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The relationship of regional longitudinal strain changes and response to cardiac resynchronization therapy in patients with left ventricular systolic dysfunction and left bundle branch block

Związek zmian regionalnego odkształcenia podłużnego miokardium z odpowiedzią na terapię resynchronizującą serca u pacjentów z dysfunkcją skurczową lewej komory i blokiem lewej odnogi pęczka Hisa

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Abstract

Introduction. Strain and strain rate (SR) are techniques, which provide local information on myocardial deformation. The aim of the study was to assess the usefulness of strain and SR measurement in cardiac resynchronization therapy (CRT) response in chronic heart failure (CHF) patients.

Materials and methods. The study included 35 CHF patients with QRS complex duration \geq 120ms with LBBB morphology. Biochemical and clinical parameters were assessed before and after six months of CRT. TTE classical and tissue Doppler echocardiography parameters (longitudinal peak systolic strain – LPS and SR for basal segment of intraventricular septum and lateral wall) were evaluated.

Results. Twenty-two patients (62.8%) benefited from CRT (the responders) and revealed improvement in septal and lateral LPS in the 6-month observation [-7.1 (-5.2– -11.1) vs -12.1 (-8.7– -14)%, p = 0.002; - 10.4 (-6.1– -17.6) vs - 13.8 (-8.9 – -17.8)%, p = 0.03; respectively]. Six months after CRT, the responders were characterised by higher increase in septal LPS comparing to the nonresponders (-4.6 \pm 6.1 vs -2.4 \pm 3.9%, p = 0.045). Septal LPS changes correlated positively with baseline cardiopulmonary exercise testing (CPET) parameters: peak oxygen uptake (r = 0.6, p = 0.004), peak carbon dioxide excretion (r = 0.62, p = 0.002) and negatively with VE/VC02 slope (r = -0.5, p = 0.037).

Conclusions. LV regional LPS appears to be a good parameter reflecting the improvement of clinical status in patients treated with CRT. The responders had better improvement of septal LPS, therefore positive response to this therapy may be related to the improvement of septal contractility.

Key words: strain, echocardiography, cardiac resynchronization therapy, chronic heart failure, left bundle branch block

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Introduction

A reliable assessment of myocardial function is crucial for the diagnosis, treatment, and prognosis of cardiovascular diseases. Echocardiography plays an indispensable role in cardiac imaging due to its real-time acquisition and wide availability. Left ventricular ejection fraction (LVEF) is one of the most widely used indicators of left ventricular (LV) heart function. This volume-based assessment of heart function suffers, however, from a lack of reproducibility and standardisation. Furthermore, newer, more sensitive techniques have shown that LV function can be reduced despite a normal LVEF. These two techniques have dominated the research area of echocardiography: 1. Doppler-based tissue velocity measurements, frequently referred to as Doppler Tissue Imaging (DTI), and 2. speckle tracking on the basis of displacement measurements (Two-Dimensional (2D) Speckle-Tracking Echocardiography (STE)). Both types of these currently available techniques allow quantitative assessment of myocardial function. Strain and strain rate (SR) are basic parameters of myocardial function used to assess local wall dynamics and to provide local information on myocardial deformation and may be assessed with the use of echocardiography and, significantly less available, cardiac magnetic resonance imaging [1]. The important advantage of strain and SR is that they reflect regional function independently of translational motion [2]. Little is known about usefulness of those parameters in the evaluation of cardiac resynchronization therapy (CRT) response in patients with chronic heart failure (CHF). The advantage of these techniques over conventional methods of LV systolic function estimation is the opportunity of early detection of myocardial dysfunction undetectable in the standard protocol echocardiography. The assessment of mechanical dyssynchrony in patients treated with or planned for CRT is a recent concept that arose from the clinical need for better patient selection and means of therapy optimisation. Although the concept is mostly accepted among experts despite recent challenges, clinical value of the approach remains to be better defined [2]. Despite promising data, quantitative assessment of the magnitude of regional LV deformation cannot be recommended at this stage because of lack of reference values, suboptimal reproducibility, and considerable inter-vendor measurement variability [3]. On the other hand, observational studies have shown, that longitudinal strain analysis reflects the segmental heterogeneity of myocardial function [4] and that the increase in global longitudinal strain correlates with the degree of LV remodelling [5]. Lim et al. [6] published very promising results derived from algorithms based on longitudinal strain peaks and the relation between peaks and end--systolic values.

