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Increased quality of life predictive factors after cardiac resynchronization therapy in heart failure patients

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Abstract. – OBJECTIVE: This study aimed to investigate the effects of cardiac resynchronization therapy (CRT) treatment on clinical and echocardiographic findings, the quality of life (QoL) in heart failure (HF) patients, and to identify possible predictors of improvement in QoL.

PATIENTS AND METHODS: A total of 97 patients (73 males and 24 females, mean age 62.8±10.6 years) with HF who underwent CRT implantation were included in this study. Demographic characteristics, laboratory findings, transthoracic echocardiography, and quality of life assessment the MOS 36- Item Short-Form Health Survey (SF-36 score) data were recorded at baseline, and 6 months after CRT. Baseline and 6th-month data were compared. The data of groups with and without improvement in QoL were analyzed, and predictors of improvement in QoL were determined.

RESULTS: According to the criteria for response to CRT, we observed good response at 6 months follow-up in at least two-thirds of heart failure patients. Significant improvement was observed in the SF-36 score of 67 patients who underwent CRT, and the procedure was considered successful in terms of improvement in QoL in these patients. In this group, baseline ejection fraction (EF), tricuspid annular plane systolic excursion (TAPSE), and right ventricular lateral peak systolic velocity (RV-lateral-S) values were significantly higher. TAPSE and RV lateral-S values were found to be significant in predicting the improvement in QoL after CRT [OR: 1.77 (1.00-3.14), 2.61 (1.02-6.69), respectively, $p<0.05$]. The cut-off values of these predictive factors were found to be 15.5 for TAPSE and 9.65 for RV lateral-S.

CONCLUSIONS: In our study, we found that TAPSE and RV Lateral-S were predictors of improved quality of life in patients who underwent CRT. Routine evaluation of right ventricular functions before the procedure can provide significant improvement in quality of life as well as clinical symptoms.

Key Words:

Cardiac resynchronization therapy, Echocardiographic findings, Heart failure, Quality of life.

Introduction

Heart failure (HF) is not a single pathological diagnosis but is a syndrome that progresses with a mortality rate of approximately 50% within 4 years from diagnosis[1]. HF significantly affects the quality of life (QoL) with functional limitations, and increased risk of depression and anxiety[2]. The World Health Organization (WHO) has defined health as a state of complete physical, mental, and social well-being, and not merely the absence of disease[3]. Therefore, it is becoming increasingly clear that for HF, QoL is as important as well-known endpoints, such as death and hospitalization.

QoL is impaired in patients with HF in several important ways. Symptoms such as dyspnea, fatigue, swelling in the feet and abdomen, and body change such as loss of muscle mass, impair physical health. HF can also affect the psychological state of the individual by triggering depression, sleep disorder, and anxiety with its negative impact on physical health and social functions[4]. Given the high prevalence and clinical and socioeconomic consequences of HF, it is important to understand the relationship between treatment options and improvement in QoL and other patient outcomes. Cardiac resynchronization therapy (CRT) is a comprehensively validated and effective treatment option in appropriately selected patient groups with symptomatic heart failure. CRT improves cardiac function, symptoms, and well-being, and reduces morbidity and mortality in an appropriately selected group of HF patients. CRT also improves quality-adjusted life-years among patients with moderate to severe HF[1]. However, approximately 30% of eligible patients do not derive significant clinical benefit from this treatment and do not respond to CRT in their mid and long-term follow-ups[5]. This study aimed to

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investigate the effects of CRT treatment on clinical, echocardiographic findings and QoL in HF patients and to identify possible predictors for improving QoL.

Patients and Methods

Patient Selection

A total of 97 patients (73 males and 24 females, mean age 62.8±10.6 years) with HF who underwent CRT implantation were included in this study. Indications for CRT implantation are based on the European Society of Cardiology (ESC) Heart Failure Guidelines with a selection of patients with left bundle branch block, QRS complex duration >130 ms, EF <35%, and sinus rhythm. The study was approved by our Institutional Ethics Committee (Bursa City Hospital, 2021-23/7). Written informed consent was obtained from all patients prior to enrolment. Inclusion criteria were as follows: patients with indications of CRT implantation, completed QoL questionnaires before the procedure and after 6 months follow-up. Exclusion criteria were as follows: malignancies, neurological disorders, presence of dementia or cognitive impairment, and patients followed up with a diagnosis of major psychiatric illness such as depression, anxiety, schizophrenia, and bipolar illness. Data on patients' demographic characteristics (age, gender), smoking habits, body mass index (BMI, kg/m^2), comorbid diseases, and drug use were recorded at the beginning. Data on laboratory findings, including blood biochemistry, complete blood count (CBC), cardiovascular risk markers [troponin, B-type natriuretic peptide (BNP)], and also 12-lead ECG and transthoracic echocardiography were recorded at baseline and after 6 months from the implant. Quality of life assessment, clinical symptoms, New York Heart Association (NYHA) class, ejection fraction, and the other echocardiographic parameters were compared before the implantation and after 6 months. Response to CRT was defined as ≥15% reduction in left ventricular end-systolic volume (LVESV) and/or ≥10% increase in ejection fraction (EF) and at least 1 class improvement in NYHA at 6 months post-CRT compared to pre-treatment findings.

