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Vectorcardiographic QRS area as a novel predictor of response to cardiac resynchronization therapy☆

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Abstract

Background: QRS duration and left bundle branch block (LBBB) morphology are used to select patients for cardiac resynchronization therapy (CRT). We investigated whether the area of the QRS complex (QRS_{AREA}) on the 3-dimensional vectorcardiogram (VCG) can improve patient selection.
Methods: VCG (Frank orthogonal lead system) was recorded prior to CRT device implantation in 81 consecutive patients. VCG parameters, including QRS_{AREA}, were assessed, and compared to QRS duration and morphology. Three LBBB definitions were used, differing in requirement of mid-QRS notching. Responders to CRT (CRT-R) were defined as patients with ≥15% reduction in left ventricular end systolic volume after 6 months of CRT.
Results: Fifty-seven patients (70%) were CRT-R. QRS_{AREA} was larger in CRT-R than in CRT non-responders (140 ± 42 vs 100 ± 40 μVs, $p < 0.001$) and predicted CRT response better than QRS duration (AUC 0.78 vs 0.62, $p = 0.030$). With a 98 μVs cutoff value, QRS_{AREA} identified CRT-R with an odds ratio (OR) of 10.2 and a 95% confidence interval (CI) of 3.4 to 31.1. This OR was higher than that for QRS duration >156 ms (OR = 2.5; 95% CI 0.9 to 6.6), conventional LBBB classification (OR = 5.5; 95% CI 0.9 to 32.4) or LBBB classification according to American guidelines (OR = 4.5; 95% CI 1.6 to 12.6) or Strauss (OR = 10.0; 95% CI 3.2 to 31.1).
Conclusion: QRS_{AREA} is an objective electrophysiological predictor of CRT response that performs at least as good as the most refined definition of LBBB.
Condensed abstract: In 81 candidates for cardiac resynchronization therapy (CRT) we measured the area of the QRS complex (QRS_{AREA}) using 3-dimensional vectorcardiography. QRS_{AREA} was larger in echocardiographic responders than in non-responders and predicted CRT response better than QRS duration and than simple LBBB criteria. QRS_{AREA} is a promising electrophysiological predictor of CRT response.

Keywords: Cardiac resynchronization therapy; QRS area; Vectorcardiography

Introduction

Cardiac resynchronization therapy (CRT) is recommended in patients with left bundle branch block (LBBB) conduction disturbances and persistent systolic heart failure despite optimal medical therapy. By simultaneous stimulation of the right (RV) and left (LV) ventricles the abnormal ventricular activation is (partly) resynchronized. This electrical resynchronization results in better LV pump function and reverse ventricular remodeling on the long term with a decrease in LV volumes, improving exercise capacity, and reducing heart failure hospitalizations and mortality [1,2].

Although the effects of CRT in large clinical trials are impressive on a group level, benefits for the individual patient vary considerably and are hard to predict. Up to half

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of the patients do not show a significant reduction in LV end systolic volume (LVESV) and around 30% of patients do not show clinical improvement [3]. Thus, to avoid invasive procedures with the risk of complications and the unnecessary use of expensive products, a reliable tool for prediction of responders to CRT is needed.

Many different strategies have been proposed, including several echocardiographic parameters [4], but up to now the ECG parameters QRS duration and QRS morphology are most widely accepted [5–8], emphasizing the importance of a good electrical substrate for this electrical therapy. Consequently, American and European guidelines for clinical decision making to implant a CRT device have included these electrical markers, i.e. QRS duration ≥150 ms with LBBB morphology for class 1A recommendation [9,10]. However, the definition of complete LBBB from the 12-lead ECG varies and the most appropriate definition is still under debate [11]. Recently, Strauss et al. [12] suggested to include the presence of mid-QRS notching or slurring. Some of their suggestions were subsequently incorporated in the American guidelines for identification of LBBB [13]. Besides the dissimilarity in how many and which leads should display QRS notching or slurring, the classification of the presence of "slurring" seems a subjective task.

We hypothesized that the QRS area (QRS_{AREA}) from the 3-dimensional (3D) vectorcardiogram (VCG), which combines QRS duration and electrical force of ventricular activation, improves prediction of the response to CRT in comparison to QRS duration on the ECG alone. Moreover, QRS_{AREA} is a continuous variable that is independent on the specific definitions of LBBB.

To this purpose we compared the predictive power of QRS_{AREA} to the conventional electrical markers QRS duration and morphology, the latter being specified using multiple LBBB criteria, prospectively in a cohort of CRT patients.