In recent years, a significant improvement of CHF patients therapy has been observed and CRT is one of the treatment methods, that may reverse the course of the disease. CRT effectiveness is based on biventricular pacing, that can improve systolic function of the heart by correcting the electromechanical dyssynchrony. That results in an improvement of patients functional capacity, as well as reduction of rehospitalisations and mortality [7]. One of the clinical assessment methods of CHF patients is cardiopulmonary exercise testing (CPET). Among the variety of CPET parameters, peak oxygen uptake (VO2 peak) remains one of the strongest prognostic values [8]. The weak point of CPET is limited availability and dependence of patient's motor skills, therefore echocardiography still plays an important role in the evaluation of those patients and the novel echocardiographic methods for CRT-response evaluation are sought after. Among a variety of parameters reflecting response to the therapy, LVEF remains one of the most commonly used, as well as one of the strongest predictors of long term prognosis. However, LVEF or left ventricle end-systolic (LVEsV) and end-diastolic volumes (LVEdV) do not provide local information on myocardial deformation. Despite prognostic properties of the regional contractility assessment, that have been confirmed by Donal et al. [9], there is no clear evidence on the use of this method in the evaluation of patients treated with CRT.

The aim of the study was: 1) to compare classical and new echocardiographic parameters — peak systolic longitudinal strain (LPS) and SR — in the assessment of LV function before and six months after CRT implantation in CHF patients, 2) to assess the value of LPS measurement usefulness in clinical and biochemical response to CRT, and 3) to determine whether they differ between CRT responders and nonresponders and may be a potential tool for postoperative optimisation of CRT.

Materials and methods

The study group

The study included 35 consecutive patients with stable, optimally pharmacologically treated CHF with LVEF lower than 35% assessed in echocardiography, who were hospitalised at the Cardiology Department from 2011 to 2014. The aetiology of heart failure included dilated (13 cases) or ischaemic cardiomyopathy (22 cases). All of these patients had sinus rhythm in ECG, QRS complex duration >120 ms and left bundle branch block (LBBB) and further underwent the procedure of CRT device implantation with the best possible location of left-ventricular electrode. The localisation of left-ventricular electrode in Table 1.

All the patients underwent the same diagnostic assessment: medical interview with the assessment of NYHA functional class, physical examination, transthoracic echocardiography (TTE), CPET, six-minute walk test (6MWT) and venous blood tests. Those measurements were obtained before implantation of CRT device and after six months

Table 1. The localization of left-ventricular electrode in patients,who benefited (the responders) and who did not benefit fromcardiac resynchronization therapy (the responders and the non-responders, respectively)

	Responders (n = 22)	Nonresponders (n = 13)
Lateral vein, % (n)	48.6 (17)	14.3 (5)
Antero-lateral vein, % (n)	17.1 (6)	2.8 (1)
Postero-lateral vein, % (n)	2.8 (1)	2.8 (1)
Great vein, % (n)	0	5.7 (2)
Posterior vein, % (n)	0	5.7 (2)

of resynchronization therapy. Patients with moderate to severe chronic lung disease were excluded from the study.

Venous blood samples were analysed for B-type natriuretic peptide (BNP), C-reactive protein (CRP), blood count, lipid profile, uric acid and creatinine concentrations in the local laboratory. The positive response to CRT was defined according to previous studies, by the improvement in clinical CHF symptoms (lower NYHA class, longer 6MWT distance) and at least a 15% relative reduction in LVESV in echocardiography, indicating reverse remodelling [10].

Echocardiography

Transthoracic echocardiography was performed with an ultrasound device (Philips iE33) with the use of transthoracic probe working with harmonic imaging within the frequency range of 1.6-3.2 MHz. Standard techniques were used to obtain M-mode, 2D and Doppler measurements in accordance with the American Society of Echocardiography and the European Association of Cardiovascular Imaging guidelines [3]. Conventional echocardiographic LV end-diastolic dimensions (interventricular septum wall thickness, LV internal dimension and LV posterior wall thickness) were obtained from the parasternal long-axis view. LVEdV and LVEsV volumes and LVEF were measured manually using the biplane Simpson's method in the 2D mode. We have adopted LVEF <50% as an abnormal LV systolic function. A decrease in LVend-systolic volume of ≥15% of the baseline value, as measured by echocardiography six months after the device implantation, was used to define a CRT responder.

Strain analysis

Echocardiographic quantification of regional myocardial function is currently based on DTI or STE techniques. Both techniques provide comparable data quality, although DTI is known to be angle-dependent and slightly more time-consuming analysis [3]. The most commonly used strain-based measure of LV global systolic function is global longitudinal strain (GLS) [11].

In our study, we used DTI technique to evaluate myocardial deformation and those data were expressed as strain and strain rate. We assessed peak longitudinal strain during LV systole, which is the most commonly used deformation parameter. DTI acquisition was performed according to the American Society of Echocardiography and the European Association of Echocardiography guidelines. Apical four-chamber views in 2D greyscale and tissue colour Doppler imaging (at a frame rate about 140 frames/sec) were acquired in all the patients. Only echocardiograms with an optimal frame rate over 100 per second were analysed.

