (56%)	0.003

6MWT, 6 min walk test; ACE, angiotensin converting enzyme; eGFR, estimated Glomerular Filtration Rate; LBBB, left bundle branch block; LVEDV, LV end-diastolic volume; LVESV, LV end-systolic volume; LVEF, LV ejection fraction; NYHA, New York Heart Association; QoL, quality of life according to the Minnesota Living with Heart Failure Questionnaire.

^aSignificant difference expected by definition of dichotomization.

capabilities in the non-LBBB vs. LBBB group (94 vs. 95%, $P = 0.389$).

Response to cardiac resynchronization therapy

Echocardiographic response to CRT after 6 months was observed in 498 patients (54%). LV reverse remodelling could not be evaluated in 54 patients because of missing follow-up echocardiographic evaluation. The response rate differed significantly between patient groups based on QRS duration and morphology. LV reverse remodelling was less frequently observed among patients with a QRS duration <150 ms compared with patients with a QRS duration ≥ 150 ms (44 vs. 59%; $P < 0.001$). Among patients with LBBB morphology, LV reverse remodelling was more frequently observed than in patients with non-LBBB morphology (56 vs. 46%; $P = 0.011$).

Long-term outcome

During a median follow-up of 59 (interquartile range 29–85) months, 423 patients reached the composite endpoint: 413 patients died, 5 patients received heart transplantation, and 5 patients underwent LVAD implantation. The survival curves for time to composite endpoint based on QRS duration and morphology accompanied by the corresponding log-rank test P -value are displayed in *Figure 1*. There were no differences in long-term survival when patients were dichotomized based on QRS duration. Despite the higher reverse remodelling rate in patients with a QRS duration ≥ 150 ms, the interaction between LV reverse remodelling and QRS duration did not reach statistical significance (HR 0.711; 95% CI 0.456–1.110; $P = 0.133$). However, when patients were dichotomized based on QRS morphology, patients with LBBB had better survival compared with patients with non-LBBB morphology. Patients with LBBB morphology and QRS duration ≥ 150 ms (reference group) and patients with LBBB morphology and QRS duration

<150 ms had comparable survival rates (HR 1.128; 95% CI 0.892–1.428; $P = 0.315$), whereas patients with non-LBBB configuration and QRS duration <150 ms (HR 1.590; 95% CI 1.130–2.238; $P = 0.008$) and patients with non-LBBB morphology and QRS duration ≥ 150 ms (HR 1.522; 95% CI 1.156–2.003; $P = 0.003$) had significantly worse survival compared to the reference group (*Figure 2*). Univariable and multivariable HR and 95% CI are displayed in *Table 2*. LBBB morphology was significantly associated with better survival (HR 0.737; 95% CI 0.584–0.931; $P = 0.010$), after correcting for age, gender, heart failure aetiology, NYHA III–IV, atrial fibrillation, AV node ablation, body mass index, diabetes mellitus, renal function, LV end-diastolic volume, LVEF, and mitral regurgitation. In contrast, there was no significant association between QRS duration ≥ 150 ms and survival (HR 0.889; 95% CI 0.726–1.088; $P = 0.252$).

Discussion

The present evaluation including a large cohort of unselected heart failure patients treated with CRT according to current recommendations shows that QRS morphology but not duration is independently associated with long-term survival.

Cardiac resynchronization therapy benefits in left bundle branch block versus non-left bundle branch block QRS morphology

Although a QRS duration ≥ 120 ms was an inclusion criterion for many randomized controlled trials on CRT, the distribution of different QRS morphologies was not balanced, and more than 70% of the included patients had LBBB morphology.^{1–4,21} QRS morphology (LBBB vs. non-LBBB) has been consistently associated with better outcomes in patients treated with CRT. For example, in the Cardiac Resynchronization-Heart

Figure 1 Kaplan–Meier survival curve for patients dichotomized twice according to QRS duration (A) and morphology (B) including univariate hazard ratios (HR) for QRS ≥ 150 ms and left bundle branch block (LBBB) morphology, respectively.

