



Evaluation of QRS dispersion and its association with tachyarrhythmia events in patients with implanted cardiac resynchronization therapy defibrillator device

Fariborz Akbarzadeh¹, Babak Kazemi¹, Elgar Enamzadeh², Nasrin Khaky², Behnaz Ghamari³, Farid Karkon-Shayan*⁴

¹ Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

² Department of Cardiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

³ Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

⁴ Medical Philosophy and History Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Article info

Article History:

Received: 01 Jan. 2018

Accepted: 01 Feb. 2018

ePublished: 10 Mar. 2018

Keywords:

Arrhythmia,

Cardiac

Resynchronization

Therapy Defibrillator,

QRS dispersion

Abstract

Introduction: Heart failure (HF) is one of the major problems of health system in the countries. In a subgroup of these patients, cardiac resynchronization therapy defibrillator (CRT-D) improves the quality of life by enhancing the function of the left ventricle (LV) and preventing of arrhythmias. The present study intends to discuss the effect of CRT-D on the QRS dispersion, as a predisposing factor to arrhythmias.

Methods: 45 patients treated with CRT-D during 2012-2015 were enrolled in this study. QRS dispersion in various V-V delays was measured and its association with the incidence of arrhythmias, at least six months after insertion, was assessed.

Results: The results showed that QRS dispersion in the intrinsic mode was significantly lower than the other modes of the CRT-D device ($P < 0.001$). Besides, it was revealed that mean QRS duration in the intrinsic mode had a higher association with arrhythmic events than max QRS duration. QRS dispersion after CRT-D implantation had a significant increase compared to the intrinsic mode. However, it did not correlate with the arithmetic events. Further decrease in the duration of QRS after CRT-D implantation improved arrhythmias.

Conclusion: QRS dispersion after CRT-D implantation is not an indicative of arrhythmia risk, and a decrease in the duration of QRS had a more significant effect on the incidence of arrhythmias.

Citation: Akbarzadeh F, Kazemi B, Enamzadeh E, Khaky N, Ghamari B, Karkon-Shayan F. **Evaluation of QRS dispersion and its association with tachyarrhythmia events in patients with implanted cardiac resynchronization therapy defibrillator device.** J Anal Res Clin Med 2018; 6(1): 43-51. Doi: 10.15171/jarcm.2018.007

Introduction

Heart failure (HF) is one of the major causes of disability and death in Iran. By changing the age pyramid of the society and the aging of the young population, its prevalence will shortly increase in Iran.^{1,2} HF significantly reduces the quality of life of the patients, and often these patients do not have a decent quality of life.^{3,4}

Despite the recent advances in the medical treatment of patients with HF, the prognosis of these patients is still not very favorable. Various paraclinical methods are used to determine the prognosis of patients with HF. Electrocardiography (ECG) is one of the main tools used to determine the prognosis of these patients.

Many HF-induced deaths are due to arrhythmias such as premature ventricular

* Corresponding Author: Farid Karkon-Shayan, Email: tabriz.drgroup@yahoo.com



© 2018 The Authors; Tabriz University of Medical Sciences

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

contraction (PVC), ventricular tachycardia (VT), left ventricular block, and atrial fibrillation (AF); and these arrhythmias are a predictor of sudden death.^{5,6} One of the non-invasive criteria that determines the risk of malignant arrhythmias in these patients is the change in the duration of the QRS wave in the 12-lead, simply called QRS dispersion.⁷ It is a rather novel predictor of mortality in HF patients and results from changes in the repolarization time of various myocardial sites.⁸ QRS dispersion indicates the instability of the myocardial electricity. It is simple and reproducible and can identify HF patients with high risk of sudden cardiac death.⁹

Different therapies are used for HF patients, which include medical treatment and cardiac resynchronization therapy defibrillator (CRT-D). CRT-D improves left ventricular function as well as hemodynamic and the quality of life in patients with severe HF by shortening the QRS duration. In addition, CRT-D may have a more effective impact on reducing arrhythmia risk in patients with more prolonged QRS duration. This might be due to its superior effects on reducing QRS duration in this set of patients.^{10,11}

Considering the importance of HF and the therapeutic methods used in these patients, this study aimed to investigate the association between dispersion of QRS and its relationship with arrhythmias in patients who are being treated with CRT.

Methods

In an analytical study, 45 patients were enrolled, who had undergone CRT-D implantation, at least six months before the study, in Shahid Madani University Hospital, Tabriz, Iran, during 2012-2015. All available sampling was included in the study. The convenient sampling method was used to select these patients.

Every patient with HF that had undergone CRT-D implantation at least six months before the study was included, and all of them had informed self-consent for

participation in this investigation. On the other hand, every patient taking any anti-arrhythmic drug, having an electrolyte imbalance, having no left ventricular lead, or being reluctant to participate in the study were excluded.

This study was in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. After approval of the Ethics Committee of Tabriz University of Medical Sciences and by considering the exclusion and inclusion criteria, and explaining the purpose of the study to the patients, 45 patients were included, and written informed consent was obtained from them. The basic information of the patients including age, sex, underlying illness, blood pressure, risk factors for heart disease, and kidney failure was gathered.