All images was transferred to an Excelera (Philips external workstation) for further processing. The data were analysed off-line by two independent investigators using the following parameters: longitudinal strain and strain rate.

From the colour-coded images of tissue Doppler, each observer measured strain and strain rate using a specific region of interest (ROI), with the same size of ROI in every measurement, that was manually positioned along the basal inferoseptal and basal anterolateral segments. The 17-segment model of LV was used in our study. The analysis of deformation included maximum strain values, that were read out in the time interval between aortic valve opening (AVO) and aortic valve closure (AVC). Each time during echocardiography AVO and AVC values were measured and reported in milliseconds (ms), than these data were entered into the Excelera system.

Cardiopulmonary exercise testing

CPET was performed using symptoms limited treadmill exercise test with RAMP protocol. The electrocardiogram was continuously monitored for the heart rate, occurrence of ST segment changes or arrhythmias. Of the numerous parameters, peak oxygen uptake (peak VO₂), peak carbon dioxide exertion (peak VCO₂) and percent (%) of predicted and the slope of the VE/VCO2 relationship from the initiation to peak exercise (VE/VCO2 slope) were used for the analysis [12].

The study is complied with the Declaration of Helsinki and was approved by the institutional medical ethics committee. Informed consent was obtained from all the individual participants included in the study.

Statistical analysis

The distribution of all variables was verified with Kolmogorov-Smirnov test. Data are expressed as mean ± standard deviation (SD) or median values with interquartile range (IQR) as appropriate. Statistical analysis was performed using Student's t-test or Mann–Whitney U test for continuous data depending on distribution. Adequately Pearson's or Spearman's correlation coefficient were used

Table 2. Characteristics of CHF patients treated with CRT at baseline and six month follow-up.

	CRT group Baseline	CRT group 6M follow-up	P value
Patients, No.	35	35	
Age (years)	66.2 ± 9.5	66.9 ± 10.6	
Female sex, % (n)	11.5 (4)	11.5 (4)	
BMI (kg/m²)	28.4 ± 4	28.9 ± 4.8	0.2
QRS duration (ms)	162.8 ± 33.8	145.2 ± 33.7	0.01
Functional parameters			
NYHA functional class, % (n)	2.8 ± 0.4	2.4 ± 0.45	< 0.001
6MWD (m)	380 (240-435)	420 (350-480)	< 0.001
Peak VO2 (ml/kg/min)	13.7 (11.8-17.6)	15.2 (11.6-20.2)	0.8
Peak VCO2 (I/min)	1.2 (0.8-1.44)	1.32 (0.7-1.85)	0.7
VE/VCO2 slope	32.5 (27.5-37.7)	29.9 (25.3-35.6)	0.02
Echocardiography			
EF bi-p (%)	22 (20-25)	33 (25-37)	< 0.001
LVDD (mm)	6.6 (6.2-7.2)	6.5 (5.8-7.2)	0.1
LVEDV (ml)	209 (175-284)	180 (129-213)	0.06
LVESV (ml)	166 (132-225)	126 (90-152)	0.02
Septal strain (%)	-7.8 (-5.311.5)	-12.1 (-8.714)	< 0.001
Septal strain rate (1/s)	1.2 (0.7-1.2)	1.47 (0.95-1.75)	0.006
Lateral strain (%)	-9.4 (-5.514.8)	-12.7 (-7.917.2)	0.006
Lateral strain rate (1/s)	1.1 (0.87-1.6)	1.25 (1-1.95)	0.05
Laboratory analyses			
BNP (pg/ml)	220 (90-705)	145 (59-374)	0.24
CRP (mg/dl)	2.15 (0.95-4)	1.6 (1-3.6)	0.21

Abbreviations: 6M follow-up – heart failure patients after six months of cardiac resynchronization therapy; 6MWD – six-minute walk test distance; BMI – body mass index; BNP – brain natriuretic peptide; CRP – C-reactive protein; EF bi-p – ejection fraction estimated with bi-plane method; LVDD – left ventricle diastolic diameter; LVEDV – left ventricle end-diastolic volume; LVESV – left ventricle end-systolic volume; Peak VC0₂ – peak carbon dioxide excretion; Peak V0₂ – peak oxygen uptake; VE/VC02 slope, minute ventilation – carbon dioxide production relationship from the initiation to peak exercise. Data are presented as mean ± standard deviation, median and interquartile range (IQR) or number and percentage.

to examine the relationship between two continuous variables. P < 0.05 was considered as statistically significant. A statistical software package Statistica 10.0 (StatSoft USA) was used for analysis.