Quality of Life Assessment

Quality of life assessment was performed with SF-36, which is a self-administration questionnaire designed for the assessment of health-related QoL[6]. The health questionnaire was determined into two main groups: Major Physical Health Score (PCS) and Mental Health Score (MCS), and 8 subgroups (Physical function, Role-physical function, Pain index, General health perception, Vitality score, Social function, Role-emotional function, Mental health index) under them, for 36 items in total[7]. Quality of life assessment was performed with the SF-36 using the patient's self-assessment before the CRT implantation procedure and after 6 months of follow-up.

Echocardiographic Assessments

Echocardiographic evaluations were made with the transthoracic echocardiography device (GE Vivid S60 Ultrasound machine, GE Healthcare, Chicago, IL, USA) before CRT implantation and after 6 months of CRT treatment. Measurements were obtained with patients at rest in the lateral decubitus position. Left ventricle (LV) end-diastolic volume and LV end-systolic volume (LVESV) and left ventricular ejection fraction (LVEF) measurements were evaluated using the Simpson biplane method. The right ventricular (RV) end-diastolic (RVED) area, right ventricular end-systolic (RVES) area, right ventricular lateral peak systolic velocity (RV lateral-S) and RV fractional area change (FAC) were evaluated by obtaining tissue Doppler images and were calculated using 'end-diastolic area – end-systolic area)/end-diastolic area × 100' formula. Tricuspid annular plane systolic excursion (TAPSE) was estimated using M-mode recordings from the apical 4-chamber view to assessing RV longitudinal function. Peak systolic velocity (S), peak early diastolic velocity (E'), and peak late diastolic velocity (A'), the trans-mitral early diastolic rapid filling (E-wave) and atrial contraction late filling (A-wave) velocities were measured with tissue doppler images of the left ventricle to calculate E/A ratio. The echocardiographic response to CRT was defined as ≥15% reduction in LVESV or ≥10% increase in ejection fraction (EF).

Statistical Analysis

The data were analyzed using SPSS, version 26.0 for Macintosh (IBM Corp., Armonk, NY, USA). The descriptive statistics were presented as mean±SD for continuous numeric variables and presented as median for discrete numeric variables. The frequency statistics were calculated. Comparisons between study groups were analyzed by independent samples Student's *t*-test for normally distributed data and Mann-Whitney U test for non-normally distributed data. Kolmogorov-Smirnov tests were used for testing normality. Comparisons between parameters before and after treatment were analyzed by paired

Table I. Clinical and demographic characteristics of the patients.

	Patients (n=97)
Age (years, mean±SD)	62.8±10.6
BMI (kg/m^2, mean±SD)	25.09±2.09
Gender (n, %)	
Male	73 (75%)
Female	24 (25%)
Presence of Hypertension (n, %)	
+	77 (79.4%)
–	20 (20.6%)
Presence of Diabetes Mellitus (yes/no, n, %)	
+	37 (38.1%)
–	60 (61.9%)
Presence of Coronary Heart Disease (n, %)	
+	67 (69.1%)
–	30 (30.9%)
Presence of Systemic Disease (n, %)	
+	92 (94.8%)
–	5 (5.2%)
History of smoking (n, %)	
+	26 (26.8%)
–	71 (73.2%)
NYHA (n, %)	
Class III	84 (86.6%)
Class IV	13 (13.4%)

BMI: Body Mass Index, NYHA: New York Heart Association Classification.

t-test. Chi-square and Fisher's Exact tests were used for comparing categorical data. A multivariate logistic regression analysis was conducted to investigate the clinical characteristics, and echocardiographic findings that impact health-related quality of life Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off values for the variables, which was found to be a predictive factor for improvement in QoL. Spearman and Pearson correlation tests were used to investigate whether baseline TAPSE and RV lateral S values are associated with 6th-month EF, pulmonary artery pressure (PAP), LVESV values, and NYHA classes. The level of statistical significance was set at $p<0.05$.

