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Clinical and classic echocardiographic features of patients with, and without, left ventricle reverse remodeling following the introduction of cardiac resynchronization therapy

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Abstract

Background: *The aim of the study was to assess clinical and classic echocardiographic data in patients with different cardiac resynchronization therapy (CRT) outcomes.*

Methods: *Sixty consecutive patients (aged 66.3 ± 8.7 years, 57 men) with chronic heart failure (CHF) in New York Heart Association (NYHA) classes III–IV despite optimized pharmacotherapy, with left ventricular end-diastolic diameter (LVEDD) > 55 mm, left ventricular ejection fraction ≤ 35% and wide QRS complex (≥ 120 ms), including individuals with permanent atrial fibrillation (AF) and single- and dual-chamber pacing, were assessed firstly before, and secondly three months after, biventricular heart stimulator implantation (excluding three patients who died during the follow-up). Patients developing ≥ 10% reduction of left ventricular end-systolic volume (LVESV) were classified as responders to CRT.*

Results: *The group of responders (n = 34, 59.7%) and the group of non-responders (n = 23, 40.3%) did not differ regarding baseline echocardiographic parameters or in terms of clinical data of age, gender, concomitant diseases, smoking or pharmacological treatment. The differences involved higher rates of ischemic CHF background, prevalence of hypertension and permanent AF, and a higher concentration of N-terminal pro-B-type natriuretic peptide (NT-proBNP) among the non-responders. In the multivariate logistic regression analysis, NT-proBNP, body mass index (BMI) and the presence of permanent AF correlated negatively with the magnitude of LVESV reduction following CRT introduction.*

Conclusions: *Classic echocardiographic data did not predict left ventricle reverse remodeling. Higher rates of ischemic CHF aetiology, hypertension, permanent AF and higher NT-proBNP concentration were found in the group without at least 10% LVESV reduction at the three month follow-up. NT-proBNP, BMI and the presence of permanent AF had negative effects on the magnitude of LVESV.* (Cardiol J 2011; 18, 2: 157–164)

Key words: heart failure, pacemakers, echocardiography

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Introduction

Cardiac resynchronization therapy (CRT) is well-established as an effective means of managing patients with drug-refractory chronic heart failure (CHF) [1]. Nonetheless, despite the clinical advantages of improved physical capacity and quality of life, and decreased morbidity and mortality related to CHF elicited by CRT, a marked percentage of individuals do not benefit from this novel therapy [2]. Various studies conducted in the past decade focused mainly on the assessment of mechanical dyssynchrony of the heart's performance, one of the key mechanisms of progressing CHF corrected by CRT, thought to be the culprit for CRT failure. Researchers have used many different techniques of dyssynchrony appraisal such as echocardiographic modalities of tissue Doppler imaging (TDI), strain, strain rate, myocardial displacement or magnetic resonance imaging. These studies have yielded inconclusive results, revealed the very often unsatisfactory reproducibility of various advanced imaging techniques, and showed the need for expensive equipment and for trained and experienced staff [3–5]. The biggest disadvantage of these methods of mechanical dyssynchrony appraisal was their inability to be practically applied. All the mainstream studies have been accompanied by an unrelenting interest in extracting efficient information to predict the outcome of CRT tests and examinations performed in daily routine. Unfortunately, trial results have been affected by the study inclusion criteria, being irrelevant to patients' heterogenous profiles treated with CRT in clinical practice e.g. permanent atrial fibrillation (AF) or previously implanted classic pacemaker patients.

The aim of our study was to assess the clinical and classic echocardiographic features including a broad array of conditions associated with poor prognosis in CHF posted in the European Society of Cardiology (ESC) guidelines in patients with, and without, left ventricle reverse remodeling, following CRT introduction [1].

Methods

Study group

Seventy two consecutive patients with chronic heart failure in stable condition for at least three months in New York Heart Association (NYHA) classes III or IV despite optimized pharmacotherapy, with left ventricle end-diastolic diameter (LVEDD) > 55 mm, left ventricular ejection fraction (LVEF) ≤ 35% and wide QRS complex (≥ 120 ms) were enrolled in our prospective study. Eight individuals met exclusion criteria; two refused the introduction of CRT; while in another two the implantation of left ventricular lead did not succeed. Eventually, 60 patients (aged 66.3 ± ± 8.7 years, 57 men: 95%, and three women: 5%) with chronic heart failure participated in the study.