Materials and methods

Patients

Patients with heart failure scheduled for implantation of a CRT device (CRT-P or CRT-D) at the Maastricht University Hospital between September 2010 and June 2012 were prospectively approached to participate in this study (n = 138). After exclusion of patients with previous RV pacing (n = 22) or an intrinsic QRS duration <120 ms (n = 13), 103 patients were included. The study was performed according to the principles of the Declaration of Helsinki and approved by the ethics committee of Maastricht University Hospital. All participants gave fully informed written consent prior to investigation.

Study design

A standard 12-lead electrocardiogram (ECG) and a 3D-VCG were recorded the day before CRT device implantation with patients at rest and in supine position.

The ECG was recorded at a paper speed of 25 mm/s and a scale of 10 mm/mV. QRS duration on the ECG was determined using the automatic calculated value given by the ECG equipment after confirmation of correctness. LBBB was classified by a single investigator (CvD), who was blinded to the echocardiographic outcome, according to three different definitions.

LBBB_1 QRS duration ≥130 ms, rS or QS pattern in lead V_1, absence of q-waves in V_5–V_6 (conventional criterion) [6].

LBBB_2 QRS duration ≥130 ms, rS or QS pattern in lead V_1, intrinsicoid deflection in lead V_6 ≥ 60 ms, mid-QRS notching or slurring in 2 or more contiguous leads of V_1, V_2, V_5, V_6, I and aVL (according to Strauss et al. [12]).

LBBB_3 QRS duration ≥130 ms, rS or QS pattern in lead V_1, intrinsicoid deflection in lead V_6 ≥ 60 ms, broad notched or slurred R wave in leads V_5, V_6, I as well as aVL (according to American guidelines) [13].

The 3D-VCG was recorded the day before CRT device implantation using 8 electrodes positioned according to the modified Frank orthogonal lead system (X, Y and Z; Coronet II System, Ortivus AB, Danderyd, Sweden) at a sampling frequency of 500Hz for 5 minutes and averaged over one minute. The VCGs were analyzed offline using customized software [14]. The magnitude and direction of the maximum QRS vector in space were expressed as amplitude (QRS_{AMPL}; mV), azimuth (angle in the transversal plane with backward vector direction being negative; degrees) and elevation (angle in craniocaudal direction with upward vector directions being >90°; degrees). QRS-T angle is the 3D-angle between maximum QRS and T vector in the preferential planes of the QRS and T vector loops. The QRS area (QRS_{AREA}; μVs) was assessed as the "3D area" between the ventricular deflection curve and the baseline from the beginning to the end of the QRS complex (J-point) in X, Y and Z direction, and calculated as $(QRSx^2 + QRSy^2 + QRSz^2)^{½}$; Fig. 1).

Ischemic etiology of heart failure was defined as presence of delayed enhancement on cardiac magnetic resonance imaging, irreversible perfusion defects on myocardial thallium scans or untreated >70% stenosis in a coronary artery according to coronary angiograms.

Echocardiography (iE33 systems, Philips Medical Systems, Best, the Netherlands) was performed the day before device implantation as well as at follow up 6 months later. CRT responders (CRT-R) and non-responders (CRT-NR) were defined as patients with ≥15% and <15% reduction in LVESV respectively, as determined using the biplane method of disks (modified Simpson's method) after 6 months of CRT. In 26 patients the apical 2-chamber view was of poor quality and volumetric response was determined solely on the apical 4-chamber view.

Assessors of echocardiography and vectorcardiography were blinded to the results from the other analyses.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics software version 20 (SPSS Inc, Chicago, Illinois)

