JOURNAL OF CLINICAL MEDICINE OF KAZAKHSTAN (E-ISSN 2313-1519)
Original Article DOI: https://doi.org/10.23950/jcmk/12113

Structural and functional characteristics of the heart before and after CRT in patients with heart failure

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Received: 2022-07-08.
Accepted: 2022-08-09

J Clin Med Kaz 2022; 19(4):44-47

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Abstract

Abstract: The aim of the study was to evaluate the clinical and hemodynamic effects of resynchronization therapy in patients with congestive heart failure.

Material and methods: Seventy-six consecutive patients underwent echocardiography, NYHA classification, 6-minute walk test and clinical assessment scale modified by Mareev, before and after cardiac resynchronization therapy. All had complete left bundle branch block, with a QRS complex duration ≥130 ms. and left ventricular ejection fraction ≤35%. Also, all patients had received optimal medical therapy for at least 3 months before inclusion to the study.

Results: We observed significant increase in left ventricular ejection fraction (35.4±3.7%, p<0.001, compared with baseline) and decrease in end-systolic volume of the left ventricle (20.2±3.0 %, p<0.001 compared with baseline). Improvement in functional class of congestive heart failure by NYHA classification by >1 was observed in 68.4% of individuals, in 26.3% of participants demonstrated no change and 5.3% of patients had worsening of CHF symptoms.

Conclusion: The response of patients with congestive heart failure to cardiac resynchronization therapy is heterogeneous. The relationship between left ventricular reverse remodeling and the functional class of the congestive heart failure was not significant.

Key words: congestive heart failure, cardiac resynchronizing therapy, optimal drug therapy

Introduction

Many different cardiovascular diseases (CVD) results in development of congestive heart failure (CHF). Despite the improvement in care, CHF remains to be a medical issue with high socio-economic burden [1-3]. Electrical disturbances, such as atrioventricular (AV) and intraventricular blocks present in most of the patients with CHF. AV conduction abnormalities lead to uncoordinated atrial and ventricular contractions, and an intraventricular contraction delay leads to uncoordinated contractions of the ventricles (ventricular dyssynchrony). Wide QRS (>120 ms) is associated with more severe CHF and is a predictor of increased overall risk of death and risk of sudden cardiac death.

Cardiac resynchronization therapy (CRT) has been used since the late 1990s to eliminate the dyssynchrony of cardiac contractions [4–7]. The number of people on CRT is growing all over the world, as well as in our country. However, there are not enough reports on the long-term clinical and hemodynamic effects of CRT, reflecting our own experience of regular follow-up of patients after the intervention.

Here we aim to evaluate the clinical and hemodynamic effects of resynchronization therapy in patients with congestive heart failure.

Material and methods

The single-center prospective observational study of consecutive unmatched patients undergoing CRT for HF between October 2019 and November 2021 evaluating clinical parameters before and after CRT. National Institute of Clinical Excellence (NICE) criteria [8] were used to enroll patients to the study. Exclusion criteria were a recent acute coronary syndrome or acute HF decompensation (<6 weeks), end-stage renal disease (on renal replacement therapy), significant cognitive impairment or terminal illness (expected survival <1 year). Postimplantation exclusions were applied in case of procedure failure or complications resulting in unsuccessful CRT pacing (eg, lead displacement/phrenic nerve pacing). Each participant underwent a preimplantation visit and follow-up at 6 months postimplant. Participants had NewYork Heart Association (NYHA) class assessment, 6 min walk test (6MWT), the clinical assessment scale modified by Mareev [9], transthoracic echocardiography and resting 12-lead electrocardiography (ECG) at all attendances. At the time of enrollment each participant were receiving optimal medicine therapy (OMT) which includes angiotensin converting enzyme inhibitors (ACE inhibitors) or angiotensin II receptor antagonists (ARA), mineralocorticoid receptor antagonists, β – blockers, antiaggregant, anticoagulants and statins for at least three months. The study protocol was approved by Institutional Research Ethic committee. All participants provided written informed consent.