The study was approved by the local ethical committee and all patients gave their informed consent.

Exclusion criteria

Exclusion criteria comprised the presence of unstable angina; acute myocardial infarction; coronary artery bypass graft or percutaneous coronary intervention within the previous three months; continuous or intermittent intravenous inotropic drug therapy; an estimated life expectancy of less than 12 months; a mechanical right-side heart valve; heart transplant; pregnancy or concurrent enrolment in a study thought to confound the results.

Study design

Before CRT implantation, and at three month follow-up (12–16 weeks), individuals were evaluated clinically as to their NYHA class, a six-minute walk test (6-MWT), and we took a history of their hospitalizations and used echocardiography (General Electric Healthcare Vivid 7; left ventricle volumes and LVEF were evaluated with biplane Simpson's method). All stored echo recordings were analyzed off-line (Echo Pack system with GE brand software) twice by an experienced physician with respect to the echocardiography norms of the European Association of Echocardiography (EAE) and the recommendations of the American Society of Echocardiography (ASE) for performance and reporting of echocardiographic studies for cardiac resynchronization therapy [3, 6]. The criteria of diagnosing different clinical and biochemical disorders were adopted from the ESC guidelines [1]. All patients undergoing CRT had had a coronarography. An ischemic background of CHF was diagnosed when there was at least 50% stenosis of one or more coronary artery branches, or when a patient had a history of coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) [7, 8].

Biventricular device implantation

Patients in sinus rhythm received an atriobiventricular stimulator (DDDR BiV: n = 47), while those with permanent AF received a biventricular device (VVIR BiV: n = 13). Patients with a history of cardiac arrest and/or malignant ventricular arrhythmias had a system with combined cardiover-

ter-defibrillator (CRT-D) implanted (18 cases). During CRT all leads were implanted transvenously. Left ventricular lead, guided by venogram, was placed in the coronary sinus tributary in a stable lateral or postero-lateral position, with a < 3.5 V capture threshold. The right ventricular lead was placed in the septal or outflow tract (RVOT) position. Leads' tip positions were verified on frontal and sagittal chest X-ray. Two patients required left ventricular lead reposition due to their dislocation. Atrioventricular (AV) delay remained standard programmed 150/120 ms, unless conduction of cardiotropic systoles was preserved. In those patients AV was shortened until ventricles were paced (five cases). Interventricular (VV) timing left nominal 5 ms, unless no signs of biventricular stimulation in the body surface ECG were observed. VV was changed then to elicit the picture of QRS fusion beats in ECG lead V1 (7 cases) as in the study of Bailey et al. [9]. Such a VV-delay optimization was there proven to correlate better with maximum rate of rise of left ventricular pressure (dp/dt_{max}) than the strategy to obtain the narrowest paced QRS complexes [9].

In patients with permanent AF, ventricles' rate control with beta-blockers and digoxin was assessed. In one patient, an unsatisfactory pharmacological effect (< 95% of biventricular stimulation) was observed and an ablation of AV junction was performed. The follow-up was prolonged over three months after the ablation.

Response to CRT criterion

Patients with at least a 10% reduction of left ventricular end-systolic volume (LVESV) after three months of follow-up were classified as responders to CRT.

Statistical analysis

Statistical analysis was performed with SAS System 9.1 (SAS Institute Inc., Cary, North Carolina, USA) by the Student's t-test, Fisher's exact test and Chi-square test. The multivariate logistic regression of the association between the magnitude of LVESV reduction and clinical variables was conducted with Proc GLM. Statistical significance was considered when $p < 0.05$.

Results

Clinical characteristics of the study group

In the studied group 61.6% were in sinus rhythm, 16.7% had paroxysmal AF and 21.7% permanent fibrillation. Conduction disorders constituted: left bundle branch block 65.0%, right bundle branch block 1.7%, ventricular conduction disturbances of other morphology 33.3%. The clinical characteristics of the study group are summarized in Tables 1 and 2.

Course of the study

Three patients died during the three-month follow-up: one of a stroke, one of myocardial infarction, and one suddenly at home of unknown cause. These individuals were excluded from further analysis. In the observation period, ten patients were hospitalized, seven of them due to CHF exacerbation. All prescriptions (medications — see Table 2) remained stable through the study.