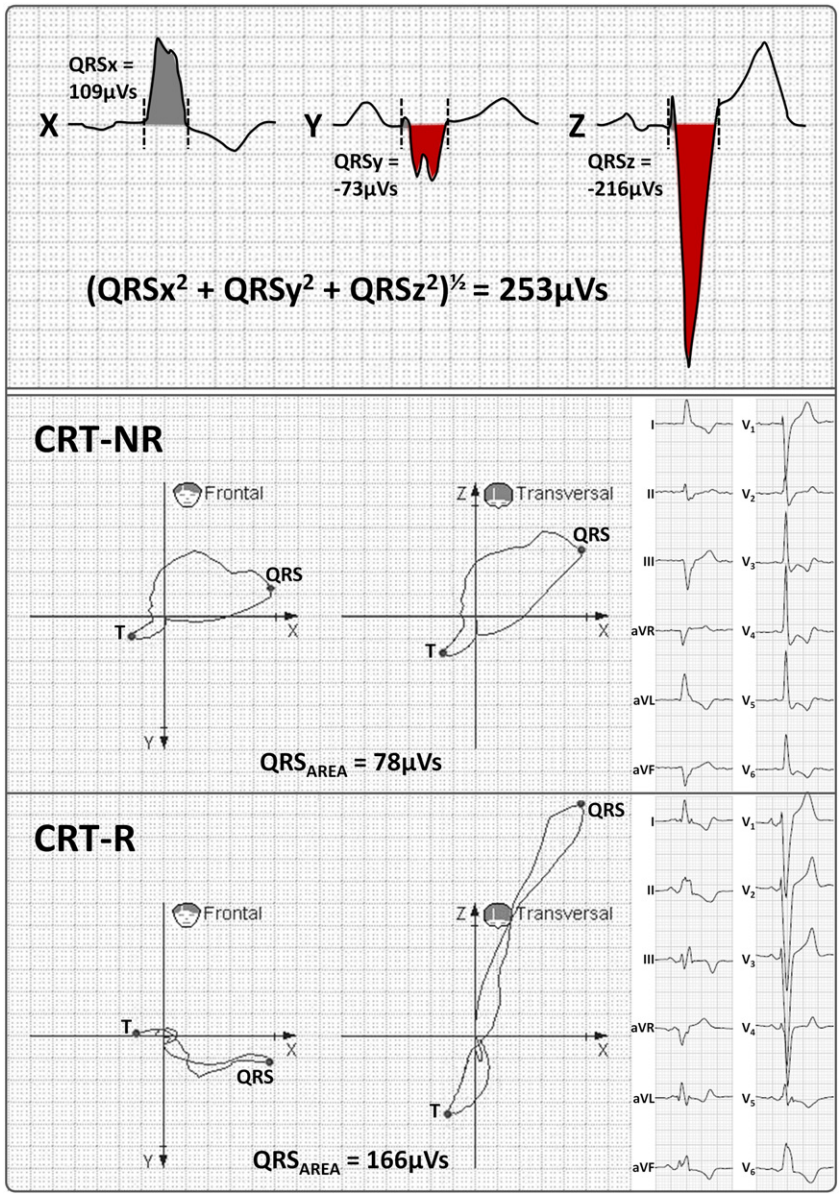

Fig. 1. Upper: Calculation of the 3-dimensional QRS area (QRS_{AREA}; µVs) using the integral between the ventricular deflection and the baseline from beginning to the end of the QRS complex in X, Y and Z. Lower: Typical vector loops in the frontal and transversal planes and corresponding ECGs for a CRT non-responder (CRT-NR) and a CRT responder (CRT-R). Note the dominant QRS vector amplitude in the transversal plane for the CRT-R, generating a larger value for QRS_{AREA} as compared to the CRT-NR. Both patients were classified as having LBBB according to conventional criteria (LBBB_1), while none of them were classified as having LBBB according to the more refined criteria (LBBB_2 or LBBB_3).

and MedCalc Software version 12.7.5 (MedCalc Software bvba, Ostend, Belgium). Continuous variables were presented as mean ± standard deviation (SD) or as median with interquartile range [IQR] in case of non-normal distribution; categorical variables as number (percentage). Linear correlations between different predictors and change in LVESV were evaluated by Pearson's correlation coefficient. Comparison between CRT-R and CRT-NR was performed by Students' T-tests or Mann–Whitney U test as appropriate (continuous variables) and χ^2 test (categorical variables). The classification performance of electrical parameters in identifying CRT response was evaluated by receiver operating characteristic (ROC) curve analysis. The significance of the difference in classification performance between parameters was evaluated by comparing the areas under the ROC curve (AUC) with the method proposed by DeLong et al. [15]. Continuous variables were dichotomized for comparison with discrete parameters by computing cut-off values with maximal sum of sensitivity and specificity. Subsequently, odds ratios (OR), sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) were calculated for all parameters. Differences were considered statistically significant at a two-sided p-value of 0.05.

Results

All patients underwent standard CRT device implantation with an RV lead implanted most frequently in the RV apex

Table 1
Baseline characteristics of 81 patients receiving CRT.