Results

The demographic and clinical characteristics of the patients are shown in Table I. A statistically significant improvement was found in all parameters of the patients' echocardiography findings, functional classification, and quality of life scale scores after CRT application. These results are shown in Table II. Significant improvement was observed in the SF-36 GH score of 67 patients who underwent CRT, and the procedure was con-

Table II. Comparisons of echocardiographic findings and health-related quality of life scores before and 6-months-after treatment.

	Baseline	6th month	*p*-value
EF (%, mean±SD)	23.8±5.2	33.3±10.0	0.000
NYHA (median, min-max)	3 (3-4)	2 (1-3)	0.000
PAP (mmHg, mean±SD)	47.8±9.5	35.6±7.9	0.000
TAPSE (mean±SD)	16.9±2.4	19.6±3.6	0.000
RV-lateral S (mean±SD)	9.9±2.0	11.9±2.6	0.000
LVESV (mean±SD)	191.9±52.9	154.1±52.2	0.000
SF-36 PF (mean±SD)	45.7±3.8	57.0±10.9	0.000
SF-36 RP (mean±SD)	31.8±9.8	54.2±17.5	0.000
SF-36 RE (mean±SD)	39.8±9.1	54.3±21.3	0.000
SF-36 VT (mean±SD)	38.0±9.9	60.0±15.3	0.000
SF-36 MH (mean±SD)	41.0±7.4	62.5±12.8	0.000
SF-36 SF (mean±SD)	48.5±8.7	66.0±13.4	0.000
SF-36 BP (mean±SD)	73.4±4.9	77.5±7.2	0.000
SF-36 GH (mean±SD)	30.5±8.8	50.4±20.7	0.000
Response to CRT			n (%)
NYHA	Remained unchanged		11 (11.3%)
	Improved by at least one NYHA class		86 (88.7%)
LVESV	Decreased by ≥15%		61 (62.9%)
EF	Increased by ≥10%		64 (66%)

EF: Ejection Fraction, NYHA: New York Heart Association Classification, PAP: Pulmonary Artery Pressure, TAPSE: Tricuspid Annular Plane Systolic Excursion, RV-Lateral-S: Right Ventricle Lateral Systolic Velocity, PF: Physical Function, RP: Physical Role, RE: Emotional Role, VT: Vitality, MH: Mental Health, SF: Social Function, BP: Bodily Pain, GH: General Health.

sidered successful in these patients. When the pre-procedural clinical features of these patients and 30 patients who did not improve in scores were compared. There was no significant difference in age, gender, BMI, smoking history, systemic disease, and NYHA classification. On the other hand, pre-procedural EF, TAPSE, and Right Ventricle lateral systolic velocity (RV-lateral-S) values were found to be significantly higher in the group with improved quality of life (Table III). When the factors that are effective in predicting the improvement in quality of life after the CRT procedure were examined, it was seen that the TAPSE and RV-lateral-S values were significant [OR 1.77 (1.00-3.14), 2.61 (1.02-6.69), respectively, $p<0.05$) (Table IV)].

The cut-off values of these predictive factors were found to be 15.5 for TAPSE and 9.65 for RV-lateral-S. Furthermore, it was found that the CRT procedure performed in patients above these values was more successful in improving the quality of life (Table V; Figure 1).

The results of correlation analyses conducted in the study are illustrated in Table VI. There was a statistically significant negative correlation among 6th month LVESV, NYHA class, PAP values, and baseline TAPSE, RV Lateral S values. Besides, we found that baseline TAPSE and RV Lateral S values had a high positive correlation with 6th-month EF values ($p<0.001$). These results strongly support the findings of our study.

Discussion

Our study's main goal was to investigate CRT treatment's effects on clinical symptoms and quality of life in heart failure patients and identify possible predictors for the outcomes of CRT treatment. The Reform study[8] showed that after 9 months of device therapy, CRT patients had improvements in disease-specific and mental component scores in measures of QoL. The study determined that improvements in QoL were associated with CRT-related physiological improvements. Based on the criteria for response to CRT, we observed good response in at least two-thirds of patients of heart failure patients at the 6th-month follow-up (Table II). The 6-month SF-36 quality of life scores of 67 patients improved com-

Table III. Comparison of initial clinical characteristics and echocardiographic findings between the patients' groups according to the improvement of HR QoL scores.