Effects of CRT

In the whole studied group, LVEF increased (21.7 ± 4.8% *vs* 26.6 ± 4.8%, $p < 0.0001$), 6-MWT distance rose (298.0 ± 107.4 m *vs* 373.1 ± 127.1 m, $p < 0.0001$), and left ventricular end-diastolic volume (LVEDV) and LVESV decreased (244.3 ± ± 83.8 mL *vs* 226.4 ± 88.6 mL, $p = 0.0002$; 192.8 ± ± 71.9 mL *vs* 168.7 ± 76.5 mL, $p < 0.0001$, respectively). Mean NYHA class dropped from 3.1 ± 0.27 to 2.2 ± 0.67 ($p < 0.0001$). The results of specialized examinations before and after biventricular stimulation introduction in the studied subgroups of responders (n = 34, 59.7%) and non-responders to CRT (n = 23, 40.3%) are shown in Table 3.

Echocardiographic parameters and clinical end point

There was no difference regarding baseline and follow-up echocardiographic parameters between patients with and without left ventricle reverse remodeling in terms of clinical endpoint i.e. history of hospitalization due to heart failure exacerbation in the observation period.

Multivariate logistic regression model

In the multivariate logistic regression analysis, having considered the parameters discriminating responders from non-responders, the magnitude of LVESV reduction [ml] in the whole study group correlated significantly with body mass index (BMI) ($r^2 = -4.18$, $p < 0.001$), the level of N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP) ($r^2 = -3.28$, $p = 0.002$) and the presence of permanent AF ($r^2 = -2.1$, $p = 0.041$).

Discussion

Clinical and echocardiographic effects of CRT

Clinical trial results (MUSTIC-SR, MIRACLE, MUSTIC-AF, PATH CHF, MIRACLE ICD, CON-

Table 1. Clinical data of the whole study group, and of responder and non-responder subgroups, according to the applied criterion of at least 10% left ventricular end-systolic volume reduction at three-month follow-up (data presented as mean value with standard deviation [SD] or number of patients with the percentage share [%] of the whole analyzed group or subgroup, p — value for comparison between responders and non-responders).

	Whole study population; n = 60	Responders; n = 34	Non-responders; n = 23	P
Age (years)	66.3 (8.7%)	65.8 (8.2%)	67.1 (9.4%)	0.60
Gender — men (%)	57 (95%)	33 (97%)	24 (92%)	0.57
Weight [kg]	74.3 (13.9%)	72.7 (12.4%)	75.6 (16.3%)	0.46
Height [cm]	168.3 (7.7%)	168.3 (7.8%)	168.2 (7.7%)	0.95
BMI [kg/m^2]	26.1 (4.3%)	26.0 (3.0%)	27.0 (5.0%)	0.33
NYHA	3.1 (0.2%)	3.1 (0.3%)	3.1 (0.2%)	0.91
Ischemic etiology of CHF	43 (71%)	21 (62%)	22 (84%)	0.04
History of myocardial infarction	38 (63.3%)	20 (59%)	18 (69%)	0.43
Permanent atrial fibrillation	13 (22%)	6 (18%)	7 (27%)	0.048
History of hypertension	39 (65%)	17 (50%)	22 (84%)	0.01
Diabetes mellitus type 2	25 (42%)	12 (35%)	13 (50%)	0.30
COPD	11 (18%)	7 (21%)	4 (15%)	0.52
Hypercholesterolemia	46 (76%)	26 (76%)	20 (76%)	0.99
Hyperuricemia	17 (28%)	9 (26%)	8 (31%)	0.56
Anaemia	2 (3%)	2 (6%)	0 (0%)	0.35
Hyponatremia	13 (22%)	9 (26%)	4 (15%)	0.32
Up-grade VVI	2 (3%)	0 (0%)	2 (8%)	0.16
Up-grade DDD	9 (15%)	6 (17%)	3 (11%)	0.47
Up-grade DDD-ICD	3 (5%)	2 (6%)	1 (3%)	0.64
CRT-D	18 (30%)	11 (32%)	7 (27%)	0.56

BMI — body mass index; CHF — chronic heart failure; COPD — chronic obstructive pulmonary disease; CRT-D — cardiac resynchronization therapy with defibrillator function; DDD — dual chamber pacemaker; DDD-ICD – dual chamber implantable cardioverter-defibrillator; NYHA — New York Heart Association functional classification; VVI — right ventricular pacemaker

Table 2. Clinical data and drug medication of the whole study group, and of responder and non--responder subgroups, according to the applied criterion of at least 10% left ventricular end-systolic volume reduction at three-month follow-up (data presented as mean value ± standard deviation [SD] or number of patients with the percentage share [%] of the whole analyzed group or subgroup, p — value for comparison between responders and non-responders).