Reproducibility analysis

Intra- and inter-observer variability of strain measurements were evaluated. To test intra-observer variability, the same primary operator analysed data sets twice at least two weeks apart. The operator was blinded to the result of the previous measurements during second evaluation. To test inter-observer variability, a second experienced observer was given data sets with no access to information regarding all prior measurements. Intra- and inter-observer variability was calculated as an absolute difference between two measurements over the mean of those measurements and presented as the mean percentage error. Intra-observer variability for strain parameters was estimated at 10%, and for inter-observer variability – 12.9%.

Ethical approval

The study was approved by the institutional medical ethics committee and is complied with the Declaration of Helsinki (1964). Informed consent was obtained from all the individual study participants.

Results

Baseline characteristics of the study group is presented in Table 2.

Six months after CRT CHF patients had a significant improvement in NYHA functional class, longer 6-MWT distance and decreased VE/VCO2 slope ratio (Table 2). According to functional parameters, the nonresponders had worse results comparing to the responders – shorter 6MWT distance, lower peak VO2 and peak VCO2 and higher VE/VCO2 slope (Table 3). BNP concentration was significantly lower in the responders six months after CRT (Table 3).

Table 3. Characteristics of CHF patients at baseline and six month follow-up qualified as the responders or the nonresponders depending
on the response to resynchronization therapy.

	Nonresponders baseline	Nonresponders 6M follow-up	P value	Responders baseline	Responders 6M follow-up	P value
Patients, No.	13	13	-	22	22	-
Age (years)	66.3 ± 9.8	66.7 ± 9.7	-	65.5 ± 9.6	65.9 ± 9.6	-
Female sex, % (n)	7.7 (1)	7.7 (1)	-	13.6 (3)	13.6 (3)	-
BMI (kg/m²)	28.2 ± 3	28.8 ± 4.8	0.8	28.5 ± 4.6	28.1 ± 3.8	0.8
QRS duration (ms)	172.3 ± 26.5	163.7 ± 31.5	0.3	163.3 ± 23.7	141 ± 21.4	0.02
Functional parameters						
NYHA functional class, % (n)	2.9 ± 0.3	2.6 ± 0.4	0.03	2.8 ± 0.5	2.29 ± 0.44	< 0.001
6MWD (m)	240 (103-380)	300 (105-450)	0.01	390 (320-460)	420 (345-480)	0.005
Peak VO2 (ml/kg/min)	12 (10.8-12.2)	13.6 (8.2-16.1)	0.7	15.3 (12.1-17)	17.6 (12.1-0.5)	0.5
Peak VCO2 (I/min)	0.96 (0.87-1.1)	1.2 (0.6-1.4)	0.8	1.2 (0.8-1.5)	1.7 (0.8-2)	0.8
VE/VCO2 slope	42.3 (36.7-50.9)	34.9 (27.3-37.7)	0.2	31.3 (26.5-35.1)	29.1 (25.2-35)	0.2
Echocardiography						
EF bi-p (%)	21 (20-22)	26 (20-33)	0.01	22 (20-26)	36 (32-39)	< 0.001
LVDD (mm)	7.2 (6.2–7.6)	7 (6.5–7.4)	0.7	6.6 (6.2-6.6)	6.1 (5.7-6.6)	< 0.001
LVEDV (ml)	284 (202-298)	250 (183-296)	0.3	195 (170-237)	145 (115–187)	< 0.001
LVESV (ml)	211 (158-249)	167 (136-251)	0.1	156 (121-193)	96 (84-129)	< 0.001
Septal strain (%)	-9.1 (-7.511.5)	-12.1 (-8.813)	0.04	-7.1 (-5.211.1)	-12.1 (-8.714)	0.002
Septal strain rate (1/s)	1.25 (1-1.7)	1.5 (1.1-1.8)	0.6	0.9 (0.6-1.4)	1.4 (0.9-1.7)	0.003
Lateral strain (%)	-9.4 (-5.510.5)	-12.1 (-6 17)	0.09	-10.4 (-6.117.6)	-13.8 (-8.917.8)	0.03
Lateral strain rate (1/s)	1.05 (0.75-1.45)	1.1 (1-1.3)	0.3	1.2 (1-2)	1.3 (1-2)	0.1
Laboratory analyses						
BNP (pg/ml)	727 (240-1409)	425 (190-548)	0.6	128 (85-297)	102 (36-166)	0.4
CRP (mg/dl)	2.4 (1-4.1)	1.8 (1.1-4.3)	0.3	1.9 (0.9–3.9)	1.4 (0.9–3.6)	0.3