First, in the intrinsic mode of CRT-D, ECG was obtained from all patients. Other ECGs were obtained from the patients 3 min after setting the device on 50-LV (left ventricle), 30-LV, only RV (right ventricle), and simultaneous modes. Then arrhythmias were extracted from the CRT-D memory and QRS wavelengths were measured by the cardiocaliper software in all 12 leads of ECGs. It should be noted that in all patients, V-V was considered to be 0 ms as the default of device after CRT-D insertion. The study protocol has been depicted in figure 1.

All the patients were informed that their information would be kept confidential, and their personal information would not be mentioned anywhere. During the study, no additional diagnostic and therapeutic interventions were performed on patients, and the patients were referred to the Cardiology Clinic of Shahid Madani Hospital in Tabriz City only for periodical analyses after CRT insertion. No additional costs were imposed on the patients and their families. The study was supported by vice-chancellor of Tabriz University of Medical Sciences.

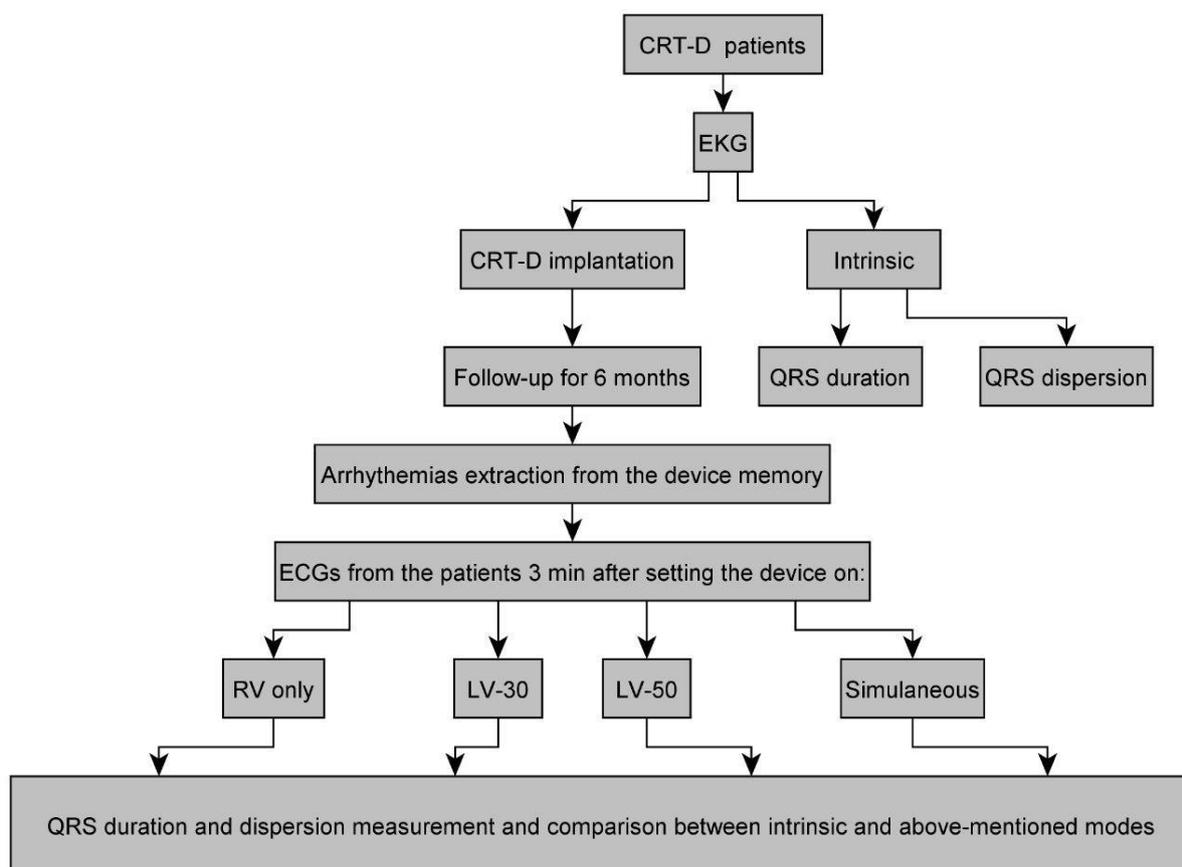


Figure 1. Study protocol

RV only: stimulation of right ventricle (RV) only, LV-30 and 50: stimulation of left ventricle (LV) 30 and 50 ms before RV
ECG: Electrocardiography; RV: Right ventricle; LV: Left ventricle

The comparison of QRS dispersion was done in two levels as more or less than 40 ms based on the previous studies.^{12,13}

The data were expressed as mean \pm standard deviation (SD), frequency, and percentage. Chi-square test was applied to compare the qualitative variables; independent t-test and one-way ANOVA were used to examine and compare the quantitative variables. All analyses were performed using SPSS (version 22, IBM Corporation, Armonk, NY, USA), and $P \leq 0.05$ was considered as statistically significant.