Patient characteristics, mean ± SD or median (IQR)	CRT-R [n = 57]	CRT-NR [n = 24]	P-value
Age [years]	67 ± 9	68 ± 8	0.572
Gender M/F [%]	56/44	75/25	0.111
BMI [kg/m^2]	28 ± 6	27 ± 5	0.981
Ischemic HF etiology [%]	39	75	0.003
Atrial fibrillation [%]	16	25	0.330
Diabetes mellitus [%]	35	21	0.205
6-MHWT [m]	409 ± 144	439 ± 136	0.506
NYHA class I/II/III/IV [%]	9/49/40/2	8/50/38/4	0.932
Minnesota [points]	33 ± 23	37 ± 26	0.646
eGFR [ml/min/1.73 m^2]	70 ± 36	65 ± 32	0.589
NT-proBNP [mmol/l]	102 (31–230)	314 (82–472)	0.116
Hb [mmol/l]	8.4 ± 1.1	8.1 ± 1.0	0.311
LVEF [%]	26 ± 7	26 ± 6	0.766
LVEDV [ml]	191 ± 57	206 ± 63	0.297
IVMD [ms]	50 ± 18	38 ± 24	0.030
RV lead Ap/S [%]	96/4	100/0	0.353
LV lead A/AL/L/IL/I [%]	0/54/16/28/2	4/63/4/29/0	0.303
Medication			
β-Blocker [%]	95	83	0.095
ACE-inhibitor/ARB [%]	88	88	0.978
Loop diuretics [%]	63	67	0.764
Ald-antagonist [%]	26	38	0.314

6-MHWT indicates six minute hall walking test; A, anterior; ACE, angiotensin-converting enzyme; AL, anterolateral; Ald-antagonist, aldosterone antagonist; Ap, apex; ARB, angiotensin II type 1 receptor blocker; BMI, body mass index; CRT, cardiac resynchronization therapy; eGFR, estimated glomerular filtration rate; F, female; Hb, hemoglobin; HF, heart failure; I, inferior; IL, inferolateral; IVMD, interventricular mechanical delay; L, lateral; LV, left ventricle; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end diastolic volume; M, male; RV, right ventricle; S, septum.

and the LV lead according to coronary venous anatomy at a position with good stability, pacing thresholds and absence of phrenic nerve stimulation. LV and RV lead positions were determined by lateral and frontal chest radiographs; Table 1. Optimization of stimulation intervals was performed according to the attending cardiologists' decision.

After exclusion due to unsuccessful LV lead implantation (n = 10), atrial fibrillation with <90% biventricular pacing at follow-up (n = 2), missing echocardiographic evaluation at 6 months follow-up (n = 7), and impossible VCG analyses due to technical disturbances or multiple ectopic beats (n = 3), 81 patients were included for analyses.

Twenty-four patients (30%) were classified as CRT-NR. Baseline characteristics did not differ between CRT-R and CRT-NR except for ischemic etiology of heart failure which was more common in the CRT-NR group and the interventricular mechanical delay (IVMD) which was larger in the CRT-R group (Table 1).

ECG and VCG parameters in responders and non-responders

Typical vector loops in the frontal and transversal planes and corresponding ECGs for a CRT-NR and a CRT-R are shown in Fig. 1. The narrow vector loops of the CRT-R were characterized by a dominant vector amplitude in the transversal plane, clearly pointing to the back of the patient.

Baseline QRS duration, QRS_{AMPL} and QRS_{AREA} were all significantly larger in the CRT-R compared to the CRT-NR group, the difference between the groups being more pronounced for the VCG parameters (Table 2, Fig. 2).

Table 2
Baseline ECG and VCG values in CRT responders and non-responders.

Predictors mean ± SD or n [%]	CRT-R [n = 57]	CRT-NR [n = 24]	P-value
QRS duration [ms]	161 ± 14	153 ± 18	0.035
LBBB_1 morphology	55 [97]	20 [83]	0.039
LBBB_2 morphology	50 [88]	10 [42]	<0.001
LBBB_3 morphology	37 [65]	7 [29]	0.003
QRS_{AMPL} [mV]	1.9 ± 0.6	1.5 ± 0.4	0.003
Azimuth [degrees]	−64 ± 10	−64 ± 18	0.963
Elevation [degrees]	88 ± 17	94 ± 26	0.233
QRS_{AMPL_X} [mV]	0.8 ± 0.4	0.6 ± 0.3	0.013
QRS_{AMPL_Y} [mV]	0.1 ± 0.5	−0.1 ± 0.5	0.185
QRS_{AMPL_Z} [mV]	−1.7 ± 0.5	−1.2 ± 0.5	0.002
QRS_{AREA} [μVs]	140 ± 42	100 ± 40	<0.001
QRS-T angle [degrees]	166 ± 8	162 ± 14	0.163

CRT-NR indicates CRT non-responder; CRT-R, CRT responder; LBBB, left bundle branch block; QRS_{AMPL}, QRS vector amplitude; QRS_{AREA}, QRS area.