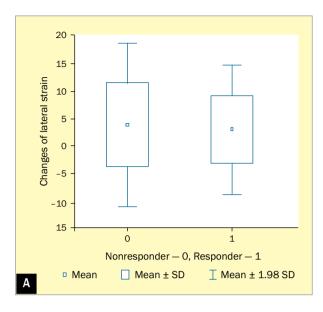
Abbreviations: 6M follow-up – heart failure patients after six months of cardiac resynchronization therapy; 6MWD – six-minute walk test distance; BMI – body mass index; BNP – brain natriuretic peptide; CRP – C-reactive protein; EF bi-p – ejection fraction estimated with bi-plane method; LVDD – left ventricle diastolic diameter; LVEDV – left ventricle end-diastolic volume; LVESV – left ventricle end-systolic volume; Peak VC02 – peak carbon dioxide excretion; Peak V02 – peak oxygen uptake; VE/VC02 slope, minute ventilation – carbon dioxide production relationship from the initiation to peak exercise. Data are presented as mean ± standard deviation, median and interquartile range (IQR) or number and percentage.

Twenty-two patients (62.8%) were the responders. There was no difference in CHF aetiology (dilated or ischaemic cardiomyopathy) between the responders and the nonresponders. There was no significant difference in baseline septal and lateral LPS measurements between the responders and the nonresponders. The baseline lateral LPS correlated with EF (r = 0.48, p = 0.01) i LVESV (r = -0.39, p = 0.035), while septal LPS correlated with intraventricular dyssynchrony (r = 0.38, p = 0.02).

In the responders group, 6-months after CRT implantation, we observed significant improvement in septal and lateral LPS values (Table 3). However, the responders were characterised by higher increase in septal LPS six months after CRT comparing to the nonresponders (-4.6 ± 6.1 vs $-2.4 \pm 3.9\%$ respectively, p = 0.045) (Figure 1A). It was reflected in the improvement in NYHA functional class $(2.8 \pm 0.4 \text{ vs } 2.3 \pm 0.4; \text{ p} < 0.001)$. Changes in septal LPS correlated positively with baseline CPET parameters, such as peak oxygen uptake (VO2 peak) (r = 0.6, p = 0.004) (Figure 2a), peak carbon dioxide production (VCO2 peak) (r = 0.62, p = 0.002) (Figure 2B) and negatively with ventilation/carbon dioxide production relation (VE/VCO2slope) (r = -0.5, p = 0.037) (Figure 2C).

The improvement in lateral LPS was observed in both groups without significant difference ($-3.0 \pm 6.0 \text{ vs} - 3.8 \pm 7.6\%$, p = 0.72) (Figure 1B). Also septal and lateral SR changes in the CRT course did not differ between those groups.

Furthermore, six months after CRT, we observed significant decrease in LVEdV and LVEsV in the responders (Table 3), while in the nonresponders group those parameters were higher at baseline and remained unchanged (Table 3).



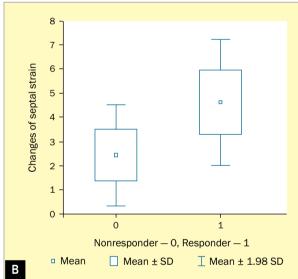


Figure 1. Changes of septal (Figure 1a) and lateral (Figure 1b) longitudinal peak strain (LPS) values in the nonresponders and the responders (six months follow-up measurement minus basic measurement).

Discussion

Overall, the response rate to CRT is still not optimal and the cause of this phenomenon is multifactorial. Beyond the influence of CRT, the clinical response is also mediated by e.g. pharmacotherapy, comorbidities and inflammatory activation [13]. This is particularly evident in the case of patients, who, despite the lack of a positive response to CRT in echocardiographic assessment demonstrate improved functional parameters, such as the 6MWD or VO2 peak. This phenomenon was also observed in our study.

An observational multicenter study (Predictors of Response to CRT) reported on the limited role of velocity

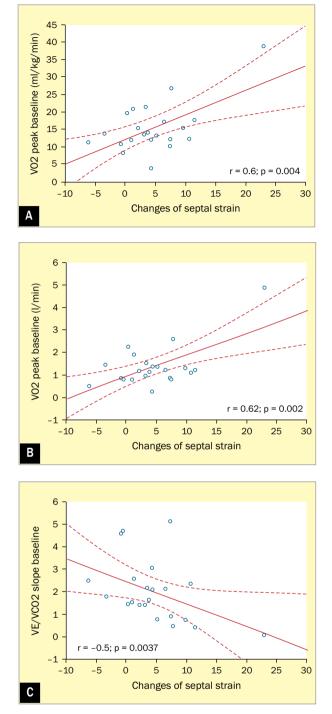


Figure 2. Correlations between changes of septal longitudinal peak strain (LPS) values in the nonresponders and the responders (six months follow-up measurement minus basic measurement) and: the baseline peak oxygen uptake, the baseline peak carbon dioxide exertion, the baseline slope of VE/VCO2 relationship from the initiation to peak exercise