Results

The mean age of the patients was 65.66 ± 11.37 years. 33 (73.3%) patients were male, and 12 (26.7%) patients were female. The results revealed that 36 (80.0%) patients had ischemic cardiomyopathy, and 9 (20.0%) patients had non-ischemic cardiomyopathy. It was found that 41 (91.1%) patients had left

bundle branch block (LBBB), and 4 (8.9%) patients had right bundle branch block (RBBB). Additionally, 40 (88.9%) patients had sinus rhythm, and 5 (11.1%) patients had AF rhythm. Table 1 represents the prevalence of risk factors and underlying diseases in patients. Table 2 shows the mean of QRS duration in the tested leads and its comparison to the simultaneous and intrinsic modes. Based on the results of this table, it was found that CRT-D implantation resulted in a significant decrease in the QRS duration in all leads.

Table 1. The prevalence of risk factors and underlying illnesses in patients

Risk factor	n (%)
Hypertension	18 (40.0)
Hyperlipidemia	8 (17.8)
Diabetes	15 (33.3)
Smoking	15 (33.3)
Renal failure	4 (8.9)
Severe mitral regurgitation	13 (28.9)

Table 2. The comparison of mean QRS duration (ms) in various cardiac resynchronization therapy defibrillator (CRT-D) modes

Lead	CRT-D mode	Intrinsic (mean ± SD)	Simultaneous (mean ± SD)	P
I		156.4 ± 24.7	131.0 ± 25.8	< 0.001
II		152.3 ± 23.9	135.1 ± 19.9	0.001
III		153.9 ± 20.3	134.9 ± 27.5	< 0.001
aVR		146.6 ± 25.7	132.3 ± 21.9	0.004
aVL		154.8 ± 24.6	132.0 ± 25.0	< 0.001
aVF		152.8 ± 21.7	133.5 ± 20.2	< 0.001
Min limb		131.0 ± 21.5	111.2 ± 17.6	< 0.001
Max limb		168.5 ± 21.2	150.0 ± 21.3	< 0.001
V1		154.1 ± 18.5	135.7 ± 18.6	0.023
V2		159.9 ± 21.7	140.1 ± 19.8	< 0.001
V3		164.6 ± 18.9	141.0 ± 20.0	< 0.001
V4		166.6 ± 20.9	147.3 ± 18.6	< 0.001
V5		165.2 ± 21.7	145.5 ± 20.2	< 0.001
V6		157.3 ± 20.8	134.1 ± 21.1	< 0.001
Min precordial		147.6 ± 18.8	125.1 ± 17.9	< 0.001
Max precordial		173.9 ± 19.5	155.5 ± 19.7	< 0.001
Total min		130.5 ± 19.9	109.3 ± 16.8	< 0.001
Total max		176.1 ± 20.2	158.4 ± 19.4	< 0.001

CRT-D: Cardiac resynchronization therapy defibrillator; Max: Maximum; Min: Minimum; SD: Standard deviation; aVR: Augmented vector right; aVL: Augmented vector left; aVF: Augmented vector foot

Moreover, because the default was based on V-V = 0 in the simultaneous mode, it was revealed that QRS dispersion increased in comparison to the intrinsic mode ($P < 0.001$).

In addition, it was found that 36 (80.0%) patients experienced VT/ventricular fibrillation (VF) arrhythmias, 18 of which had sustained VT/VF. The following tables

(Tables 3 and 4) compare the QRS duration in all the 12 leads in the patients with or without VT/VF (non-Sustained or sustained) in the intrinsic and simultaneous modes.

According to these tables, there was a significant difference in QRS duration in the pre-ordial and limb leads between patients with total VT/VF and no arrhythmia ($P = 0.004$ and $P = 0.040$, respectively).

Table 3. The comparison of mean QRS duration (ms) based on ventricular tachycardia/ventricular fibrillation (VT/VF) in the intrinsic mode

Lead	Patients group	Total VT/VF (mean ± SD)	Without VT/VF (mean ± SD)	P	Sustained VT/VF (mean ± SD)	Non-sustained VT-VF (mean ± SD)	P
I		155.1 ± 23.2	161.5 ± 31.2	0.524	149.6 ± 23.4	160.4 ± 25.1	0.200
II		147.3 ± 21.5	171.0 ± 24.3	0.011	146.0 ± 23.2	155.9 ± 24.0	0.224
III		148.5 ± 17.0	174.1 ± 19.9	0.001	147.6 ± 15.6	158.0 ± 21.9	0.110
aVR		144.2 ± 25.5	155.6 ± 25.9	0.270	136.6 ± 25.9	152.4 ± 24.2	0.067
aVL		151.4 ± 25.2	167.6 ± 12.2	0.100	149.9 ± 22.2	157.6 ± 26.0	0.355
aVF		147.8 ± 19.4	171.7 ± 20.7	0.004	150.2 ± 20.7	154.4 ± 22.6	0.580
Min limb		128.3 ± 19.5	141.1 ± 22.2	0.119	124.7 ± 20.2	134.7 ± 20.1	0.153
Max limb		164.9 ± 19.6	181.8 ± 22.7	0.043	163.0 ± 18.5	171.7 ± 22.3	0.227
V1		150.8 ± 17.9	167.1 ± 14.4	0.023	149.4 ± 18.5	157.0 ± 18.0	0.219
V2		156.3 ± 22.2	176.2 ± 8.8	0.019	151.8 ± 19.6	165.5 ± 21.5	0.059
V3		154.9 ± 31.5	182.2 ± 12.8	0.023	158.7 ± 18.9	161.8 ± 36.0	0.764
V4		160.9 ± 19.6	187.8 ± 8.2	0.001	160.0 ± 21.0	170.4 ± 20.3	0.140
V5		160.8 ± 19.9	181.7 ± 21.0	0.013	157.4 ± 19.1	169.7 ± 22.1	0.092
V6		156.1 ± 21.3	156.1 ± 21.3	0.497	150.6 ± 20.0	160.9 ± 20.8	0.156
Min precordial		144.7 ± 17.6	158.5 ± 20.5	0.066	141.0 ± 18.7	151.5 ± 18.1	0.096
Max precordial		169.3 ± 18.8	191.1 ± 10.5	0.004	166.6 ± 16.8	178.2 ± 20.0	0.078