Clinical assessment scale modified by Mareev

For a comprehensive analysis of the functional state of the patient and their response the clinical assessment scale (CAS) modified by Mareev V.Yu. were used [9]. This scale includes patient complaints (shortness of breath, weight changes, feeling of heart rhythm disturbances), objective data (orthopnea, cervical venous overload signs, fine crackles in the lower lobes of the lungs, gallop rhythm, liver span, edema of lower extremities), systolic and diastolic blood pressure. Summary of points corresponds to functional classes (FC): 0 points - no signs of CHF, I FC - ≤3 points, II FC - from 4 to 6 points, III FC - from 7 to 9, IV FC - ≥9 points.

Transthoracic echocardiography

All underwent transthoracic echocardiography (Vivid 7, GE Healthcare, Horten, Norway) for LV volumetric assessment performed on the same machine by the same operator for each study visit. LV ejection fraction was estimated using the biplane modified Simpson's method [10].

Statistical analysis

Basic descriptive statistics for all participants (means, standard deviations) were conducted. Continuous variables were presented using means and for categorical variables were presented using percentages. Student's t-test was used to compare continuous independent variables.

Results

Baseline characteristics

Baseline characteristics are shown in the Table 1. A total of 76 patients were enrolled to the study. 40 of them were male and 36 female. The average age at the time of enrollment was 61.1±1.2. Two thirds of patients had acute myocardial infarction and 37 patients had coronary artery disease (CAD) + arterial hypertension. Based on NYHA class assessment 15 patients had class II, 43 – class III and 18 patients had class IV. The average time of 6MWT was 238.22±11.1 minutes, and average CAS score was 9.0±0.43 points. Average QRS duration was 156.8±2.56 ms.

Table 1 Baseline characteristics

Demographics		
	Age (years, mean ±SD)	61.1 ± 10.2
	Male (n, %)	40 (53%)
Etiology (n, %)		
	Ischemic + hypertension	40 (53%)
	Hypertension	23 (30 %)
	Dilatational cardiomyopathy	13 (17%)
NYHA (n, %)		
	II	15 (19.7%)
	III	43 (56.6%)
	IV	18 (23.7%)
6MWT (M, mean ±SD)		238.22 ± 11,1
CAS score (points, mean ±SD)		9,0 ± 0,43
ECG		
	QRS duration (ms, mean ±SD)	156,8 ± 2,56 ms.
	LBBB (n, %)	76 (100%)

Table 2 Structural and functional parameters of the heart before and 6 months after CRT

Echo-parameters	Baseline	6 months after CRT	p
Left atrium, (cm, mean ±SD)	4.4 ± 0.08	4.2 ± 0.07	<0.001
LVEDD (cm, mean ±SD)	7.1 ± 0.1	6.6 ± 0.1	< 0.001
LVESD (cm, mean ±SD)	6.0 ± 0.1	5.4± 0.1	< 0.001
LVEDV (mm, mean ±SD)	262.3 ± 10.47	230.5 ± 9.76	< 0.001
LVEDVI (ml/m2, mean ±SD)	136.3 ± 5.28	119.8 ± 4.87	< 0.001
LVESV (mm, mean ±SD)	186.7 ± 8.59	144.8 ± 7.89	< 0.001
LVESVI (ml/m2, mean ±SD)	97.2 ± 4.48	75.3 ± 4.02	< 0.001
SV (mm, mean ±SD)	77.2 ± 2.35	84.8 ± 3.04	< 0.01
SVI (ml/m2, mean ±SD)	40.0 ± 1.2	44.1 ± 1.49	< 0.01
LVEF (%, mean ±SD)	27.7 ± 0.72	36.4 ± 0.91	< 0.001
ePASP (mm Hg, mean ±SD)	50.7 ± 1.8	45.4 ± 1.44	< 0.01
Mitral regurgitation (level, mean ±SD)	2.4 ± 0.07	1.9 ± 0.07	< 0.001
Tricuspid regurgitation (level, mean ±SD)	1.7 ± 0.07	1.7± 0.07	>0.01

Effects of CRT on cardiac function

Structural and functional parameters of the heart before and 6 mo. after CRT are shown in the Table 2. It is shown that the most significant changes were in LV ejection fraction (EF) (increase on average by 35.4±3.7% compared with the baseline, p<0.001) and LV end systolic volume (ESV) (decrease by 20.2±3.0% vs baseline, p<0.001).

