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Relationship between parameters of myocardial electrical remodeling and parameters of contractile function, deformation and myocardium work in patients with chronic heart failure with low left ventricular ejection fraction and atrial fibrillation

Aim To compare electrocardiographic parameters and characteristics of myocardial contractility by echocardiography data in patients with chronic heart failure (CHF) with low left ventricular ejection fraction (LV EF) and atrial fibrillation (AF).

Material and methods The study included 66 patients with CHF and LV EF ≤40%. Electrocardiography was used to assess the QRS complex duration, QRS fragmentation, frontal QRS-T angle (fQRS-Ta), and 3D vectorcardiographic parameters, including the planarity of QRS loop, and the spatial QRS-T angle (sQRS-Ta). Echocardiography assessed LV EF, global longitudinal strain (GLS), global work index (GWI), global constructive work (GCW), global wasted work (GWW), and global work efficiency (GWE).

Results Statistically significant correlations between electrocardiographic parameters and LV EF were not found. The presence of QRS fragmentation was associated with impaired GLS, higher GWW values, and lower GWE. A number of weak but significant correlations was observed: GLS worsened with increasing QRS duration, fQRS-Ta, and sQRS-Ta and decreasing QRS planarity index; GWW increased with increasing QRS duration; GWI, GCW, and GWE decreased as the QRS planarity index decreased. GWI decreased with increasing sQRS-Ta; GCW decreased with increasing fQRS-Ta and sQRS-Ta; GWE decreased with increasing QRS duration, fQRS-Ta and sQRS-Ta.

Conclusion Correlations were found between indicators of myocardial electrical remodeling and parameters of myocardial contractility, strain, and performance in CHF patients with low LV EF and AF. Further study of these parameters may be promising for assessing the severity of changes in myocardial structure and function in patients with various cardiovascular pathologies.

Keywords Chronic heart failure; myocardial performance; QRS fragmentation; QRS-T angle

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Introduction

Chronic heart failure (CHF) is a serious health concern. Echocardiography plays a vital role in both the diagnosis of CHF and the evaluation of its treatment success.

Currently, it became possible during the echocardiography to assess not only the left ventricular ejection fraction (LVEF) but also more complex indicators characterizing the left ventricular (LV) contractile function. Speckle tracking echocardiography (STE) is a new technique.

Global longitudinal strain (GLS) is a sensitive and reproducible parameter estimated by STE and used to assess the LV contractile function during sinus rhythm and atrial fibrillation (AF). It has a high predictive value in patients with CHF. This technique is limited by its dependence on afterload.

To overcome this limitation, a method to measure the efficacy of the LV myocardial performance has been developed that combines GLS analysis with the measurement of the LV cavity pressure (LV pressure-strain loop). LV myocardial strain is evaluated considering the blood pressure measured by sphygmomanometry. This technique enables a comprehensive examination of the LV contractile function in patients with CHF including during various therapies [1].

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Despite wide availability and low cost, electrocardiography is still of limited significance in the diagnosis of CHF. AF is the main electrocardiographic (ECG) abnormality that allows suspecting left ventricular systolic dysfunction [2].

It has been shown in recent years that ECG indicators, such as QRS fragmentation, spatial and frontal QRS-T angles, have predictive value for CHF patients. However, it is unknown what pathogenetic mechanisms lead to abnormal changes in those indicators.

Our objective was to compare ECG indicators with myocardial contractility assessed by echocardiography in CHF patients with reduced LVEF and AF.

Material and methods

The study included 66 patients with CHF and reduced LVEF (≤40%) in combination with AF who were treated at the Myasnikov Institute of Clinical Cardiology of the Academician Chazov National Medical Research Center (Russian Federation). Diagnosis was established in accordance with the guidelines based on the standard clinical examination.

All patients signed the informed consent before being included in the study. The study protocol was approved by the local ethics committee.

Patients with acute myocardial infarction and paced ventricular rhythm were excluded.

All patients received the best-possible drug therapy for CHF in accordance with the current guidelines [3] and had compensated CHF at the time of the examination.

Electrocardiography

Digital 12-lead ECGs were acquired and processed using a PC-based Easy ECG device (Ates Medica, Russian Federation).