	Improved QoL (n=67 patients)	Non-improved QoL (n=30 patients)	*p*-value
Age (years, mean±SD)	63.4±11.4	61.5±8.6	0.435
BMI (kg/m^2, mean±SD)	24.9±2.1	25.3±2.0	0.839
Gender (n, %)			
Male	51	22	0.769
Female	16	8	
History of smoking (n, ±)	50	21	0.634
	17	9	
Presence of systemic disease (n, ±)	62	30	0.124
	5	0	
EF (%, mean±SD)	25.4±5.0	20.3±3.9	0.000
NYHA (median)			
Class III	60	24	0.202
Class IV	7	6	
PAP (mmHg, mean±SD)	47.0±9.7	49.8±9.0	0.152
TAPSE (mean±SD)	17.9±1.8	14.5±2.0	0.000
RV-lateral S (mean±SD)	10.7±1.8	8.2±1.0	0.000
Difference in EF (mean±SD)	13.1±6.4	1.4±3.6	0.000
Difference in PAP (mean±SD)	12.8±6.9	10.9±6.4	0.369
Difference in TAPSE (mean±SD)	3.5±1.7	1.0±0.9	0.000
Difference in RV-lateral S (mean±SD)	2.5±1.0	0.9±0.9	0.000

QoL: Quality of Life, BMI: Body Mass Index, EF: Ejection Fraction, NYHA: New York Heart Association, PAP: Pulmonary Artery Pressure, TAPSE: Tricuspid Annular Plane Systolic Excursion, RV-Lateral-S: Right Ventricle Lateral Systolic Velocity.

Table IV. Multivariate Logistic Regression Analysis for predictive factors of improvement in HRQoL

	Odds Ratio	95% CI	*p*-value
Age	1.04	0.97-1.11	0.190
Gender (reference category: female)	1.66	0.36-7.51	0.511
BMI	0.88	0.63-1.23	0.457
NYHA	3.16	0.51-19.50	0.216
EF	0.99	0.83-1.18	0.971
PAP	1.03	0.95-1.12	0.358
TAPSE	1.81	1.02-3.20	0.039
RV-lateral-S	2.71	1.03-7.13	0.043

Nagelkerke R^2: 0.651.
CI: Confidence Interval, BMI: Body Mass Index, NYHA: New York Heart Association Classification EF: Ejection Fraction, PAP: Pulmonary Artery Pressure, TAPSE: Tricuspid Annular Plane Systolic Excursion, RV Lateral-S: Right Ventricle Lateral Systolic Velocity.

pared to the pre-CRT procedure, consistent with the CRT response rate. Moreover, this significant improvement was seen in all 8 subscales of the SF-36 score. A study[9] reported an improvement in all parameters of the patients' SF-36 scores, an increase in EF, and a decrease in LVESV in 3-month follow-up after CRT. Another study[10] showed that CRT improved QoL, NYHA class, and EF with a significant positive correlation between changes in SF-36 indices and EF. Similarly, in our study, besides the improvement in QoL, an increase in EF, a decrease in pulmonary artery pressure and LVESV, and an improvement in NYHA class were observed after CRT. In addition, there were increases in TAPSE and RV lateral-S, which are indicators of right ventricular functions (p<0.000). When we compared the groups with improved and non-improved QoL, TAPSE, RV-lateral-S, and EF were significantly higher before the procedure in the group with improved QoL (p<0.000). Consistent with the literature, these findings show that poor right ventricular and left ventricular systolic functions are negative prognostic factors in terms of procedural success and improvement in QoL in heart failure patients. CARE-HF study[11] shows that patients with baseline low TAPSE were associated to a weak LVEF at 18 months' follow-up. Ghio et al[12] studied 379 patients with moderate to severe HF and showed that a low right ventricular ejection fraction (low right ventricular ejection fraction defined as TAPSE on echocardiogram <14 mm) was an independent predictor of survival. Another study[13] found a significant correlation between TAPSE and LVESV reduction, it was shown that the TAPSE cut-off value of 17 mm was the best predictor of LV reverse remodeling 6 months after CRT (sensitivity 67.8%, specificity 54.2%; area under the curve: 0.615; p=0.0076). Similarly, we found a statistically significant inverse correlation between baseline TAPSE and RV Lateral-S and 6th-month LVESV values, NYHA class, pulmonary arterial pressure, and a positive correlation with 6th-month EF. Alpendurada et al[14] demonstrated that low RVEF and TAPSE values before the CRT procedure were strongly associated with less LV remodeling and a higher number of hospitalizations and death after CRT. It was stated that right ventricular dysfunction is an indicator of response to CRT and clinical outcome[14,15]. In our study, in Multivariate Logistic Regression Analysis, TAPSE, and RV lateral-S were found to be important predictive factors for improvement in QoL after CRT treatment. The cut-off values were 15.5 for TAPSE and 9.65 for RV lateral-S. Our results are in very good agreement with the cited literature.