CRT-R patients fulfilled the morphology definitions to all 3 different LBBB criteria more frequently than CRT-NR patients (Table 2). Almost all patients fulfilled the LBBB_1 definition (n = 75), whereas classification of LBBB_2 and especially LBBB_3 definitions remained more selective (n = 60 and n = 44 respectively).

Correlation between ECG and VCG parameters and volumetric CRT response

Using LVESV as a continuous variable, an inverse correlation was observed between QRS_{AMPL} or QRS_{AREA} and the percentage change in LVESV at 6 months of CRT (r = −0.54 and r = −0.57 respectively). These correlations were stronger than the correlation between QRS duration and change in LVESV (r = −0.20; Fig. 2).

Predictive value of ECG and VCG parameters for CRT response

In Fig. 3, ROC curves are displayed, showing the abilities of QRS duration, QRS_{AMPL} and QRS_{AREA} to predict CRT-R. The area under the ROC curve was largest for QRS_{AREA} (AUC = 0.78), followed by QRS_{AMPL} (AUC = 0.71) and QRS duration (AUC = 0.62). The AUC for QRS_{AREA} was significantly larger than for QRS duration (p = 0.030), indicating a more accurate prediction of CRT response. Using a cutoff value for QRS_{AREA} of 98 μVs, the odds ratio for predicting CRT response was much higher (OR = 10.2; 95% confidence interval (CI) 3.4 to 31.1) than for QRS duration >156 ms (OR = 2.5; 95% CI 0.9 to 6.6), LBBB_1 (OR = 5.5; 95% CI 0.9 to 32.4) and LBBB_3 (OR = 4.5; 95% CI 1.6 to 12.6), while LBBB_2 had a comparable OR (OR = 10.0; 95% CI 3.2 to 31.1; Table 3).

QRS duration >156 ms falsely diagnosed 23 patients as CRT-NR (60% sensitivity and 63% specificity; Table 4 and Fig. 3). In comparison, QRS_{AREA} >98 μVs only falsely diagnosed 8 patients as CRT-NR (86% sensitivity and 63%