The QRS duration (QRSd) was determined based on all leads.

The QRS fragmentation was considered as the presence of one or more additional R (R') waves or a S wave notch at QRSd < 120 msec or the presence of more than two R (R'') waves or more than two S wave notches in two adjacent leads at QRSd ≥120 msec.

The QRS-T frontal angle (fQRS-Ta) was calculated as the absolute difference between the QRS axis and the T axis. When this figure was more than 180°, it was subtracted from 360°.

Synthesized vector cardiograms (VCGs) were automatically calculated using special linear transformations.

Planarity of the spatial QRS loop (P/S) was calculated as the ratio of the area of the projection of the QRS loop onto the plane and the true area of the QRS loop in space. The QRS-T spacial angle (sQRS-T) was calculated as the spacial angle between the QRS and T integral vectors.

Echocardiography

Echocardiogram was performed in the patient's left lateral position using an expert ultrasound scanner (Vivid E9, GE, Norway) and an M5Sc-D matrix transducer. Digital copies of the echocardiogram were saved for offline analysis. Left ventricular end-diastolic (LVEDV) and end-systolic (LVESV) volumes were evaluated; LVEF was determined by the Simpson method (biplane) in 4- and 2 chamber views.

Digital cine loop was recorded from the apical view (at the level of chambers 4, 2 and 3), from the parasternal long-axis view, and the short-axis view at the levels of the mitral valve, papillary muscles, and the LV apex, to assess LV strain in the STE mode. The images were analyzed in 2 D Strain on EchoPac PC workstation (GE Healthcare, USA). The protocol for AF patients included 5 to 8 cycles with mean R-R interval, which made allowed using cycles with approximately the same R-R intervals in the GLS analysis during post-processing.

Myocardial work was assessed by the following indicators: global work index (GWI), – complete work performed by LV from mitral valve closing to opening; global constructive work (GCW) – work to eject blood during systole; global wasted work (GWW) – work that does not contribute to the ejection of blood from the LV cavity; global work efficiency (GWE) – the ratio of constructive work to the sum of constructive and wasted work percentages. Since the work performed by the left ventricle over certain time is defined as the area of the pressure-strain loop, the pressure is measured in mm Hg, and the strain is measured in %, therefore the myocardial work is expressed mm Hg %.

Statistical analysis

Statistical analysis of the data was performed using MedCalc (MedCalc Software BVBA, Belgium). Continuous variables were expressed as the medians and interquartile ranges [Q25; Q75]. Qualitative variables were presented as the absolute and relative values. The Mann – Whitney test was used to estimate the differences between two independent quantitative variables. Spearman's rank correlation analysis was applied to determine the correlation between variables. The level of statistical significance was $p < 0.05$.

Results

Characteristics of the study group are provided in Table 1.

Table 1. Characteristics of the study group

Parameter		Value
Male, n (%)		54 (82)
Age, years		58 [53; 64]
Leading cause of CHF	CAD, PICS, n (%)	28 (43)
	DCM, n (%)	22 (33)
	HHD, n (%)	16 (24)
CHF NYHA class	II, n (%)	31 (47)
	III, n (%)	35 (53)
AF	Paroxysmal, n (%)	38 (58)
	Permanent, n (%)	28 (42)
HR, bpm		70 [60; 84]

Data is presented as a median and interquartile range (Me [Q25; Q75]), the number of patients – n (%); CHF, chronic heart failure; CAD, coronary artery disease; PICS, postinfarction cardiosclerosis; DCM, dilated cardiomyopathy; HHD, hypertensive heart disease; NYHA, New York Heart Association; AF, atrial fibrillation; HR, heart rate.