VT: Ventricular tachycardia; VF: Ventricular fibrillation; Max: Maximum; Min: Minimum; SD: Standard deviation; aVR: Augmented vector right; aVL: Augmented vector left; aVF: Augmented vector foot

Table 4. The comparison of mean QRS duration (ms) based on ventricular tachycardia/ ventricular fibrillation (VT/VF) in the simultaneous mode

Patients group	Total VT/VF (mean ± SD)	Without VT/VF (mean ± SD)	P	Sustained VT/VF (mean ± SD)	Non-sustained VT-VF (mean ± SD)	P
Lead						
I	133.0 ± 33.7	129.8 ± 25.6	0.798	127.6 ± 24.4	135.5 ± 36.3	0.422
II	139.1 ± 21.0	131.6 ± 24.2	0.362	138.5 ± 18.0	137.0 ± 24.0	0.816
III	135.0 ± 21.3	134.1 ± 41.9	0.928	137.1 ± 22.7	133.3 ± 28.4	0.636
aVR	134.4 ± 24.6	134.5 ± 25.5	0.988	133.7 ± 19.2	134.8 ± 27.8	0.884
aVL	132.1 ± 25.4	136.8 ± 26.2	0.625	130.5 ± 24.7	134.8 ± 26.1	0.584
aVF	134.8 ± 19.7	136.1 ± 24.7	0.870	134.4 ± 20.9	135.5 ± 20.6	0.866
Min limb	112.6 ± 17.7	111.1 ± 21.9	0.826	111.3 ± 18.3	112.9 ± 18.7	0.782
Max limb	153.4 ± 28.1	151.4 ± 29.7	0.849	150.6 ± 19.2	154.6 ± 33.0	0.646
V1	131.6 ± 17.7	139.3 ± 14.5	0.067	130.2 ± 18.4	137.1 ± 18.6	0.135
V2	140.5 ± 20.1	147.1 ± 18.7	0.081	139.4 ± 19.9	143.5 ± 20.7	0.335
V3	138.7 ± 17.4	144.5 ± 16.3	0.140	139.2 ± 18.1	141.6 ± 19.2	0.820
V4	140.2 ± 18.3	145.4 ± 16.9	0.110	142.1 ± 21.2	144.4 ± 19.5	0.570
V5	139.2 ± 15.6	142.2 ± 19.1	0.900	142.4 ± 14.1	145.7 ± 20.5	0.630
V6	142.7 ± 21.8	144.5 ± 21.6	0.694	139.6 ± 21.2	143.0 ± 19.3	0.132
Min precordial	115.4 ± 13.6	116.5 ± 14.2	0.950	117.2 ± 11.3	118.0 ± 12.9	0.890
Max precordial	159.2 ± 20.7	161.3 ± 19.8	0.980	157.6 ± 19.7	161.2 ± 21.3	0.475

VT: Ventricular tachycardia; VF: Ventricular fibrillation; Max: Maximum; Min: Minimum; SD: Standard deviation; aVR: Augmented vector right; aVL: Augmented vector left; aVF: Augmented vector foot

This means that patients with a more extended QRS duration had fewer arrhythmias or, in the other words, CRT-D effect on decreasing arrhythmias is more evident in patients who previously had wider QRS.

Moreover, it was revealed that mean QRS duration in the intrinsic mode had a higher association with arrhythmic events than max QRS duration (Table 5).

The following table (Table 6) compares the mean duration of QRS among patients with or without VT/VF (non-sustained or sustained) in the various modes of the CRT-D device.

The results also showed that QRS dispersion in the intrinsic mode was

significantly lower than the other modes of the CRT-D device ($P < 0.001$), as shown in table 7.

Table 8 represents the frequency and comparison of QRS dispersion and its relation to arrhythmia incidence among patients with sustained or non-sustained VT/VF in various modes of CRT-D device.