	Study group; n = 60	Responders; n = 34	Non-responders; n = 23	P
History of stroke	4 (6.7%)	3 (9%)	1 (3%)	0.62
Chronic renal disease	20 (33.3%)	8 (23%)	12 (46%)	0.09
Smoking	9 (15%)	6 (17%)	3 (11%)	0.71
History of smoking	14 (23.3%)	9 (26%)	5 (19%)	0.55
Hypotension	4 (7%)	0 (0%)	4 (15%)	0.02
History of hospitalization for CHF	50 (83%)	28 (82%)	20 (77%)	0.74
History of cardiac arrest	4 (7%)	2 (6%)	2 (8%)	0.53
Pulmonary rales	21 (35%)	10 (29%)	11 (42%)	0.13
Complex ventricular arrhythmias	18 (30%)	11 (32%)	7 (27%)	0.56
Q waves in an electrocardiogram	17 (28%)	10 (29%)	7 (27%)	0.58
Enlarged right ventricle	33 (55%)	18 (53%)	15 (58%)	0.64
Pulmonary hypertension	28 (47%)	16 (47%)	12 (46%)	0.79
Restrictive mitral filling pattern	13 (22%)	9 (26%)	4 (15%)	0.73
Medication: ACEI/ARB	51 (85%)	30 (88%)	21 (81%)	0.48
Beta-blocker	58 (96.7%)	33 (97%)	25 (96%)	0.99
Loop diuretic	53 (88.3%)	28 (82%)	25 (96%)	0.12
Potassium-sparing diuretic	40 (66.7%)	25 (73%)	15 (58%)	0.27
Digoxin	13 (21.7%)	8 (23%)	5 (19%)	0.76
Amiodarone	18 (30%)	9 (26%)	9 (35%)	0.39

ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin II receptor blocker; CHF — chronic heart failure

Table 3. Specialized examination results of responders and non-responders according to the applied criterion of at least 10% left ventricular end-systolic volume reduction at three month follow-up. Each parameter presented as arithmetic mean with standard deviation (SD); p — for the difference between initial and three months follow-up values of the same parameter; #p < 0.05 — for the difference between initial parameters of responders and non-responders; *p< 0.05 — for the difference between parameters of responders and non-responders measured after three months of follow-up.

	Responders (n = 34, 59.7%)			Non-responders (n = 23, 40.3%)		
	Initially	After three months	P	Initially	After three months	P
LVEDD [mm]	73.2 (7.4)	69.9 (8.3)	< 0.001	73.5 (10.9)	73.9 (11.5)	0.47
LVESD [mm]	62.0 (7.9)	58.1 (9.4)	0.003	63.0 (12.7)	64.2 (13.0)*	0.13
LVEDV [mL]	246.3 (61.1)	209.5 (58.7)	< 0.001	241.3 (110.7)	251.4 (117.6)	0.054
LVESV [mL]	194.5 (55.9)	153.0 (51.4)	< 0.001	190.3 (92)	191.8 (99.9)	0.68
SV [mL]	51.6 (12.8)	56.3 (12.4)	0.002	51.4 (21.3)	59.6 (22.2)	0.002
MR (%)	25.6 (14)	18.4 (11)	0.001	23.7 (11)	24.4 (11)	0.62
QRS [ms]	179 (28)	153 (20)	0.001	199 (27)	152 (17)	0.001
LVEF (%)	21.5 (4.9)	27.1 (4.8)	< 0.001	21.9 (4.7)	24.5 (4.7)*	0.003
6-MWT [m]	315.7 (112.1)	392.3 (109.5)	< 0.001	271.9 (96)	344.7 (147.4)	0.001
NYHA	3.1 (0.3)	2.1 (0.5)	< 0.001	3.1 (0.2)	2.5 (0.8)	0.001
NT-proBNP [pg/mL]	2005.6 (1632)	1512.0 (1148)	0.012	3150.5 (2034)#	2509.5 (1403)*	0.32
SPWMD [ms]	98.9 (36)	99.2 (56)	0.86	85.5 (60.1)	62.2 (57)	0.79
IVMD [ms]	58.8 (25)	46.6 (22)	0.047	57.8 (26)	35.6 (30)	0.037
VV-sep. [cm]		8.1 (2.9)			8.9 (2.3)	