dyssynchrony measurements by colour DTI in predicting the response to CRT. However, the study had several important limitations, including the enrollment of patients who did not meet criteria for CRT (20% of patients with EF>35%), overall low feasibility and reproducibility of DTI measurements, and using ultrasound systems and software from different vendors, including systems that had lower temporal resolution than the time intervals to be measured [14]. Currently, for patients with QRS durations < 120 msec, the existing data do not support using DTI or M-mode measurements for the selection of patients for CRT [15]. On the other hand, a recent single-centre study showed, that radial dyssynchrony assessed by STE can be of value in predicting changes in LV volumes and EF after CRT in patients with QRS durations of 100 to 130 msec [16]. Another recent study showed, that the combination of timing and magnitude of longitudinal strain could predict the response to resynchronization [17].

In our study, the baseline septal and lateral LPS did not differ between the responders and the nonresponders. Bernard A. et al. [18] also showed, that the responders and the nonresponders had similar baseline values of regional peak strain, while the other investigators observed significantly higher baseline values longitudinal strain in the CRT responders [19].

In our study we observed significant improvement in values of septal and lateral LPS, as well as decrease in LVEdV and LVEsV in the responders after six months of CRT. Furthermore, our analyses of septal and lateral strain curves showed significant improvements in septal strain during systole in the responders patients with LBBB, that is consistent with other analysis [20]. We showed only slight improvement of lateral wall contractility in both groups of patients. In another studies, at follow-up, significant improvements of midlateral LPS were noted only in the responders, whereas a decrease of LPS was observed in the nonresponders [18].

Kang Y et al. [21] observed, that longitudinal strain and LBBB combined with a wide QRS can help to predict positive response to CRT effectively and reliably. In another study, none of the longitudinal strain indices was different between echocardiographic responders and nonresponders to CRT [22]. Similarly, Maffè et al. [23] on univariate and multivariate analysis showed, that only interventricular mechanical delay (IVMD), not longitudinal strain, was significantly associated with a complete echocardiographic response to CRT. In our study, the baseline septal and lateral LPS did not differ between the responders and the nonresponders and therefore this measurements are not relevant in predicting CRT-related improvement.

In our study, LPS values correlated well with EF, which is consistent with investigations of other authors [24].

This study showed, for the first time, the strong correlation of strain measurements and CPET parameters reflecting cardiopulmonary functional capacity, such as peak oxygen consumption or VE/VCO2 slope. This is important finding, because it has been shown, that peak VO₂, as well as VE/VCO₂ slope are important markers of prognostic values [25]. In our study, the changes of septal LPS in the course of CRT correlated with CPET oxygen and carbon dioxide exchange parameters at baseline, while after six months those observations were significant for measurements at anaerobic threshold. This fact highlights, that the most relevant information of patients clinical status is given by the anaerobic threshold level and the accompanying efficiency of the gas exchange. These correlations were not observed in classical echocardiographic parameters, therefore septal LPS appears to be a better marker of clinical capacity improvement comparing to e.g. LVEF.

Conclusions

LV regional LPS appears to be a good parameter in reflecting the improvement of clinical status in patients treated with CRT. Patients, who benefited from CRT had better improvement of septal LPS, therefore positive response to this therapy may be related to the improvement of septal contractility.

Limitations

Combined assessment of baseline longitudinal strain and its acute reduction after CRT may have clinical implications for predicting the responders, and thus patients' care. Although our findings are promising, literature data are divergent. A limitation of the study is the lack of echocardiographic measurements directly after the device implantation. Further, our study was based on relatively small number of selected, optimally treated stable CHF patients, therefore this group may be not representative of whole CHF patients.

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Conflicts of interest

The Authors declare no conflict of interest.

Streszczenie

Wstęp. Odkształcenie miokardium i tempo tego odkształcania (strain i SR, strain rate) to metody w tkankowej echokardiografii doplerowskiej wnoszące informacje o regionalnej kurczliwości mieśnia. Celem badania była ocena przydatności pomiarów strain i SR w ocenie odpowiedzi na terapię resynchronizującą (CRT) u chorych z przewlekłą niewydolnością serca (CHF).

Materiał i metody. Do badania włączono 35 pacjentów z CHF i czasem trwania zespołów QRS ≥ 120 ms i morfologią LBBB. Parametry biochemiczne i kliniczne były oceniane przed implantacją i 6 miesięcy po wszczepieniu CRT. Analizie poddano wybrane parametry z badania echokardiograficznego przezklatkowego i metodą Dopplera tkankowego – odkształcenie podłużne miokardium na szczycie skurczu – (LPS, *longitudinal peak systolic strain*) i tempo odkształcania (SR, *strain rate*) mierzone dla segmentu przypodstawnego przegrody międzykomorowej i ściany bocznej lewej komory.