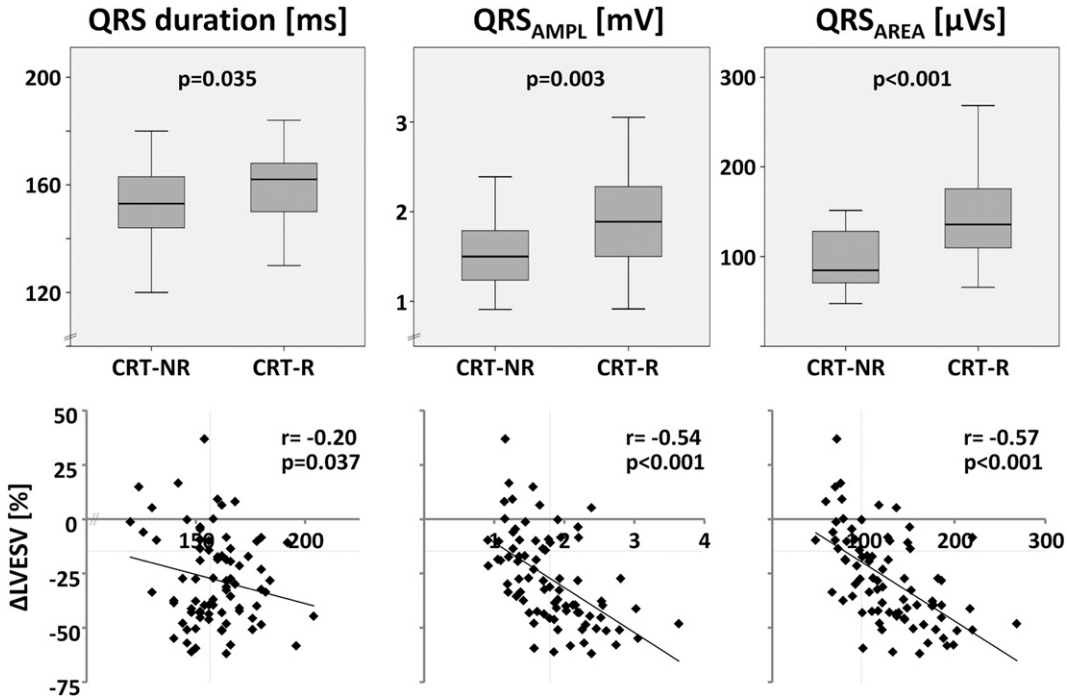

Fig. 2. Boxplots showing the median and interquartile range for QRS duration, QRS_{AMPL} and QRS_{AREA} between CRT-NR and CRT-R (upper panels) and the relation between these variables and the relative change in left ventricular end systolic volume (LVESV) after 6 months of CRT (lower panels).

specificity). The sum of sensitivity and specificity in predicting CRT-R was highest for QRS_{AREA} >98 μVs.

QRS_{AREA} in relation to other markers and different patient characteristics

Fig. 4 shows plots of QRS_{AREA} versus QRS duration. The figure depicts that at a given QRS duration patients with a LBBB_2 morphology displayed larger QRS_{AREA} compared to those with non-LBBB_2 morphologies. Similarly, among LBBB patients, QRS_{AREA} was smaller in patients with an ischemic etiology of heart failure compared to those with a non-ischemic etiology. Furthermore, in patients with non-LBBB and ischemic etiology of heart failure, QRS duration may be prolonged without an increase in QRS_{AREA}. Overall, QRS_{AREA} was significantly smaller in patients with an ischemic etiology of heart failure (108 ± 39 μVs vs 148 ± 43 μVs, $p < 0.001$). QRS_{AREA} was not significantly different in males versus females (123 ± 43 μVs vs 137 ± 48 μVs, $p = 0.183$), and not related to age ($r = -0.15$, $p = 0.095$) or BMI ($r = -0.17$, $p = 0.060$).

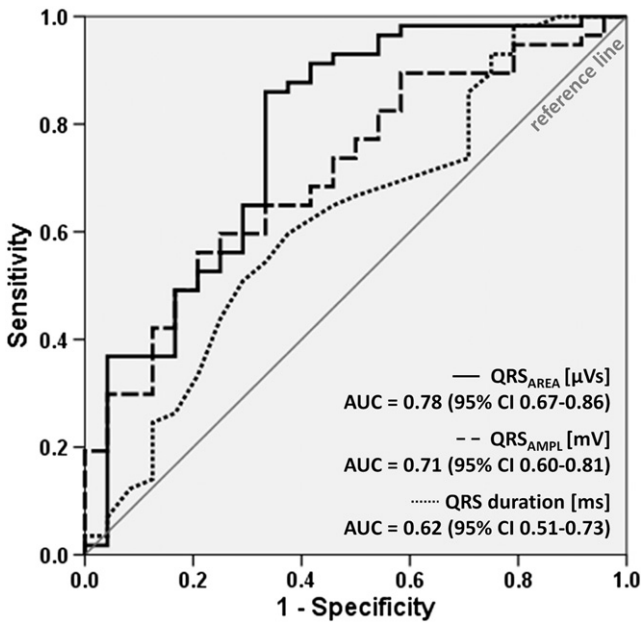

Fig. 3. Receiver operating characteristics (ROC) curves for QRS duration (dotted line), QRS_{AMPL} (dashed line) and QRS_{AREA} (straight line). Area under the receiver operating curve (AUC) signifies performance of each parameter in identifying CRT response and is given for each parameter with the 95% confidence interval (CI).

Discussion

The present prospective study demonstrates that the VCG parameter QRS_{AREA} predicts volumetric CRT response at 6 months better than QRS duration or the presence of conventionally defined LBBB morphology. Moreover, the predictive power of QRS_{AREA} is comparable to that of the most refined definition of LBBB, while it has the advantage of being objectively quantifiable as a continuous parameter. The predictive value of QRS_{AREA} may be explained because it appears to reflect both the presence of LBBB and the etiology of heart failure.

QRS_{AREA} as a predictor of response to CRT

Strong unopposed electrical forces, generated within the heart, are the likely underlying mechanism of a large QRS_{AREA}. This is typically the case in dyssynchronous ventricular activation like LBBB, where ventricular activation wavefronts propagate to the left and back of the patient

Table 3
Univariate analysis of predictors of CRT response.