Table 2. Echocardiography and ECG findings in the study group

Parameter	Value	Normal (according to the literature)
LVEDV, mL	206 [170; 240]	<150 (m), <106 (f) [4]
LVEDVI, mL/m²	98 [80; 119]	<74 (m), <61 (f) [4]
LVESV, mL	130 [105; 165]	<61 (m), <42 (f) [4]
LVESVI, mL/m²	65 [50; 82]	<31 (m), <24 (f) [4]
LVEF, %	34 [30; 39]	>52 (m), >54 (f) [4]
GLS, %	–6 [-8; – 4]	–20 [-21; – 18] [1]
GWI, mm Hg%	488 [357; 668]	1896 [1292; 2505] [1]
GCW, mm Hg%	717 [530; 949]	2232 [1582; 2881] [1]
GWW, mm Hg%	188 [137; 246]	78.5 [53; 122] [1]
GWE, %	76 [70; 81]	96 [94; 97] [1]
QRSd, ms	112 [102; 128]	<124 (m), <114 (f) [5]
fQRS-Ta, °	151 [110; 166]	23.9 ± 24.0 [6]
sQRS-Ta, °	152 [138; 164]	< 117 (m), < 105 (f) [5]
P/S, %	86 [63; 92]	96.8 ± 0.2 [7]

Data is presented as the medians and interquartile ranges (Me [Q25; Q75]) or the means and standard deviation (M ± SD); LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; LVESV, left ventricular end-systolic volume; LVESV, left ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global wasted work; GWE, global work efficiency; QRSd, QRS duration; fQRS-Ta, frontal QRS-T angle, sQRS-Ta, spatial QRS-T angle, P/S, QRS loop planarity index, m, male; f, female.

Table 2 contains the echocardiographic and ECG values obtained in the study group and their normal values available in the literature.

QRS fragmentation was observed in 53 (80%) patients. The presence of QRS fragmentation was associated with higher QRSd values (114 [103; 130] ms and 102 [93; 114] ms, respectively, p=0.02). The indicators of myocardial work in the presence and absence of QRS fragmentation are presented in Table 3.

Several correlations of ECG indicators with LV volumes and LV contractility characteristics were identified. Statistically significant coefficients of the correlation between echocardiographic and ECG findings are presented in Table 4. There were no statistically significant correlations of ECG indicators with LVEF in the studied group, which is likely to be explained by the fact that the included patients had minimal LVEF variations.

Case studies

Case 1

Figure 1shows ECG and VCG of a 43-year-old patient. Diagnosis: Dilated cardiomyopathy Abnormal heart rhythm: permanent AF, normosystole. CHF IIB with reduced LVEF, NYHA class II.

Figure 2shows LVGLS (bovine eye), a pressure-strain loop, and the myocardial work of the same patient.

Case 2

Figure 3shows ECG and VCG of a 68-year-old patient. Diagnosis: Dilated cardiomyopathy Abnormal heart rhythm: permanent AF, normosystole. CHF IIB with reduced LVEF, NYHA class III.

Figure 4shows LVGLS (bovine eye), a pressure-strain loop, and the myocardial work of the same patient.

In the presented cases, the second patient had more severe pathological myocardial electrical remodeling and more significant reduction of LVEF (30%), LVGLS, and myocardial parameters compared, that the first patient (LVEF 37%).

Table 3. Indicators of myocardial work in the presence and absence of QRS fragmentation

Parameter	QRS fragmentation		p
	Yes	No	
GLS, %	-6 [-8; -4]	-8 [-10; -7]	p=0.006
GWI, mm Hg %	451 [345; 633]	592 [502; 789]	p=0.05
GCW, mm Hg %	661 [514; 883]	907 [738; 1011]	p=0.05
GWW, mm Hg %	204 [155; 261]	138 [108; 191]	p=0.01
GWE, %	74 [69; 79]	82 [78; 89]	p=0.002

Data is presented as the medians and interquartile ranges (Me [Q25; Q75]); GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global wasted work; GWE, global work efficiency.

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Table 4. Echocardiography and ECG correlation coefficients