Discussion

Based on the current guidelines, CRT-D was indicated for patients who were on medical treatment and had moderate to severe HF, individuals with left ventricular ejection fraction of 35% or less, or patients with QRS duration of more than 120 ms.⁵

Table 5. The comparison of mean QRS duration (ms) based on ventricular tachycardia/ ventricular fibrillation (VT/VF) between intrinsic and simultaneous modes

Patients group	Total VT/VF (mean ± SD)	Without VT/VF (mean ± SD)	P	Sustained VT/VF (mean ± SD)	Non-sustained VT-VF (mean ± SD)	P
Variable						
Total min QRS (Int)	127.8 ± 18.9	140.5 ± 21.5	0.798	123.5 ± 18.7	134.6 ± 19.8	0.097
Total max QRS (Int)	171.0 ± 18.9	195.3 ± 12.0	0.112	168.2 ± 17.1	180.7 ± 20.8	0.065
Total min QRS (Sim)	109.3 ± 16.9	109.6 ± 22.0	> 0.999	108.4 ± 18.3	110.1 ± 17.6	0.762
Total max QRS (Sim)	160.3 ± 25.9	161.3 ± 22.0	0.967	156.9 ± 12.3	162.6 ± 28.3	0.478
Mean QRS (Int)	153.1 ± 16.8	171.5 ± 13.4	0.007	151.0 ± 17.1	160.3 ± 17.5	0.130
Mean QRS (Sim)	136.8 ± 11.1	139.0 ± 23.5	0.758	135.7 ± 15.6	138.3 ± 20.1	0.649

VT: Ventricular tachycardia; VF: Ventricular fibrillation; Int: Intrinsic; Sim: Simultaneous; Max: Maximum; Min: Minimum; SD: Standard deviation

Table 6. The comparison of mean QRS duration (ms) based on ventricular tachycardia/ ventricular fibrillation (VT/VF) in different cardiac resynchronization therapy defibrillator (CRT-D) modes

Patients group	Total VT/VF	Without VT/VF	P	Sustained VT/VF	Non-sustained VT-VF	P
CRT-D mode	(mean ± SD)	(mean ± SD)		(mean ± SD)	(mean ± SD)	
Max QRS (Int)	179.8 ± 18.4	187.5 ± 13.1	0.278	185.1 ± 19.1	178.8 ± 16.5	0.279
Max QRS (Sim)	161.7 ± 20.5	169.2 ± 19.9	0.330	166.9 ± 12.7	160.7 ± 18.6	0.323
Max QRS (RV only)	194.7 ± 26.1	199.1 ± 20.7	0.648	204.9 ± 23.7	189.6 ± 24.2	0.047
Max QRS (LV-30)	160.3 ± 26.9	161.7 ± 25.3	0.902	153.1 ± 25.8	164.2 ± 26.0	0.297
Max QRS (LV-50)	170.3 ± 26.7	162.7 ± 21.4	0.436	178.9 ± 26.9	161.8 ± 22.8	0.028
Min QRS (Int)	126.4 ± 19.2	129.4 ± 17.4	0.820	159.5 ± 20.0	154.6 ± 18.0	0.422
Min QRS (Sim)	108.6 ± 14.5	117.0 ± 20.6	0.955	134.5 ± 18.5	128.0 ± 22.3	0.313
Min QRS (RV only)	139.4 ± 21.9	144.5 ± 25.1	0.780	167.8 ± 18.7	157.0 ± 20.6	0.089
Min QRS (LV-30)	115.4 ± 20.5	119.8 ± 23.6	0.865	128.6 ± 25.9	132.4 ± 22.8	0.691
Min QRS (LV-50)	124.0 ± 23.6	131.8 ± 24.9	0.546	140.3 ± 25.8	129.4 ± 26.1	0.181

VT: Ventricular tachycardia; VF: Ventricular fibrillation; CRT-D: Cardiac resynchronization therapy defibrillator; Int: Intrinsic; Sim: Simultaneous; RV: Right ventricle; LV: Left ventricle; Max: Maximum; Min: Minimum; SD: Standard deviation

In many patients with HF, the duration of QRS was less than 120 ms,¹⁴ and thus CRT-D is not recommended; however, electrocardiographic studies indicated that 50% of these patients had dyssynchrony evidence, and therefore can benefit from CRT-D implantation.^{15,16} As discussed earlier, CRT-D can improve ventricular hemodynamics and the quality of life in patients with congestive HF.^{10,11,17,18} In addition, HF is considered as a source of arrhythmias, and some studies have pointed to a reduction in the HF-associated arrhythmias with the use of CRT-D.¹⁹⁻²¹ On the other hand, measurements of interlead changes in QRS duration during a twelve-lead ECG, which is called QRS dispersion, is a non-invasive simple method for detecting regional differences in the relaxation time of contracted ventricle.^{22,24} This study was conducted to provide a hypothesis

regarding the probable relationship between QRS duration changes in patients with or without arrhythmias after CRT-D implantation.

In the present study, 45 HF patients with CRT-D implantation were studied. During the study, the QRS dispersion was evaluated in different functioning modes of the device, and its association with arrhythmic events was investigated. Based on the results of the study, the mean duration of QRS in the simultaneous mode was significantly lower than that of the intrinsic mode (indicating the function of the device). However, there was no significant difference between different modes of CRT-D related to the association of QRS dispersion and arrhythmia events (VF/VT). Besides, according to the results of this study, the effect of CRT-D on decreasing arrhythmias was more prominent in patients with wider QRS wave.