Wyniki. Dwudziestu dwóch pacjentów (62,8%) odniosło korzyść z CRT i wykazało poprawę w zakresie wartości przegrodowego i bocznego LPS w obserwacji 6-miesięcznej [odpowiednio: -7,1 (-5,2- -11,1) vs – 12,1 (-8,7- -14)%, p = 0,002; -10,4 (-6,1- -17,6) vs –13,8 (-8,9- -17,8)%, p = 0,03]. Osoby odnoszące korzyść z CRT po 6 miesiącach wykazywały większy wzrost przegrodowego LPS w stosunku do nonresponderów (-4,6 ± 6,1 vs -2,4 ± 3,9%, p = 0 045). Zmiany LPS w obrębie przegrody pozytywnie korelowały z wyjściowymi parametrami uzyskanymi w badaniu ergospirometrycznym: szczytowym pochłanianiem tlenu (r = 0,6, p = 0,004), szczytowym wydalaniem dwutlenku węgla (r = 0 62, p = 0 002) oraz negatywnie z VE/VC02 slope (r = -0,5, p = 0,037).

Wnioski. Regionalne odkształcenie podłużne wybranych segmentów lewej komory jest parametrem odzwierciedlającym poprawę stanu klinicznego pacjentów leczonych terapią resynchronizującą. Chorzy odnoszący korzyść z terapii resynchronizującej wykazują lepszą poprawę przegrodowego LPS, w związku z czym pozytywna odpowiedź na terapię może mieć związek z poprawą kurczliwości w obrębie przegrody międzykomorowej.

Słowa kluczowe: odkształcenie miokardium, echokardiografia, terapia resynchronizująca serca, przewlekła niewydolność serca, blok lewej odnogi pęczka Hisa

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References

- Buckert D, Tibi R, Cieslik M, et al. Myocardial strain characteristics and outcomes after transcatheter aortic valve replacement. Cardiol J. 2018; 25(2): 203–212, doi: 10.5603/CJ.a2017.0121, indexed in Pubmed: 29064540.
- Mor-Avi V, Lang RM, Badano LP, et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. J Am Soc Echocardiogr. 2011; 24(3): 277–313, doi: 10.1016/j. echo.2011.01.015, indexed in Pubmed: 21338865.
- Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015; 28(1): 1–39.e14, doi: 10.1016/j.echo.2014.10.003, indexed in Pubmed: 25559473.
- Klimusina J, De Boeck BW, Leenders GEH, et al. Redistribution of left ventricular strain by cardiac resynchronization therapy in heart failure patients. Eur J Heart Fail. 2011; 13(2): 186–194, doi: 10.1093/eurjhf/hfq197, indexed in Pubmed: 21106543.
- Delgado V, Ypenburg C, Zhang Q, et al. Changes in global left ventricular function by multidirectional strain assessment in heart failure patients undergoing cardiac resynchronization therapy. J Am Soc Echocardiogr. 2009; 22(6): 688–694, doi: 10.1016/j.echo.2009.04.008, indexed in Pubmed: 19501328.

- Lim P, Donal E, Lafitte S, et al. Multicentre study using strain delay index for predicting response to cardiac resynchronization therapy (MUSIC study). Eur J Heart Fail. 2011; 13(9): 984–991, doi: 10.1093/ /eurjhf/hfr073, indexed in Pubmed: 21810831.
- Anand IS, Carson P, Galle E, et al. Cardiac resynchronization therapy reduces the risk of hospitalizations in patients with advanced heart failure: results from the Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) trial. Circulation. 2009; 119(7): 969–977, doi: 10.1161/CIRCULATIONAHA.108.793273, indexed in Pubmed: 19204305.
- Mancini D, LeJemtel T, Aaronson K. Peak VO(2): a simple yet enduring standard. Circulation. 2000; 101(10): 1080–1082, indexed in Pubmed: 10715250.
- Donal E, Coquerel N, Bodi S, et al. Importance of ventricular longitudinal function in chronic heart failure. Eur J Echocardiogr. 2011; 12(8): 619– -627, doi: 10.1093/ejechocard/jer089, indexed in Pubmed: 21727079.
- Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. Circulation. 2008; 117(20): 2608–2616, doi: 10.1161/CIRCULATIONAHA.107.743120, indexed in Pubmed: 18458170.
- Voigt JU, Pedrizzetti G, Lysyansky P, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. Eur Heart J Cardiovasc Imaging. 2015; 16(1): 1–11, doi: 10.1093/ehjci/jeu184, indexed in Pubmed: 25525063.