ECG assessment

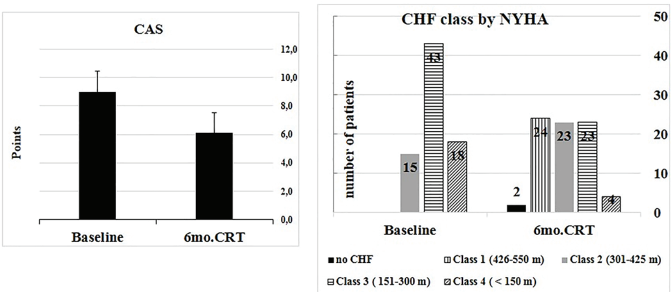
On ECG assessment, the duration of the QRS complex shortened from 156.8±2.56 ms to 128.5±2.79 ms (p<0.001), i.e. there was a significant decrease in the width of the ventricular ECG complex. Overall improvement of all indicators of the structural and functional state of the heart was more pronounced in individuals with an initially wider ventricular complex (≥150 ms) than in the group with a complex width of less than 150 ms, however, the difference was statistically insignificant.

In our study, 51 (67.1%) of 76 patients had an increase in LV EF by ≥15%, 18 (23.7%) - less than 15%, the remaining 7 (9.2%) - a decrease in this score compared to baseline. LV end-systolic volume decreased by ≥ 15% and < 15% in 40 (52.6%) and 24 (31.6%) patients, respectively, and 12 (15.8%) patients experienced an increase in ESV.

Clinical assessment

According to CAS, the average points decreased from 9.0±0.43 to 6.1±0.37 points ($p<0.001$) 6 months after CRT implantation. The 6-minute walk test showed that the average distance increased from 238.2±11.13 meters to 363.6±14.81 meters, i.e. by 73.44±11.56% compared with the baseline ($p<0.001$). It should be noted that 46 (60.52%) out of 76 subjects showed an increase in the distance by ≥25% compared with the baseline.

Figure 1 - Clinical assessment of patients before and after CRT implantation



At the follow-up clinical symptoms corresponding to NYHA class I were in 24 patients, class II - in 23, and class III - in 23, and class IV were in only 4 patients. Two patients walked more than 551 m (600 and 563), i.e. they did not have signs of heart failure according to the test criteria (Figure 1). Analysis of individual data showed that a positive response (decrease in CHF class according to NYHA ≥ 1) was observed in 52 (68.4%) of 76 individuals; 20 (26.3%) patients showed no changes in the class, and 4 (5.3%) patients had deterioration (an increase by one class of NYHA). In the group of individuals with an increase in LV EF ≥ 15%, the changes in CHF class was as follows: decrease - in 35 (68.6%), unchanged - in 15 (29.4%), increase - in 1 (2%) of 51 patients, among those with an increase in LVEF < 15% - in 13 (72.2%), 3 (16.7%) and 2 (11.1%) of 18 subjects, respectively; even among 7 individuals with a decrease in LV EF compared with the baseline, exercise tolerance was different: 4 people had a decrease (improvement) in CHF class by ≥1, 1 had an increase (deterioration) and 2 remained unchanged.

There was direct correlation between the distance in 6MWT and LVEF ($r=0.338$, $p=0.003$) and a negative correlation between the ESV and the distance in 6MWT ($r=- 0.244$, $p=0.03$).