6-MWT — 6-minute walk test distance; IVMD — interventricular mechanical delay; LVEDD — left ventricular end-diastolic diameter; LVEDV — left ventricular end-diastolic volume; LVEF — left ventricular ejection fraction; LVESD — left ventricular end-systolic diameter; LVESV — left ventricular end-systolic volume; MR — mitral regurgitation presented as percentage of left atrium area; NT-proBNP — N-terminal pro-B-type natriuretic peptide; NYHA — New York Heart Association functional classification; SPWMD — septal to posterior wall motion delay; SV — stroke volume; VV-sep. — right and left ventricular electrodes tips' separation on sagittal chest X-ray

TAK CD, MIRACLE ICD II, COMPANION, CARE HF) show that CRT leads to reduction in NYHA class by 0.5–0.8 points and improves physical capacity estimated via 6-MWT distance by 20% [5]. The effects of CRT regarding those parameters were similar in our study. Also, the reduction of LVESV rate as a sign of reversal of left ventricle remodeling is similar to values met in the literature. In the PROSPECT study, a more pronounced decrease of LVESV (≥ 15%) as an end point was noted in 56.3% of participants, but the follow-up was longer: up to six months [10].

Rationale for response to CRT criterion choice

Despite the subjectivity of clinical and echocardiographic assessment and multiplicity of response to CRT criteria, cardiac resynchronization therapy is an efficient treatment for advanced CHF [11, 12]. Among the factors offering a positive long-term prognosis in patients undergoing CRT, the presence of left ventricle reverse remodeling observed a few months after CRT introduction with at least 10% LVESV reduction, is the best marker [13, 14].

Conditions of poor prognosis in CHF

Taking into account the effects of CRT, it should be emphasized that decreased morbidity and mortality related to CHF, and improved physical capacity and quality of life observed in patients following biventricular heart stimulator implantation are conditioned by numerous factors such as age, concomitant diseases, BMI, physical activity, and compliance. CRT is only a part of a complex CHF treatment [1]. Some researchers also claim that a huge proportion of this phenomenon can be attributed to the placebo effect [15]. Numerous prognostic factors of CRT failure have been identified in the literature including: NYHA IV class; left ventricle dilatation (LVEDD > 65–70 mm); low LVEF (< 30%); the presence of scar tissue in the myocardium; suboptimal left ventricular lead position; valvular defects with advanced mitral insufficiency; inadequate ventricles' rate control in patients with permanent AF without AV junction ablation; lack of initial mechanical dyssynchrony; ineffective biventricular stimulation; unsuitable stimulator settings of AV and VV delay [1, 2, 5, 16]. It is worth noting that the optimal dyssynchrony assessment, left ven-

tricular lead positioning and device programming, despite a good deal of investigation being done into the issues, have yet to be elaborated.

In our study, ischemic etiology of CHF, permanent AF, higher prevalence of hypertension and hypotension and higher NT-proBNP concentrations were observed in the group without ≥ 10% LVESV reduction in the follow-up. Negative effects of NT-proBNP, BMI and the presence of permanent AF on the magnitude of LVESV reduction following CRT introduction were found in the multivariate logistic regression model.