Parameter	QRSd	fQRS-Ta	sQRS-Ta	P/S
Age	0.28 (p=0.02)	0.33 p=0.008	–	–0.27 (p=0.03)
LVEDV	0.32 (p=0.01)	–	0.26 (p=0.037)	–0.26 (p=0.037)
LVEDVI	0.29 (p=0.02)	–	0.31 (p=0.01)	–0.32 (p=0.01)
LVESV	0.34 (p=0.006)	–	0.27 (p=0.028)	–0.32 (p=0.01)
LVESVI	0.31 (p=0.01)	–	0.32 (p=0.01)	–0.35 (p=0.005)
GLS	0.26 (p=0.035)	0.34 (p=0.006)	0.39 (p=0.002)	–0.39 (p=0.002)
GWI	–	–	–0.30 (p=0.016)	0.31 (p=0.01)
GCW	–	–0.26 (p=0.037)	–0.43 (p=0.001)	0.45 (p=0.0001)
GWW	0.34 (p=0.005)	–	–	–
GWE	–0.31 (p=0.01)	–0.37 (p=0.003)	–0.34 (p=0.007)	0.39 (p=0.002)

LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; LVESV, left ventricular end-systolic volume; LVESV, left ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global wasted work; GWE, global work efficiency; QRSd, QRS duration; fQRS-Ta, frontal QRS-T angle, sQRS-Ta, spatial QRS-T angle, P/S, QRS loop planarity index.

Discussion

New approaches to the treatment of CHF encourage the development of more effective diagnostic techniques that enable targeted selection of candidates for different treatment methods and evaluation of treatment efficacy. The echocardiographic assessment of the effectiveness of myocardial work is a promising diagnostic method.

In our pilot study, we compared ECG indicators with echocardiographic parameters characterizing LV contractility in CHF patients with reduced LVEF and AF.

QRSd is a well-known marker of myocardial electrical remodeling. QRSd was positively correlated with GWW in our study.

QRS fragmentation in a population-based study [8] was observed in almost 20% of middle-aged people; it was not associated with an increased risk of death in individuals without cardiovascular diseases and increased the risk of all-cause death almost 2 times and cardiovascular death 2.5 times in patients with cardiovascular disease.

QRS fragmentation is an independent predictor of all-cause death in CHF patients with reduced LVEF [9] and is associated with left ventricular dyssynchrony in patients with DCM and QRS complex narrowing [10]. QRS fragmentation can be caused by myocardial fibrosis, abnormal ionic currents, and violations in neuroregulatory mechanisms [11]. The presence of QRS fragmentation was associated in the study group with worse GLS, higher GWW values, and lower GWE. The subjective nature of QRS fragmentation, which is high intra- and inter-operator variability, is a disadvantage of the assessment method [10].

The QRS loop planarity is a promising indicator for the detection of structural heart disease [12]. In our

Figure 1. ECG and VCG of a 43-year-old patient with DCM.
QRS fragmentation is shown by arrows. QRSd 110 ms, fQRS-Ta 112°, sQRS-Ta 138°, P/S 96 %