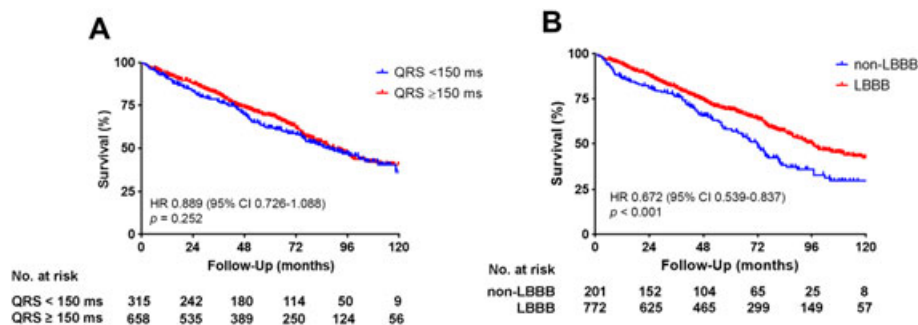


Figure 2 Kaplan–Meier survival curves for patients subdivided into four groups based on QRS morphology and duration. LBBB, left bundle branch block; HR, hazard ratios.

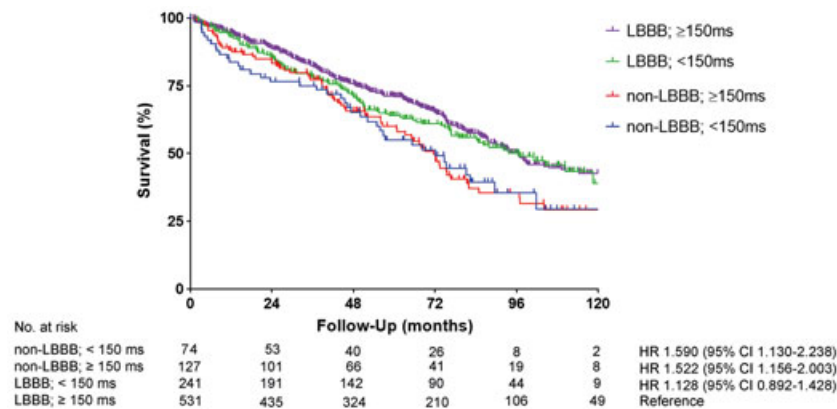


Table 2 Cox proportional hazards model

	Univariable HR (95% CI)	P-value	Multivariable HR (95% CI)	P-value
Age (year)	1.036 (1.025–1.047)	<0.001	1.020 (1.007–1.032)	0.002
Gender (male)	1.593 (1.247–2.035)	<0.001	1.310 (0.992–1.729)	0.057
Aetiology (ischaemic)	1.867 (1.524–2.309)	<0.001	1.461 (1.161–1.840)	0.001
NYHA III–IV	1.976 (1.516–2.576)	<0.001	1.501 (1.127–1.999)	0.005
6MWT (m)	0.996 (0.995–0.997)	<0.001		
QoL	1.016 (1.011–1.022)	<0.001		
Atrial fibrillation	1.591 (1.243–2.036)	<0.001	1.354 (1.014–1.808)	0.040
AV node ablation ^a	2.045 (1.221–3.426)	0.007	1.423 (0.773–2.619)	0.257
Body mass index (units)	0.972 (0.949–0.995)	0.017	0.964 (0.938–0.991)	0.009
Diabetes mellitus	1.643 (1.323–2.039)	<0.001	1.576 (1.238–2.006)	<0.001
eGFR (mL/min/1.73 m ²)	0.974 (0.970–0.979)	<0.001	0.981 (0.976–0.987)	<0.001
Echocardiography				
LVEDV (mL)	1.002 (1.001–1.003)	<0.001	1.002 (1.000–1.003)	0.035
LVESV (mL)	1.003 (1.002–1.004)	<0.001		
LVEF (%)	0.970 (0.958–0.983)	<0.001	0.990 (0.976–1.005)	0.195
Mitral regurgitation grade 3–4+	1.789 (1.421–2.254)	<0.001	1.324 (1.032–1.699)	0.027
ECG				
QRS duration (≥150 ms)	0.889 (0.726–1.088)	0.252		
QRS morphology (LBBB)	0.672 (0.539–0.837)	<0.001	0.737 (0.584–0.931)	0.010

CI, confidence interval; HR, hazard ratio; other abbreviations as in Table 1.