- Ptaszynska-Kopczynska K, Szpakowicz A, Marcinkiewicz-Siemion M, et al. Interleukin-6 signaling in patients with chronic heart failure treated with cardiac resynchronization therapy. Arch Med Sci. 2017; 13(5): 1069– 1077, doi: 10.5114/aoms.2016.58635, indexed in Pubmed: 28883848.
- Brouwers C, Versteeg H, Meine M, et al. Association between brain natriuretic peptide, markers of inflammation and the objective and subjective response to cardiac resynchronization therapy. Brain Behav Immun. 2014; 40: 211–218, doi: 10.1016/j.bbi.2014.03.017, indexed in Pubmed: 24704567.
- Sanderson JE. Echocardiography for cardiac resynchronization therapy selection: fatally flawed or misjudged? J Am Coll Cardiol. 2009; 53(21): 1960–1964, doi: 10.1016/j.jacc.2008.12.071, indexed in Pubmed: 19460608.
- Beshai JF, Grimm RA, Nagueh SF, et al. RethinQ Study Investigators. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med. 2007; 357(24): 2461–2471, doi: 10.1056/ /NEJMoa0706695, indexed in Pubmed: 17986493.
- Oyenuga O, Hara H, Tanaka H, et al. Usefulness of echocardiographic dyssynchrony in patients with borderline QRS duration to assist with selection for cardiac resynchronization therapy. JACC Cardiovasc Imaging. 2010; 3(2): 132–140, doi: 10.1016/j.jcmg.2009.09.020, indexed in Pubmed: 20159638.
- Lim P, Buakhamsri A, Popovic ZB, et al. Longitudinal strain delay index by speckle tracking imaging: a new marker of response to cardiac resynchronization therapy. Circulation. 2008; 118(11): 1130–1137, doi: 10.1161/CIRCULATIONAHA.107.750190, indexed in Pubmed: 18725491.
- Bernard A, Donal E, Leclercq C, et al. Impact of Cardiac Resynchronization Therapy on Left Ventricular Mechanics: Understanding the Response through a New Quantitative Approach Based on Longitudinal Strain Integrals. J Am Soc Echocardiogr. 2015; 28(6): 700–708, doi: 10.1016/j.echo.2015.02.017, indexed in Pubmed: 25819341.
- Ma CY, Liu S, Yang J, et al. Evaluation of global longitudinal strain of left ventricle and regional longitudinal strain in the region of left

ventricular leads predicts the response to cardiac resynchronization therapy in patients with ischemic heart failure. Cell Biochem Biophys. 2014; 70(1): 143–148, doi: 10.1007/s12013-014-9870-2, indexed in Pubmed: 24619820.

- 20. De S, Popović ZB, Verhaert D, et al. Comparison of left ventricular torsion and strain with biventricular pacing in patients with underlying right bundle branch block versus those with left bundle branch block. Am J Cardiol. 2015; 115(7): 918–923, doi: 10.1016/j.amjcard.2015.01.018, indexed in Pubmed: 25779616.
- Kang Yu, Cheng L, Cui J, et al. A new score system for predicting response to cardiac resynchronization therapy. Cardiol J. 2015; 22(2): 179–187, doi: 10.5603/CJ.a2014.0089, indexed in Pubmed: 25428735.
- Ghani A, Delnoy PP, Adiyaman A, et al. Response to cardiac resynchronization therapy as assessed by time-based speckle tracking imaging. Pacing Clin Electrophysiol. 2015; 38(4): 455–464, doi: 10.1111/ /pace.12589, indexed in Pubmed: 25684239.
- Maffè S, Paffoni P, Dellavesa P, et al. Role of echocardiographic dyssynchrony parameters in predicting response to cardiac resynchronization therapy. J Cardiovasc Med (Hagerstown). 2015; 16(11): 725–735, doi: 10.2459/JCM.00000000000111, indexed in Pubmed: 25004003.
- Altman M, Bergerot C, Aussoleil A, et al. Assessment of left ventricular systolic function by deformation imaging derived from speckle tracking: a comparison between 2D and 3D echo modalities. Eur Heart J Cardiovasc Imaging. 2014; 15(3): 316–323, doi: 10.1093/ehjci/ /jet103, indexed in Pubmed: 24047866.
- 25. Ptaszyńska-Kopczyńska K, Krentowska A, Sawicka E, et al. The strengths and weaknesses of non-invasive parameters obtained by echocardiography and cardiopulmonary exercise testing in comparison with the hemodynamic assessment by the right heart catheterization in patients with pulmonary hypertension. Adv Med Sci. 2017; 62(1): 39–44, doi: 10.1016/j.advms.2016.06.001, indexed in Pubmed: 28187374.