Predictors CRT-R	Odds ratio	95% CI	*P*-value
QRS duration >156 ms	2.5	0.9–6.6	0.072
LBBB_1 morphology	5.5	0.9–32.4	0.059
LBBB_2 morphology	10.0	3.2–31.1	<0.001
LBBB_3 morphology	4.5	1. 6–12.6	0.004
QRS_{AMPL} >1.8 mV	3.8	1.3–11.1	0.013
QRS_{AREA} >98 μVs	10.2	3.4–31.1	<0.001

Table 4
Diagnostic performance of ECG and VCG parameters.

Predictors CRT-R	Sensitivity	Specificity	PPV	NPV
QRS duration >156 ms	60	63	79	39
LBBB_1 morphology	96	17	73	67
LBBB_2 morphology	88	58	83	67
LBBB_3 morphology	65	71	84	46
QRS_{AMPL} >1.8 mV	56	75	84	42
QRS_{AREA} >98 μVs	86	63	84	65

NPV indicates negative predictive value; PPV, positive predictive value.

without simultaneous cancellation from wavefronts to the right and front of the patient [16]. This idea is supported by a study demonstrating that a larger QRS integral obtained with 120-channel body surface imaging strongly correlated to the presence of interventricular dyssynchrony obtained by Doppler echocardiography [17]. However, these investigators found that there was no standard body surface ECG lead to use for investigation of the QRS integral, because of dependency on the mean electrical axis of the heart. QRS_{AREA}, which is the 3D-VCG QRS integral, can overcome this problem, because it is independent of QRS axis. According to a recent study using the same methodology as we employed, the average QRS_{AREA} in healthy adult subjects was found to be 34 μVs [18], a value of only one third of that in LBBB. Moreover, several studies have provided evidence that the more dyssynchronous the baseline situation (especially LBBB), the better the substrate for CRT [19,20].

On the other hand, QRS_{AREA} is smaller in patients with an ischemic etiology of heart failure and this etiology is known to decrease the chance of response to CRT. The lower QRS_{AREA} in these hearts may be explained by the presence of non-conducting fibrotic tissue which also decreases the amount of tissue that can be recruited by CRT. Similarly, a lower QRS_{AREA} may arise from consequences of severe hypertrophic remodeling such as electrical uncoupling between cells as a consequence of fibrosis or deranged expression or location of connexins [21]. These considerations might explain the power of QRS_{AREA} for prediction of CRT response, but more research is required to better understand all determinants of QRS_{AREA}.

QRS_{AREA} is a stronger predictor of CRT response as compared to QRS duration and LBBB morphology

In the present study, an optimal cutoff value for QRS duration of >156 ms was calculated, close to the value used in large clinical trials (150 ms) [5,7,8]. However, we found that the power to predict CRT response was less than using QRS_{AREA} >98 μVs. This difference may be explained because QRS duration only includes the time of depolarization, while QRS_{AREA} also reflects the electrical substrate for CRT response, as discussed above [22].

Recently, several studies have already reported that a LBBB morphology on the ECG is a stronger predictor of CRT response than QRS duration [6–8] and this is now incorporated in the current guidelines for class 1A recommendation [9,10]. However, until now conventional criteria for the definition of complete LBBB were used, which may include patients with a combination of LV hypertrophy, LV enlargement and incomplete LBBB [23], thus patients that possibly lack an ideal electrical substrate for resynchronization therapy. In addition, none of the conventional definitions have incorporated the presence of mid-QRS notching or slurring in 2 or more contiguous leads (V_1, V_2, V_5, V_6, I and aVL) as suggested by Strauss et al. [12]. This refinement of the definition of LBBB morphology has shown to significantly improve the performance of predicting CRT response and clinical outcome as compared to the conventional definition [24,25]. In the present study, the use of a definition of LBBB that includes the presence of mid-QRS notching or slurring according to Strauss et al. appeared to be more accurate in predicting CRT response than the presence of QRS notching or slurring according to American guidelines or the conventional definition of LBBB. However, the predictive power of even the most refined LBBB definition was not better than having a QRS_{AREA} of >98 μVs. Though LBBB and QRS_{AREA} >98 μVs were strongly related to each other, the benefit of using QRS_{AREA} may be the objective measurement, avoiding the subjective interpretation of presence of notching or slurring and the dependence on correct ECG lead positioning. Moreover, it provides a continuous measurement, making it possible to adapt the cutoff value according to the desired sensitivity and specificity. If an almost 100% specificity is wanted (i.e. no non-responders), a high cutoff value for QRS_{AREA} should be applied.