^aTime-dependent co-variate.

Failure (CARE-HF) trial, which randomized 813 patients to CRT + optimal medical therapy or optimal medical therapy alone, 94% of patients had LBBB morphology while only 5% of patients had right bundle branch block QRS configuration.⁶ The presence of right bundle branch block morphology was independently associated with the composite primary outcome of all-cause mortality and unplanned hospitalization for management of major cardiovascular events (HR 2.043, 95% CI 1.332–3.157; $P = 0.001$).⁶ In addition, the sub-study of the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) trial, including 1817 patients with sinus rhythm at baseline ECG, showed that the presence of LBBB morphology was associated with a 53% reduction in the risk of heart failure events or all-cause mortality

of patients randomized to CRT with defibrillator compared with patients treated with implantable cardioverter defibrillator (ICD) alone whereas patients with non-LBBB QRS morphology did not show clinical benefit from CRT.⁷ Subsequent meta-analysis pooling data from 5356 patients enrolled in four randomized trials showed that LBBB morphology was associated with significant reduction in the composite adverse clinical events of patients treated with CRT (risk ratio 0.64, 95% CI 0.52–0.77; $P < 0.0001$) whereas patients with non-LBBB configuration failed to show clinical benefit.⁹ Recently, the analysis of data from 31 892 heart failure patients treated with CRT (76% with LBBB QRS morphology) included in the National Cardiovascular Data Registry and the ICD registry showed that after a median follow-up of 3 years,

patients with LBBB morphology had 24% lower mortality risk than patients with non-LBBB morphology (HR 0.76, 95% CI 0.72–0.80; $P < 0.001$).²² Similarly, the present study, including unselected heart failure patients treated with CRT demonstrated that LBBB morphology was independently associated with superior survival. Therefore, LBBB morphology is an important criterion to select patients who will likely benefit from CRT.

Cardiac resynchronization therapy benefits in QRS duration <150 versus ≥ 150 ms

However, QRS duration has also been shown to be an important determinant of the clinical benefits of CRT. In the COMPANION trial, a QRS duration >148 ms was associated with significant reductions in all-cause mortality in patients treated with CRT.¹ In addition, the results of the randomized trials on CRT including patients with NYHA functional class II heart failure symptoms consistently showed that QRS duration ≥ 150 ms is associated with significantly reduced risk of all-cause mortality and heart failure hospitalization and larger LV reverse remodelling compared with patients with QRS duration <150 ms.^{3,4,21} In the MADIT-CRT trial, a QRS duration ≥ 150 ms [present in 1175 (64%) patients] was associated with lower risk of all-cause mortality or non-fatal heart failure (HR 0.48, 95% CI 0.37–0.64) compared with QRS duration <150 ms (HR 1.06, 95% CI 0.74–1.52; $P = 0.001$ for interaction).³ A recent meta-analysis, pooling data from 5813 patients included in five randomized trials, showed that QRS duration ≥ 150 ms was associated with clinical benefit from CRT (risk ratio 0.60, 95% CI 0.53–0.67; $P < 0.001$) whereas patients with QRS duration between 120 and 143 ms did not benefit from CRT (risk ratio 0.95, 95% CI 0.82–1.10; $P = 0.49$).⁸ In contrast, the substudy of the CARE-HF trial demonstrated that QRS duration was not associated with the composite primary outcome of all-cause mortality and unplanned hospitalization for management of major cardiovascular event.⁶ Of note, only 11% of patients had a QRS duration <150 ms, which may explain the lack of statistically significant association between QRS duration and outcome. Although the present study included a larger percentage of patients with a QRS duration <150 ms (32%), the results are in agreement with those observed in the CARE-HF substudy⁶ and QRS duration was not associated with long-term survival.