Table 7. The comparison of QRS dispersion based on ventricular tachycardia/ ventricular fibrillation (VT/VF) in different cardiac resynchronization therapy defibrillator (CRT-D) device modes

Patients group	Total VT/VF	Without VT/VF	P	Sustained VT/VF	Non-sustained VT-VF	P
CRT-D mode	(mean ± SD)	(mean ± SD)		(mean ± SD)	(mean ± SD)	
Intrinsic	21.9 ± 12.1	22.4 ± 14.7	0.911	22.7 ± 10.3	21.5 ± 13.9	0.763
Simultaneous	31.3 ± 12.5	37.6 ± 16.3	0.946	32.3 ± 13.4	32.7 ± 13.6	0.644
RV only	33.6 ± 16.9	33.2 ± 17.1	0.207	35.0 ± 17.7	32.5 ± 16.6	0.940
LV-30	26.5 ± 13.8	30.1 ± 12.5	0.532	22.1 ± 11.3	30.6 ± 13.6	0.107
LV-50	35.3 ± 17.0	29.2 ± 13.5	0.324	38.6 ± 18.6	31.1 ± 14.5	0.139

VT: Ventricular tachycardia; VF: Ventricular fibrillation; CRT-D: Cardiac resynchronization therapy; RV: Right ventricle; LV: Left ventricle; SD: Standard deviation

Table 8. The frequency and comparison of QRS dispersion (more or less than 40 ms) and its relation to arrhythmia incidence among patients with sustained or non-sustained ventricular tachycardia/ventricular fibrillation (VT/VF) in various modes of cardiac resynchronization therapy defibrillator (CRT-D) device

Patients group	Sustained VT/VF [n (%)]	Non-sustained VT/VF [n (%)]	P
CRT-D mode			
Intrinsic > 40 ms	1 (2.2)	3 (6.6)	0.640
Intrinsic < 40 ms	17 (37.7)	24 (53.3)	
Simultaneous > 40 ms	6 (13.3)	9 (20.0)	> 0.999
Simultaneous < 40 ms	12 (26.6)	18 (40.0)	

VT: Ventricular tachycardia; VF: Ventricular fibrillation; CRT-D: Cardiac resynchronization therapy

In one study, Benn et al. investigated arrhythmogenic right ventricular cardiomyopathy (ARVC) patients and measured QT dispersion. The results of this study showed that there was no significant difference in QT dispersion between patients with low and high risk of arrhythmias.²⁵ On the other hand, Peters et al. showed that QT dispersion in the QRS complexes of pre-cordial leads is a non-invasive predictor for frequent arrhythmias in this group of patients.²⁶

Turrini et al. also studied the importance of ECG findings such as QRS dispersion in estimating the risk of sudden cardiac death in patients with ARVC. During the study, patients were divided into four groups: 1) 20 patients with sudden death from the disease; 2) 20 patients living with the disease; 3) 20 patients with ARVC with PVCs ≤ 3 ; and 4) 20 subjects as the control group. Based on the findings of this study, the QRS-QT dispersion was higher in the first group than that of the second and third groups. Moreover, they found that QRS dispersion (40 ms) is a strong and non-dependent predictor of sudden death in ARVC patients.²⁷ However, in the present study, there was no significant association between QRS dispersion (≥ 40 ms) and arrhythmogenic events. These controversies can be due to the choice of the patients, the underlying conditions and the status of the LV of the patients.

Several studies have pointed to improved cardiac function and increased ejection fraction with the CRT-D implantation. Thus, it is likely to be effective in reducing arrhythmias by improving the function of the LV and reducing its size.^{21,28} In addition, based on the results of this study, it was found that

mean QRS association with arrhythmic events in the intrinsic mode was higher than that of max QRS duration. Because max QRS duration is considered as an indication for CRT-D implantation, it can be stated that QRS mean is probably a better indication for CRT-D implantation. However, this should be considered in the future studies.

Additionally, Anastasiou-Nana et al. examined the usefulness of QRS dispersion in the prognosis of patients with congestive HF. During the study, 104 patients with HF (ejection fraction $\leq 35\%$) who did not take any anti-arrhythmic drugs were studied. During the 20-month period of the study, 13 non-sudden and 10 sudden cardiac deaths occurred. They showed that the average length of QRS in the dead patients was significantly more than that of the other patients. The study revealed that QRS dispersion is an independent predictor of non-sudden cardiac death, and in general, mortality rate in people with a QRS dispersion ≥ 46 ms, is 3.9 folds higher than other individuals.²⁹

In another study, Kearney et al. assessed 553 patients with congestive HF and sudden cardiac death. They found that high cardiothoracic ratio, high QRS dispersion, high corrected QT dispersion, and VT are predictors of sudden cardiac death in these patients.³⁰ In a study by Tsagalou et al. the relationship between QT and QRS dispersion and mortality in patients with congestive HF was evaluated. During the 20-month period of follow-up, 13 non-sudden and 10 sudden cardiac death occurred. They showed that QT and QRS dispersion was higher in these individuals than survivors indicating that QRS dispersion is an

independent risk factor that predicts sudden cardiac deaths in HF patients.³¹

Until now, all studies that have demonstrated the effect of QRS dispersion on the incidence of arrhythmic events have been performed before CRT-D implantation. One of the novelties of this study was that by implantation of CRT-D, the effect of QRS dispersion on patients with severe HF, who were highly susceptible to sudden death due to the arrhythmias, was evaluated.

