Original Article

Comparison of the Response to Cardiac Resynchronization Therapy Defibrillator Implantation Between Patients With and Without Fragmented QRS in Electrocardiography

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ABSTRACT

Background: Myocardial scars cause heterogeneous ventricular activation, which results in fragmented QRS (f-QRS) complexes and the resultant left ventricular (LV) dysfunction and dyssynchrony and thus further mortality. The accurate management of this patient population is essential to lessen mortality and improve the quality of life.

Methods: The present cross-sectional study recruited 80 patients (40 with f-QRS and 40 with non–f-QRS) who underwent cardiac resynchronization therapy defibrillator (CRT-D) implantation and followed them up for 6 months. The 2 groups were compared, before and after CRT-D implantation, concerning the New York Heart Association functional class; the quality of life; the incidence of all arrhythmias, including tachyarrhythmias; echocardiographic findings; the number of hospitalization; and mortality.

Results: The study population consisted of 80 patients at a mean age of 62.05±11.25 years: 40 cases with f-QRS and 40 with non–f-QRS. Men comprised 68.8% (n=55) of the patients. Ischemic cardiomyopathy was detected in 62.5% of the patients, nonischemic cardiomyopathy in 37.5%, and sinus rhythm in 76 cases. The mean values of the LV ejection fraction, the LV end-diastolic diameter, and the LV end-systolic diameter in both groups were 17.12±5.77, 6.44±0.81, and 5.70±0.81, respectively ($P<0.05$). An improvement was observed among the patients with non–f-QRS in echocardiography after CRT-D implantation, which was not related to the incidence of ischemic or nonischemic LV dysfunction. Dyspnea on exertion and mitral regurgitation improved in both groups ($P>0.05$).

Conclusions: The presence of f-QRS in patients with heart failure could confirm a diminished response to CRT-D implantation according to echocardiographic findings and could be considered an accurate patient selection guide. ***(Iranian Heart Journal 2021; 22(2): 77-82)***

KEYWORDS: Fragmented QRS, MR, DOE, NYHA class, CRT-D

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Received: February 22, 2020 **Accepted:** May 9, 2020

Fragmented QRS (f-QRS) indicates the depolarization of the ventricular myocardium, and it may occur due to ischemia, fibrosis, or scars in the myocardium. [1] f-QRS complexes are also termed "high-frequency components", and they are more common among patients with prior myocardial scars and also among patients with the enlargement of the right ventricle or the left ventricle (LV). [2] The presence of f-QRS and in particular, late potentials has been investigated as a possible new tool to identify the high-risk cardiac population. [3] Fragmented electrical activity is present in all patients with LV aneurysms. Nonetheless, patients with ventricular tachycardias have fragmented electrical activity in a larger proportion of the endocardial border zone and have more prolonged electrograms in this zone than patients without ventricular tachycardias. [4] It has been postulated that mapping endocardial electrical activity and detecting fragmented activity are useful tools in surgically guided therapy for ventricular aneurysms and ventricular tachycardias. [5]

The latest definition of the f-QRS was presented by Das et al [6] as the presence of an additional R-wave (R') or notching in the nadir of the S-wave, or the presence of more than 1 R' in 2 contiguous leads, corresponding to a major coronary artery territory on the resting 12-lead electrocardiogram (ECG) with a filter range of 0.16 to 100 Hz, an AC filter of 60 Hz, a paper speed of 25 mm/s and 10 mm/mv. The fragmentation of wide QRS complexes (bundle branch blocks [BBBs] and paced rhythms) was also defined by Das et al [6] as various rSr' patterns with or without a Q-wave, featuring more than 2 R-waves (R') or more than 2 notches in the R-wave, or more than 2 notches in the downstroke or upstroke of the S-wave in 2 contiguous leads corresponding to a major coronary artery territory. [4] The present study was designed to compare the efficacy of cardiac resynchronization therapy defibrillator (CRT-D) implantation between patients with f-QRS and patients with non–f-QRS. To that end, the response to CRT-D was assessed, and improvements in prognosis and the left ventricular ejection fraction (LVEF) were investigated to streamline patient selection for CRT-D implantation.

METHODS

Patient Selection

Eighty patients who underwent CRT-D implantation were enrolled in this case-control study. The study population was divided into 2 groups: 40 patients in the f-QRS group and 40 in the non–f-QRS group. The patients were followed up for 6 months. Intragroup and intergroup comparisons were made before and after CRT-D implantation concerning the New York Heart Association (NYHA) functional class; the quality of life; the incidence of all arrhythmias and in particular, tachyarrhythmias; echocardiographic findings, including LVEF, mitral regurgitation, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and dyspnea on exertion; the number of hospitalization; and mortality. The demographic data and past medical history of the study patients were obtained from the outpatient clinic and medical data sheet records in our center.