Integration of QRS morphology and duration versus outcome after cardiac resynchronization therapy

The aforementioned separate analyses showing that QRS duration and morphology are important determinants of clinical

benefits of CRT have led to the investigation of the interaction between QRS duration and morphology and its effects on CRT outcomes.^{5,10,23,24} The sub-analysis of the RAFT trial (after excluding patients with ventricular pacing and permanent atrial fibrillation) showed that regardless the QRS duration, patients with LBBB morphology who were randomized to CRT with defibrillator function showed a reduction in the rates of the primary outcome (composite endpoint of all-cause mortality and heart failure hospitalization) (HR 0.640; 95% CI 0.524–0.781; $P < 0.001$).⁵ In addition, there was a continuous relationship between QRS duration and greater benefit from CRT is these patients. In contrast, patients with non-LBBB morphology allocated to the CRT arm showed a clinical benefit only when the QRS duration was 160 ms or longer (HR 0.52, 95% CI 0.29–0.96; $P = 0.033$).⁵ In addition, an individual patient meta-analysis on data from 3872 patients randomized in five clinical trials showed that patients with LBBB morphology exhibited larger benefit from CRT than patients with non-LBBB morphology, although the difference was not statistically significant.²³ Importantly, QRS duration was significantly associated with reductions in all-cause mortality and the rates of the composite endpoint, particularly when QRS duration exceeded 140 ms.²³ Based on this evidence, current guidelines have modified the recommendations and consider CRT a class I indication for heart failure patients with LBBB morphology (regardless the QRS duration) and class IIa for patients with non-LBBB and QRS duration ≥ 150 ms and IIb for non-LBBB and QRS duration between 120–150 ms.¹³ However, it is important to note that these observations of substudies and meta-analyses of randomized clinical trials include selected patients and may not represent the ‘real-world’ patients being treated with CRT.

Data from the National Cardiovascular Data Registry, which included 24 169 patients aged 65 years or more who underwent CRT implantation, showed that the adjusted risk of 3 year mortality was lowest for the patients with LBBB and ≥ 150 ms QRS duration (20.9%) and highest for the patients with non-LBBB and <150 ms QRS (32.3%).¹⁰ There were no statistically significant differences in the adjusted risk of all-cause mortality between the groups of patients with LBBB configuration and QRS duration <150 ms (26.5%) and the patients with non-LBBB configuration and QRS duration ≥ 150 ms (30.7%). Therefore, it seems that patients with LBBB morphology and patients with wider QRS complex are more likely to benefit from CRT. These results are extended to a younger population in the present study, which demonstrates that QRS morphology but not duration is independently associated with long-term survival. Probably, the smaller patient groups have precluded us from observing significant differences between subgroups based on QRS morphology and duration. However, since these registries did not include a control group of patients who did not undergo CRT implantation, the efficacy of CRT could not be compared, and therefore, conclusions regarding the survival benefits of CRT in

patients with non-LBBB morphology and QRS duration between 120 and 149 ms remain unclear.

Limitations

Some limitations should be acknowledged. The present analysis was retrospective and single centre introducing a bias. However, the present study extends the results to a younger unselected population compared with previous series.¹⁰ In addition, comparisons between patients undergoing CRT implantation vs. patients who were medically treated or received a conventional dual-chamber ICD were not possible. Furthermore, beyond QRS duration and morphology, previous study has demonstrated the relevance of other ECG parameters (PR interval, QRS axis, amplitude, and durations of each component of the QRS complex, QRS notching, QRS hiroglyphs that suggest myocardial scar) in predicting CRT response.^{25,26} These parameters were not considered in the present study.

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Conclusions

In this large population of unselected heart failure patients treated with CRT according to contemporary guidelines, QRS morphology but not duration was independently associated with long-term survival.

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Conflicts of Interest

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