This study had some limitations which may affect its results. First, the effects of changes in the ejection fraction and LV size on the arrhythmic events in HF patients could not be assessed. Therefore, the effects of QRS dispersion on these events should also be evaluated independently of these parameters. Second, the sample size was small, and thus studies with larger sample size are of top priority in this regard.

Conclusion

In conclusion, it was found that CRT-D implantation in HF patients significantly reduced the QRS duration and increased QRS dispersion. However, this increase in the QRS dispersion was not associated with an increase in the incidence of cardiac arrhythmias. Moreover, it was found that using mean QRS duration before CRT-D implantation is more related to arrhythmic events than max QRS duration. Further studies are necessary in this field for better decision making.

Acknowledgments

None.

References

1. Malek-Afzali H, Mehrabi Y. Population and health in Iran in future decades. *Pajouhesh Dar Pezeshki* 2001; 26(3): 41-7. [In Persian].
2. Hekmatpour D, Mohammadi E, Ahmadi F, Arefi S, Rafie M. The effectiveness of applying "making sensitivity to re-admission caring model. *Razi J Med Sci* 2010; 17(75): 33-50. [In Persian].
3. Shih ML, Chen HM, Chou FH, Huang YF, Lu CH, Chien HC. Quality of life and associated factors in patients with heart failure. *Hu Li ZaZhi* 2010; 57(6): 61-71. [In Chinese].
4. Shojaei F. Quality of life in patients with heart failure. *Hayat* 2008; 14(2): 5-13. [In Persian].
5. Givertz MM, Colucci WS, Braunwald E. Clinical

Authors' Contribution

Study concept and design: Fariborz Akbarzadeh, Babak Kazemi

Acquisition of data: Elgar Enamzadeh, Nasrin Khaky, Farid Karkon-Shayan

Analysis and interpretation of data: Elgar Enamzadeh, Nasrin Khaky, Farid Karkon-Shayan

Drafting of the manuscript: Elgar Enamzadeh, Nasrin Khaky, Behnaz Ghamari

Critical revision of the manuscript for important intellectual content: Fariborz Akbarzadeh, Babak Kazemi

Statistical analysis: Behnaz Ghamari, Farid Karkon-Shayan

Administrative, technical, and material support: Fariborz Akbarzadeh, Babak Kazemi

Study supervision: Fariborz Akbarzadeh, Babak Kazemi.

Funding

This paper is based on Nasrin Khaky's specialty dissertation (93/3-6/7) submitted to the School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Conflict of Interest

Authors have no conflict of interest.

Ethical Approval

This study was approved by the Regional Medical Ethics Committee of Tabriz University of Medical Sciences under the number 93.3-6.7.

aspects of heart failure; high-output heart failure; pulmonary edema. In: Braunwald E, Zipes DP, Libby P, editors. *Braunwald's heart disease: a textbook of cardiovascular medicine*. Philadelphia, PA: Saunders; 2005. p. 534-61.

6. Albert NM. Ventricular dysrhythmias in heart failure. *J CardiovascNurs* 2004; 19(6 Suppl): S11-S26.
7. Antzelevitch C. Transmural dispersion of repolarization and the T wave. *Cardiovasc Res* 2001; 50(3): 426-31. DOI: 10.1016/S0008-6363(01)00285-1
8. Mesquita ET, Deus FC, Guedes CR, Maia ER, Subieta CG, Villacorta H, et al. Effects of propranolol on the QT dispersion in congestive heart failure. *Arq Bras Cardiol* 1999; 73(3): 295-8.