Table V. ROC analysis for cut-off value of TAPSE and RV-lateral-S for predicting improvement in HRQoL.

	AUC	95% CI	p-value	Cut-off value
TAPSE	0.887	0.802-0.972	0.044	15.5
RV-lateral-S	0.896	0.831-0.960	0.033	9.65

AUC: Area Under Curve, CI: Confidence Interval.

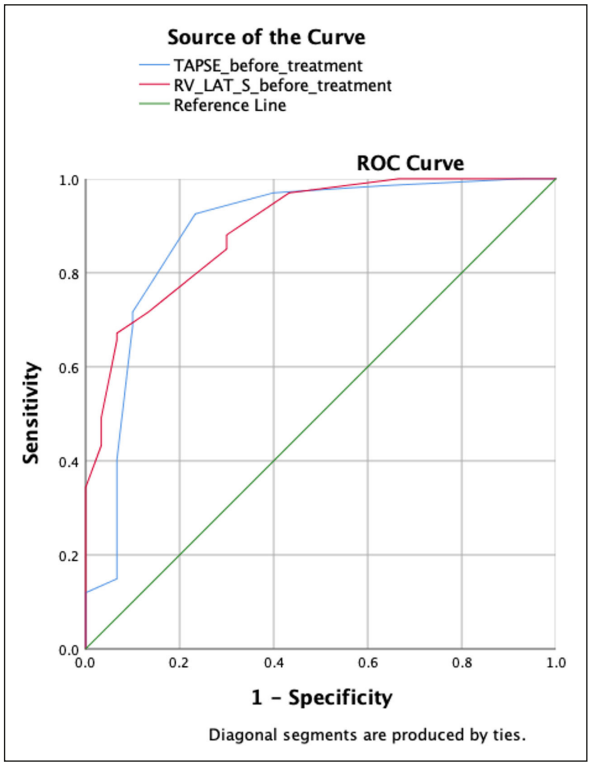

Figure 1. ROC Analysis.

CRT improves cardiac functions, clinical symptoms, and well-being, reduces hospitalization, and morbidity and mortality in an appropriately selected group of HF patients[1]. Heart failure-specific QoL combines physical, socioeconomic, and psychological impairments into a single dimension[9]. Therefore, improvement in QoL is another important endpoint for heart failure management as well as clinical and symptomatic improvement. CRT has been shown to improve heart failure-specific QoL with multiple clinical endpoints, including heart failure symptoms, exercise capacity, hospitalization rates, and longevity[9,16,17]. However, there is not enough data on which parameters are associated with the improvement in QoL before the procedure. Previous studies[18,19] have associated improvements in clinical, symptomatic, and QoL with improvement in left ventricular function, achieved by correcting left ventricular dyssynchrony due to intraventricular and interventricular conduction delay. Our study shows that TAPSE and RV lateral-S are predictors of improvement in QoL. Based on the funding of our study, the increase in EF due to the reduction in LVESV after CRT and the resulting improvement in left ventricular functions are associated with preserved right ventricular functions before the procedure. The authors agree that routine evaluation of the right ventricle should be considered in the selection of patients who are candidates for CRT, as suggested in some studies, and that this evaluation will significantly improve QoL as well as clinical and symptomatic improvement.

Limitations

The limitations of our study are the limited number of patients included in the study, and it is not known whether the etiology of heart failure is ischemic or non-ischemic. More scientific studies on the subject are needed.

Conclusions

In conclusion, in our study, we found that preserved right ventricular function improves left ventricular functions and leads to an increase in quality of life in patients undergoing CRT. We are of the opinion that right ventricular functions should be evaluated routinely before the procedure, and as a result, with appropriate patient selection, a significant improvement can be achieved in quality of life as well as clinical symptoms.

Table VI. Correlation analysis between baseline TAPSE and RV lateral S values and 6th-month EF, PAP, LVESV values, and NYHA classes.

	Baseline TAPSE		Baseline RV Lateral S	
	r	p	r	p
LVESV 6th month	-.437	.000	-.386	.000
EF 6th month	.636	.000	.642	.000
PAP 6th month	-.274	.007	-.207	.042
NYHA 6th month	-.457	.000	-.488	.000

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This study received no financial assistance.

Conflict of Interest
The authors have no conflicts of interest to declare.

Informed Consent
Written informed consent was obtained from all patients prior to enrolment.

Ethics Approval
The study was approved by the Bursa City Hospital Ethics Committee (2021-23/7).

Authors' Contributions
Concept, Design, Supervision, Funding, Materials, Data Collection and/or processing, Analysis and/or interpretation, Literature search, Writing, Critical review: DT, BU.

Data Availability
Data are available upon request.

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