Discussion

Based on our results, there are no uniform direction of changes in hemodynamics and the clinical condition of patients at the baseline and after CRT. There is no strict relationship between gross reverse remodeling of the left ventricle and the changes of CHF class, which is consistent with a number of previously reported studies [11, 12]. The direct correlation between the distance in 6MWT and LVEF and negative correlation between the ESV and the distance in 6MWT confirm that the responses of patients with CHF to resynchronization therapy are heterogeneous. Therefore, in our work, we avoided the concepts of "responders, non-responders, super-responders", given the relatively small number of patients and the observation period. In most cases we observed that OMT and CRT improved clinical condition of patients (68.54%), their tolerance to physical stress increased and reverse heart remodeling were observed. Especially, the LVEF (an increase by an average of 35.4±3.7 %, $p<0.001$) 54%) and ESV of the left ventricle (decrease by 20.2±3.0%, $p<0.001$) changed to the greatest extent. If patient has no changes or increase (worsening) in CHF class and insufficient reverse heart remodeling after CRT, this patient generally considered to be a "non-responder" [13-16]. Different studies consider the heterogeneity of patients by cause of CHF, the presence of myocardial scar, suboptimal (not-optimal) position of the ventricular electrode and low degree of biventricular stimulation as a reason behind the poor response to CRT. There is also no unanimity in the timing of assessment of the response to CRT, although in most published studies, 6 or 12 months were chosen as an intermediate period for determining the reliability of CRT [17-22]. The results of our study show that even with a slight LVEF or a decrease in ESV (<15% compared with baseline), the clinical condition of most patients improves, therefore, in our opinion, they should not be classified as "non-responders". Even if CHF class remains unchanged and left ventricular remodeling is not worsening, then, in our opinion, this should be considered as acceptable result and we should continue our follow-up with precise control of pharmacotherapy and echocardiogram parameters.

The ambiguity of the literature data when choosing the timing of assessment the response to CRT and insufficient positive changes of the structural and functional parameters of the heart are indicating the need for a better approach to the selection of patients and the need to establish an uniform criteria and optimal timing for determination the effectiveness of resynchronization therapy. To achieve good results, it is important to achieve a high percentage of biventricular stimulation and an optimal position of the electrode in the non-scared region of the myocardium.

Thus, the results of the study confirmed the clinical efficacy and positive changes in the parameters of the structural and functional state of the heart compared to the baseline six-month after the resynchronization therapy in patients with severe heart failure. To verify the results of resynchronization therapy, it is necessary to carefully select patients, monitor their device programming parameters, and search for new approaches to pharmacotherapy.

Conclusions

1. CRT implantation along with optimal medication therapy in patients with severe CHF (LVEF ≤ 35%) with sinus rhythm and LBBB resulted in improvement of structural and functional parameters of the heart and clinical symptoms. Especially, the LVEF (an increase by an average of 35.4±3.7 %, $p<0.001$) 54%) and ESV of the left ventricle (decrease by 20.2±3.0%, $p<0.001$) changed to the greatest extent. The decrease in CHF class by more than 1 was observed in 68.6% of patients, 26.3% of patients had no change in CHF class and 5.3% patients had worsening or increase in CHF class by 1.

2. The response of the patients to the CRT implantation was not uniform. There was no relationship between reverse remodeling of the left ventricle and CHF class changes. There was direct correlation between the distance in 6MWT and LVEF ($r=0.338$, $p=0.003$) and a negative correlation between the ESV and the distance in 6MWT ($r= - 0.244$, $p=0.03$).

Disclosures: There is no conflict of interest for all authors.

Acknowledgements: None.

Funding: This study was supported by the research grant of the Ministry of Healthcare of the Republic of Kazakhstan BR 11065383 "Development of innovative and highly effective technologies aimed at reducing the risk of premature death from cardiovascular diseases, chronic respiratory diseases and diabetes" (State registration number 0121RK00850)

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