In the MIRACLE study, LVEF rose by less in patients with a non-ischemic CHF background. This has not been confirmed in other trials [17, 18]. Interestingly, it is the presence of scar tissue that is thought to be of major importance here. In the study by Jansen et al. [19] on the role of scar in the heart muscle, 15% of patients with a diagnosed ischemic background of CHF, based on history of CABG, PCI, myocardial infarction and results of the coronarography, did not have features of transmural scar in magnetic resonance imaging (MRI); whereas in 19% of individuals with idiopathic cardiomyopathy, such signs were present. The negative influence of coronary artery disease on the reversal of malfunctional left ventricle remodeling induced by biventricular stimulation seems thus also to involve aspects other than the presence of scar. The course of hypertension is associated with myocardial architecture changes, which might impede CHF left ventricle remodeling regression following CRT introduction [20]. Hypotension is a sign of severe CHF with a heavily damaged heart muscle, an accepted risk factor of poor prognosis. So the fact that all four patients with hypotension were found in the group with no response to CRT came as no surprise [21]. Increased BMI, especially in the obese, is associated with CHF progression, more severe symptoms and worsening of well-being. BMI in our study has affected negatively the reverse remodeling. The results of meta-analysis by Upadhyay et al. on 1,164 CRT recipients, released after the latest ESC guidelines on cardiac pacing and CRT were published, indicate similar echocardiographic and clinical effects of CRT in patients with permanent AF with pharmacological ventricles' rate control *vs* individuals in sinus rhythm. Our findings do not comply with those observations but are in consent with some small trials [22–24].

Echocardiography

In our study, responders did not differ from non-responders in respect of baseline left ventricular end-diastolic and end-systolic diameters and volumes, or the size of mitral regurgitation. Responders presented a decrease in the aforementioned parameters, while non-responders did not show reduced LVEDD, left ventricular end-systolic diameter (LVESD), LVEDV, LVESV or degree of severity of mitral regurgitation. Interestingly, the group with no response to CRT according to the adopted criterion, despite lacking left ventricle reverse remodeling, also gained benefit from the therapy. This might be explained by the fact that clinical and echocardiographic responses to CRT may not always appear simultaneously, and patients who respond clinically may not exhibit reverse remodeling and *vice versa* [11].

Classic echocardiographic-derived dyssynchrony parameters

Two of the simplest parameters of mechanical dyssynchrony deriving from classic echocardiographic examination techniques are septal to posterior wall motion delay (SPWMD) and interventricular mechanical delay (IVMD).

SPWMD (being based on measurements to the peak of systolic wave of heart walls) suffers from error of interaction between active and passive movements of myocardial segments, something emphasized by Marcus et al. [25] in the 79 participants of the CONTAK-CD trial. The PROSPECT study revealed unsatisfactory intra- and interobserver reproducibility of this parameter [10]. ASE does not recommend the use of M-mode as an isolated method of mechanical dyssynchrony appraisal, but indicates that it might provide some accessory information to the results gained with other techniques such as TDI [3].

IVMD, although reproducible and easily calculated in daily practice, has little efficacy in predicting response to CRT as compared to intraventricular dyssynchrony assessment [10]. In our study, both groups presented marked but comparable inter- and intraventricular dyssynchrony assessed with IVMD and SPWMD (normal values proposed by ASE expert consensus statement are for IVMD < 20 ms and for SPWMD < 50 ms) [3]. The index SPWMD was not altered by CRT in responders and non-responders, while biventricular stimulation significantly improved IVMD.

Biochemical markers of CHF

Results of studies confirm that CRT improving heart function leads to a decrease of B-type natriuretic peptide (BNP) and NT-proBNP levels. Additionally, patients with persistently high concen-

trations after CRT introduction have higher all-cause mortality in the long-term observation (data from CARE-HF study on 813 individuals with mean 37.6 months follow-up and NT-proBNP assessment three months after CRT implantation) [26–28]. In our study, individuals without left ventricle reverse remodeling had a higher concentration of NT-proBNP initially and after the given follow-up period. NT-proBNP decreased only in patients with reverse remodeling, and its baseline level correlated negatively with the magnitude of LVESV reduction when the whole study group was considered. This suggests that left ventricle reverse remodeling is associated with an improvement in the biochemical parameters of CHF.

QRS complex duration

In most papers, QRS complex width did not carry prognostic value of variously defined response to CRT. QRS duration would not differ initially and after certain periods of the follow-up between groups with and without response to CRT [29, 30]. In our study, baseline QRS width diminished but we observed no difference between initial and final values of the analyzed groups.

Conclusions

Classic echocardiographic data do not predict left ventricle reverse remodeling. Significantly higher prevalence of hypertension and permanent AF and higher NT-proBNP concentration were found in the group without at least 10% LVESV reduction in the three-month follow-up. NT-proBNP, BMI and the presence of permanent AF had negative effects on the magnitude of LVESV reduction following CRT introduction.

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