Statistical Analysis

All the statistical analyses were conducted using SPSS, version 17 (SPSS Inc, Chicago, III). The mean and standard deviations for qualitative variables were determined. Differences between the 2 groups were analyzed by using the Student *t*-test and log transformations for continuous variables and the χ^2 test for categorical variables. The one-sample Kolmogorov test was used to evaluate normal distributions in the 2 groups. A *P* value of less than 0.05 (2-tailed) was considered significant.

RESULTS

The study population consisted of 80 patients (55 [68.8%] male) at a mean age of 62.05±11.25 years. The patients were divided into 2 groups of 40: the f-QRS group and the non–f-QRS group. Ischemic cardiomyopathy was reported in 62.5% of the patients, nonischemic cardiomyopathy in 37.5%, and sinus rhythm in 76 patients. Sex, age, rhythm, NYHA functional class, and LV size distribution were assessed and were almost similar in both groups. The mean values of LVEF, LVEDD, and LVESD in both groups were 17.12±5.77, 6.44±0.81, and 5.70±0.81, respectively. Mild LV enlargement was detected in 12 patients (15%), of whom 8 had f-QRS. Moderate LV dysfunction was observed in 16 patients (20%), of whom 7 had f-QRS. Severe LV enlargement was seen in 50 patients (62.5%), of whom 23 had f-QRS. Normal-sized LV was reported in 2 patients, both of whom had f-QRS. At 6 months' follow-up, mild LV dysfunction was reported in 13 patients (16.3%), of whom 3 had f-QRS; while normal LV function was reported in 19 patients (23.8%), of whom 8 had f-QRS. An improvement was observed in terms of LV size in both groups, with the difference between the groups failing to constitute statistical significance (*P*=0.05) (Table 1).

DISCUSSION

On the subject of MR comparison between the two groups before and after CRT implantation the results of the base line echocardiography in the patients showed, 36 of the cases (45%) had mild MR (16 cases with f-QRS), 27 patients (33.8%) had moderate MR (16 cases with f-QRS), 9 cases (11.3%) had moderate to severe MR (eight cases with f-QRS), 5 patients (6.3%) had sever MR (four cases with f-QRS). Consequently, in contrast MR assessing between the two groups showed a recovery by implantation of CRT so as to be appeal in clinics, however no significance relationship was found (*P*=0.08).

Table 1: Comparison of LVESD and LVEDD between the 2 groups of f-QRS and non–f-QRS before and after CRT-D implantation and the differences at 6 months' follow-up

	f-QRS		Percentiles								
			Difference			Follow-up			Baseline		
			25	50 (Median)	75	25	50 (Median)	75	25	50 (Median)	75
Weighted Average (Definition I)	LVEDD	Yes	5.4	6.5	7	5.6	6.45	7.075	-1	-1	.1
		No	6	6.7	7.2	5.8	6.5	7	-1	.2	.2
	LVESD	Yes	4.8	5.9	6.2	4.8	5.85	6.4	-2	.0	.175
		No	5	6	6.2	4.825	5.8	6	.125	-.3	.3
	LVEF	Yes	10	15	20	10	15	23.75	.0	.00	5
		No	15	5	20	15	20	25	-5	-5	.0
Tukey's Hings	LVEDD	Yes	5.4	6.5	7	5.6	6.45	7.05	-1	-1	.1
		No	6	6.7	7.2	5.8	6.5	7	.1	.2	.2
	LVESD	Yes	4.8	5.9	6.2	4.8	5.85	6.4	-2	.0	.15
		No	5.05	6	6.2	4.85	5.8	6	15	.3	.3
	LVEF	Yes	10	15	20	10	15	22.5	0	.0	5
		No	12	15	20	15	20	25	-5	-5	.0

LVESD, Left ventricular end-systolic diameter; LVEDD, Left ventricular end-diastolic diameter; LVEF, Left ventricular ejection fraction

NYHA classification before CRT-D implantation were compared between the two groups and it showed that 18 cases (22.5%) had NYHA class 1 (6 cases with f-QRS), 56 (70%) had NYHA class III (31 cases with f-QRS), 6 (7.5%) had NYHA class IV (three with f-QRS), 26 (32.5%) had NYHA class I (eight cases with f-QRS), 48 (60%) had NYHA class II (27 with f-QRS) and 6 (7.5%) had NYHA class three (5 cases with f-QRS). Clinical characteristics and functional class in both groups were improved significantly and most of the patients who had NYHA class II after CRT implantation had f-QRS in ECG, although no significant relationship was found between the 2 groups regarding NYHA class (P=0.15).