Potential clinical implications

VCG is an easy and non-invasive technique. While we used a dedicated 3D-VCG system in the present study, most commercially available ECG machines have algorithms to construct VCGs using the inverse Dower or Kors' regression transformation [18,26]. From this, an automatic calculated QRS area can be generated. However, the accuracy of the inverse transformations has yet to be demonstrated for patients with heart failure and wide QRS complex. Furthermore, the present study emphasizes the importance of including mid-QRS notching or slurring in the criteria for LBBB, especially when present in 2 or more contiguous leads of V_1, V_2, V_5, V_6, I and aVL.

Limitations

Although the number of patients included in this single center study is modest and too small for subgroup analyses, this is to our knowledge, the first study investigating 3D-

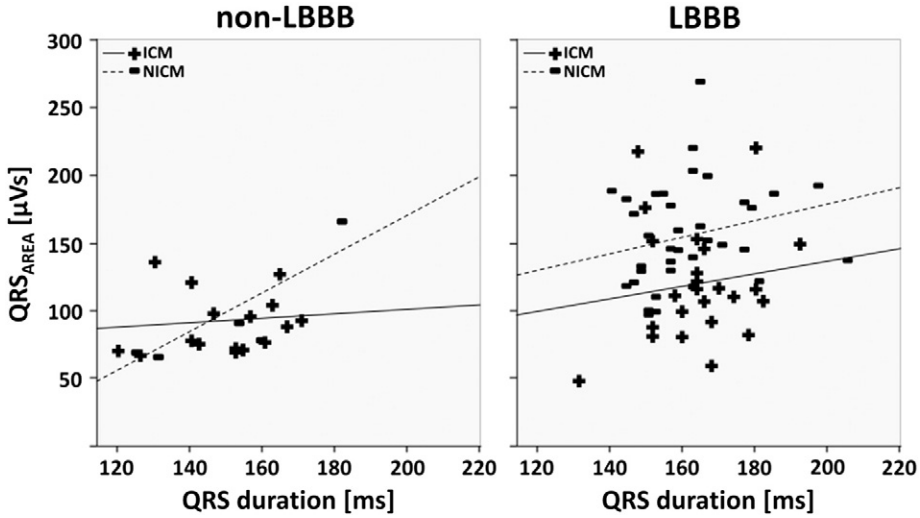

Fig. 4. QRS_{AREA} plotted against QRS duration for patients without (left) and with (right) LBBB_2 morphology, and subdivided into presence of ischemic etiology of heart failure (ICM; plus sign) or non-ischemic etiology of heart failure (NICM; hyphen). Regression lines are given for subgroups. Note that among patients with non-LBBB and ICM, the QRS duration can prolong without an increase in QRS_{AREA}. In LBBB patients, QRS_{AREA} was smaller in patients with ICM compared to those with NICM.

VCG derived parameters as predictors of response to CRT. Assessment of LBBB was performed by a single reviewer, and an independent training and test set for the calculation of a cutoff value for QRS_{AREA} was lacking. Multicenter prospective studies with a larger amount of patients are required to confirm our results. These larger studies should also search for confirmation of the predictive power of QRS_{AREA} with regard to clinical outcome, hospitalization admissions and survival rate.

Conclusion

QRS_{AREA} is a more powerful predictor of CRT response compared to QRS duration or conventionally defined LBBB morphology. Since it can be automatically computed, this parameter can be easily applied in daily clinical practice, thereby better identifying appropriate candidates for CRT and potentially preventing ineffective, invasive and costly CRT device implantations.

What is new?

- The best definition for predicting CRT response includes mid-QRS notching in ≥ 2 leads contiguous leads of V_1, V_2, V_5, V_6, I and aVL.
- Such LBBB definition improves the selection of patients that respond to CRT by a factor of 4 compared to using QRS duration > 150 ms and by a factor 2 as compared to conventional LBBB definitions.
- Selection of CRT candidates with good response is at least as good with the objective and direction insensitive QRS_{AREA}, derived from the VCG.
- 3D VCG is a promising tool for better application of CRT.

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Author contribution

Van Deursen: data analysis, drafting article; Vernooy: critical revision, data analysis; Dudink: data analysis; Bergfeldt: critical revision; Crijns: critical revision; Prinzen: funding, critical revision and final approval of article; Liliane Wecke: concept development, drafting, final approval.

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