9. Barr CS, Naas A, Freeman M, Lang CC, Struthers AD. QT dispersion and sudden unexpected death in chronic heart failure. *Lancet* 1994; 343(8893): 327-9. DOI: 10.1016/S0140-6736(94)91164-9
10. Medina-Ravell VA, Lankipalli RS, Yan GX, Antzelevitch C, Medina-Malpica NA, Medina-Malpica OA, et al. Effect of epicardial or biventricular pacing to prolong QT interval and increase transmural dispersion of repolarization: does resynchronization therapy pose a risk for patients predisposed to long QT or torsade de pointes? *Circulation* 2003; 107(5): 740-6. DOI: 10.1161/01.CIR.0000048126.07819.37
11. Guerra JM, Wu J, Miller JM, Groh WJ. Increase in ventricular tachycardia frequency after biventricular implantable cardioverter defibrillator upgrade. *J CardiovascElectrophysiol* 2003; 14(11): 1245-7. DOI: 10.1046/j.1540-8167.2003.03303.x
12. Jessup M. Aldosterone blockade and heart failure. *N Engl J Med* 2003; 348: 1380-2. DOI: 10.1056/NEJMe030030
13. Bradley DJ, Bradley EA, Baughman KL, Berger RD, Calkins H, Goodman SN, et al. Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. *JAMA* 2003; 289(6): 730-40. DOI: 10.1001/jama.289.6.730
14. Wingate S, Wiegand DL. End-of-life care in the critical care unit for patients with heart failure. *Crit Care Nurse* 2008; 28(2): 84-95.
15. Yu CM, Lin H, Zhang Q, Sanderson JE. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. *Heart* 2003; 89(1): 54-60. DOI: 10.1136/heart.89.1.54
16. Hawkins NM, Petrie MC, MacDonald MR, Hogg KJ, McMurray JJ. Selecting patients for cardiac resynchronization therapy: Electrical or mechanical dyssynchrony? *Eur Heart J* 2006; 27(11): 1270-81. DOI: 10.1093/eurheartj/ehi826
17. Shukla G, Chaudhry GM, Orlov M, Hoffmeister P, Haffajee C. Potential proarrhythmic effect of biventricular pacing: Fact or myth? *Heart Rhythm* 2005; 2(9): 951-6. DOI: 10.1016/j.hrthm.2005.05.019
18. Bai R, Yang XY, Song Y, Lin L, Lu JG, Ching CK, et al. Impact of left ventricular epicardial and biventricular pacing on ventricular repolarization in normal-heart individuals and patients with congestive heart failure. *Europace* 2006; 8(11): 1002-10. DOI: 10.1093/europace/eul110
19. Auricchio A, Stellbrink C, Block M, Sack S, Vogt J, Bakker P, et al. Effect of pacing chamber and atrioventricular delay on acute systolic function of paced patients with congestive heart failure. The Pacing Therapies for Congestive Heart Failure Study Group. The Guidant Congestive Heart Failure Research Group. *Circulation* 1999; 99(23): 2993-3001. DOI: 10.1161/01.CIR.99.23.2993
20. Saxon LA, De MT, Schafer J, Chatterjee K, Kumar UN, Foster E. Effects of long-term biventricular stimulation for resynchronization on echocardiographic measures of remodeling. *Circulation* 2002; 105(11): 1304-10. DOI: 10.1161/hc1102.105730
21. van Rees JB, de Bie MK, Thijssen J, Borleffs CJ, Schalij MJ, van EL. Implantation-related complications of implantable cardioverter-defibrillators and cardiac resynchronization therapy devices: a systematic review of randomized clinical trials. *J Am CollCardiol* 2011; 58(10): 995-1000. DOI: 10.1016/j.jacc.2011.06.007
22. Day CP, McComb JM, Campbell RW. QT dispersion: An indication of arrhythmia risk in patients with long QT intervals. *Br Heart J* 1990; 63(6): 342-4. DoI: 10.1136/hrt.63.6.342
23. Higham PD, Campbell RW. QT dispersion. *Br Heart J* 1994; 71(6): 508-10. DOI: 10.1136/hrt.71.6.508
24. Higham P, Hilton C, Aitchison D, Furniss S, Bourke J, Campbell R. QT dispersion does reflect regional variation in ventricular recovery. *Circulation* 1992; 86(Suppl): 392.
25. Benn M, Hansen PS, Pedersen AK. QT dispersion in patients with arrhythmogenic right ventricular dysplasia. *Eur Heart J* 1999; 20(10): 764-70. DOI: 10.1053/euhj.1998.1400
26. Peters S, Peters H, Thierfelder L. Risk stratification of sudden cardiac death and malignant ventricular arrhythmias in right ventricular dysplasia-cardiomyopathy. *Int J Cardiol* 1999; 71(3): 243-50. DOI: 10.1016/S0167-5273(99)00142-4
27. Turrini P, Corrado D, Basso C, Nava A, Bauce B, Thiene G. Dispersion of ventricular depolarization-repolarization: A noninvasive marker for risk stratification in arrhythmogenic right ventricular cardiomyopathy. *Circulation* 2001; 103(25): 3075-80. DOI: 10.1161/01.CIR.103.25.3075
28. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005; 352(15): 1539-49. DOI: 10.1056/NEJMoA050496
29. Anastasiou-Nana MI, Nanas JN, Karagounis LA, Tsagalou EP, Alexopoulos GE, Toumanidis S, et al. Relation of dispersion of QRS and QT in patients with advanced congestive heart failure to cardiac and sudden death mortality. *Am J Cardiol* 2000; 85(10): 1212-7. DOI: 10.1016/S0002-9149(00)00730-X
30. Kearney MT, Fox KA, Lee AJ, Brooksby WP, Shah AM, Flapan A, et al. Predicting sudden death in patients with mild to moderate chronic heart failure. *Heart* 2004; 90(10): 1137-43. DOI: 10.1136/hrt.2003.021733
31. Tsagalou EP, Anastasiou-Nana MI, Karagounis LA, Alexopoulos GP, Batziou C, Toumanidis S, et al. Dispersion of QT and QRS in patients with severe congestive heart failure: Relation to cardiac and sudden death mortality. *Hellenic J Cardiol* 2002; 43: 209-15.