DISCUSSION

The correlations between f-QRS and ischemic and nonischemic cardiomyopathy and reduced LV function have been investigated in some studies. In some of these investigations, f-QRS was present in 23% to 75% of patients with dilated cardiomyopathy (DCM) and narrow QRS complexes and was common in patients with ischemic cardiomyopathy. Moreover, f-QRS was associated with intraventricular dyssynchrony in patients with nonischemic DCM and was useful in identifying patients who would benefit from CRT. [1-5]

A previous study reported that a wide QRS complex was observed in 14% to 47% of patients with heart failure. Consequently, a wide QRS complex, especially a left BBB, was associated with more advanced myocardial injury, worse LV function, and higher mortality than a narrow QRS complex. [7]

In another investigation, f-QRS and a wide QRS complex were associated with worse prognoses in patients with DCM. Additionally, in patients with nonischemic DCM (EF<40%), f-QRS was a strong predictor of arrhythmic events, event-free survival, and mortality in patients with f-QRS or a wide QRS complex. [5] According to another study, f-QRS was an independent predictor of lethal arrhythmic events (HR=7.62) in patients with ischemic or nonischemic DCM who had received an implantable cardioverter-defibrillator (ICD) for primary or secondary prophylaxis. Nevertheless, it could not predict death in that population. The authors concluded that if the subjects had been limited to patients suffering from DCM (both ischemic and nonischemic) with primary prevention through an ICD, the usefulness of f-QRS for predicting arrhythmic events might have been lost. [8]

Another investigation demonstrated that f-QRS was not associated with a higher risk of both arrhythmic events and mortality in patients with an ICD for primary prevention. [4]

Despite the wide availability of clinical and investigational imaging modalities for the evaluation of patients' response to CRT with variable accuracy rates, a simple 12-lead remains the standard test for patient selection. Several ECG parameters are drawn upon to predict response to CRT; they include baseline rhythm, QRS duration, QRS morphology, LV activation sequence, and the PR interval. Prior studies have failed to demonstrate improved response rates to CRT when adding echocardiographic measures of dyssynchrony. Thus, the QRS width is currently the sole criterion for treatment in eligible patients, resulting in a non-uniform effect of this costly technology in implanted patients.

f-QRS represents an underlying arrhythmogenic substrate, and the distortion and fragmentation of QRS occur when normally smooth myocardial activation is disrupted. [9] The course of the disruption

may be either structural or functional changes. In patients with coronary artery disease, f-QRS is a better marker of prior myocardial infarction than the Q-wave. [6]
Myocardial scars and conduction disturbances result in dyssynchrony in LV systolic function. In patients with a narrow QRS complex, f-QRS is associated with intraventricular systolic dyssynchrony; in addition, patients with f-QRS might benefit from CRT. [10, 11]
In the present study, we focused on simple baseline ECG parameters associated with favorable reverse remodeling effects in patients with CRT-D implantation. We showed a strong association between f-QRS and non-response to CRT in terms of reverse remodeling. Further, our results demonstrated no difference between patients with an ischemic etiology in heart failure and patients with nonischemic cardiomyopathy. Independent of our patients' characteristics, the presence of f-QRS was associated with a poor response to CRT-D.
For the assessment of functional myocardial remodeling after CRT-D implantation, we monitored the development of LVEF, LVEDD, and LVESD during follow-up visits. While LVESD and LVEDD were introduced as good indicators of reverse remodeling in previous investigations, LVEF is better established insofar as it can be measured with comparably low intra- and interobserver variations during routine echocardiography.

CONCLUSIONS

The past decade has witnessed substantial research on the complex topic of response to CRT. For all the substantial knowledge about CRT, a significant proportion of patients with heart failure do not respond to CRT. However, a careful analysis of simple ECG can yield impressive data difficult to be replaced by any of the available, more sophisticated clinical tools.
We demonstrated that f-QRS, as detected by standard 12 lead ECG, was a prognostic maker for non-response to CRT-D, regardless of the etiology of heart failure. Large clinical trials are required to evaluate the role of f-QRS in patient selection for CRT-D implantation.
The salient limitation of our study was its non-randomized, retrospective analysis of a relatively small number of patients.

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