

Moving Beyond QRS Duration: QRS Voltage-Time-Integral (Area) is a Superior Predictor of Clinical Response to Cardiac Resynchronization Therapy 2



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Background

Cardiac resynchronization therapy (CRT) can alleviate left ventricular (LV) electrical dyssynchrony mediated systolic heart failure (HF). 15% reduction in LV end systolic volume (LVESV) with CRT is a validated surrogate of improved clinical outcomes. Prolonged baseline QRS duration (QRSd) is the only conventional quantitative ECG criteria to assess left ventricular electrical dyssynchrony.

Objective

In addition to QRS duration, we evaluated the baseline QRS voltage-time-integral (VTI) and its reduction after CRT as predictors of LV reverse remodeling.

Methods and Materials

We included 595 patients (68.1±11.5 yr, 32.6% women, 43.9% ischemic cardiomyopathy) who underwent CRT-defibrillator implant for clinical indications 2012-2019 and analyzed their ECGs before and after CRT. Orthogonal X, Y, Z leads were reconstructed from 12-lead ECG using Kors's matrix. VTIQRS-X, Y, Z and VTIQRS-3D were obtained from integration over the duration of QRS in X, Y, Z, and root-mean-squared (3D) ECGs respectively.

We reviewed echocardiogram reports to obtain LV measures before and 3-12 months after CRT, including ejection fraction (LVEF), internal dimensions in diastole (LVIDd) and systole (LVIDs), end-diastolic (LVEDV) and LVESV. We used linear regression models to evaluate ECG variables as predictors of change in LV measures. We further used unadjusted and multivariable-adjusted logistic regression models to predict ≥15% reduction in LVESV from ECG variables.

Table 1. P-values from unadjusted linear associations between ECG and change in echocardiographic variables (3-12 months post CRT vs. pre-CRT).

	Δ LVEF (n=586)	Δ LVIDd (n=560)	Δ LVIDs (n=559)	Δ LVEDV (n=403)	Δ LVESV (n=400)
Baseline ECG					
QRS duration	0.03	0.002	0.03	0.07	0.01
QRS _{VTI-3D}	0.0006	0.0008	0.0002	0.01	0.0004
QRS _{VTI-Z}	0.0004	<0.0001	<0.0001	0.03	0.0002
Change post CRT					
Δ QRS duration	0.001	<0.0001	0.005	0.7	0.4
Δ QRS _{VTI-3D}	<0.0001	0.0001	0.004	0.002	0.0004
Δ QRS _{VTI-Z}	<0.0001	0.0002	0.0002	0.005	0.0002

Results

Baseline LVEF was 25.8±8.3%, LVIDd 5.7±0.9 cm, LVIDs 4.8±0.9 cm, LVEDV 164±67 and LVESV 109±56 mL. QRSd reduced from 153±26 to 137±22 ms with CRT. VTIQRS-3D and VTIQRS-Z of 104±49 and 75±44 respectively improved to 67±34 and 33±24 μVs. Baseline and change in VTIQRS-Z and VTIQRS-3D were more significantly associated with change in echo variables as compared to baseline and change in QRSd (Table 1). ≥15% reduction in LVESV was independently predicted by baseline VTIQRS-Z ≥71 μVs (OR 2.0, 95% CI 1.3-3.0, p=0.0009) and Δ VTIQRS-Z ≥42 μVs (OR 2.1, 1.4-3.1, p=0.004).

Table 2. Logistic regressions of ECG variables categorized by median cutoff predicting ≥15% reduction in LV end systolic volume on 3-12-month post CRT echocardiogram compared to pre-CRT baseline.

N=400	Cutoff	≥15% Reduction in LVESV				
		Unadjusted O.R. (95% CI)	p-value	Multivariable* adjusted O.R. (95% CI)	p-value	
Baseline ECG						
	QRS duration (ms)	155	1.3 (0.9, 2.0)	0.2	1.4 (0.9, 2.1)	0.1
	QRS _{VTI-3D} (μVs)	97	1.8 (1.2, 2.6)	0.006	1.7 (1.1, 2.6)	0.01
	QRS _{VTI-Z} (μVs)	71	2.1 (1.4, 3.1)	0.0003	2.0 (1.3, 3.0)	0.0009
Change post CRT						
	Δ QRS duration (ms)	21	1.7 (1.1, 2.6)	0.009	1.7 (1.1, 2.5)	0.02
	Δ QRS _{VTI-3D} (μVs)	35	1.8 (1.2, 2.6)	0.005	1.7 (1.1, 2.6)	0.01
	Δ QRS _{VTI-Z} (μVs)	42	2.1 (1.4, 3.2)	0.0002	2.1 (1.4, 3.1)	0.004

* Adjusted for age, sex, ischemic cardiomyopathy and baseline LV ejection fraction

Conclusion

In patients undergoing CRT baseline QRS VTI from Z (anteroposterior) axis ECG ≥71 μVs independently predicted 2 times higher odds of salutary reverse LV remodeling post CRT. Further, a reduction in VTIQRS-Z ≥42 μVs also predicted more than 2 times odds of reverse remodeling.

VTIQRS-Z is a superior automatically calculable quantitative summary ECG marker for CRT patient selection and prognostication as compared to QRS duration.

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