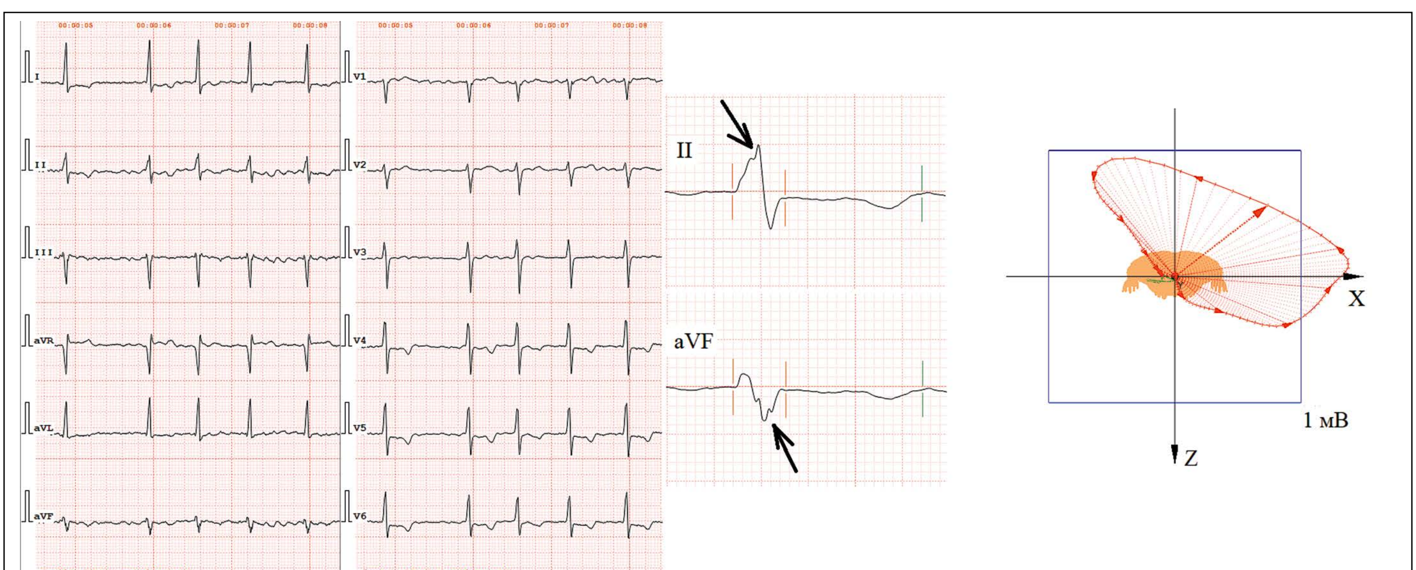


Figure 2. LVGLS (bovine eye), pressure-strain loop, and myocardial work of a 43-year-old patient. GLS 8 %, GWI 571 mm Hg %, GCW 914 mm Hg %, GWW 266 mm Hg %, GWE 77 %, BP 110/70 mm Hg

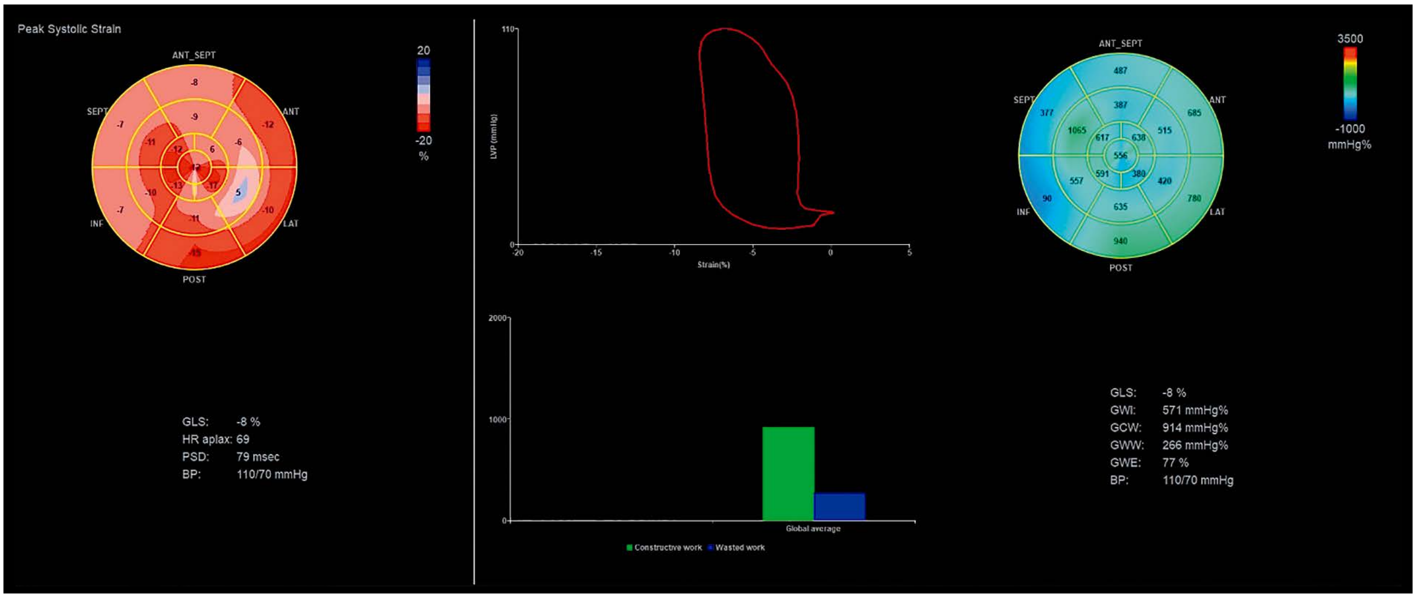
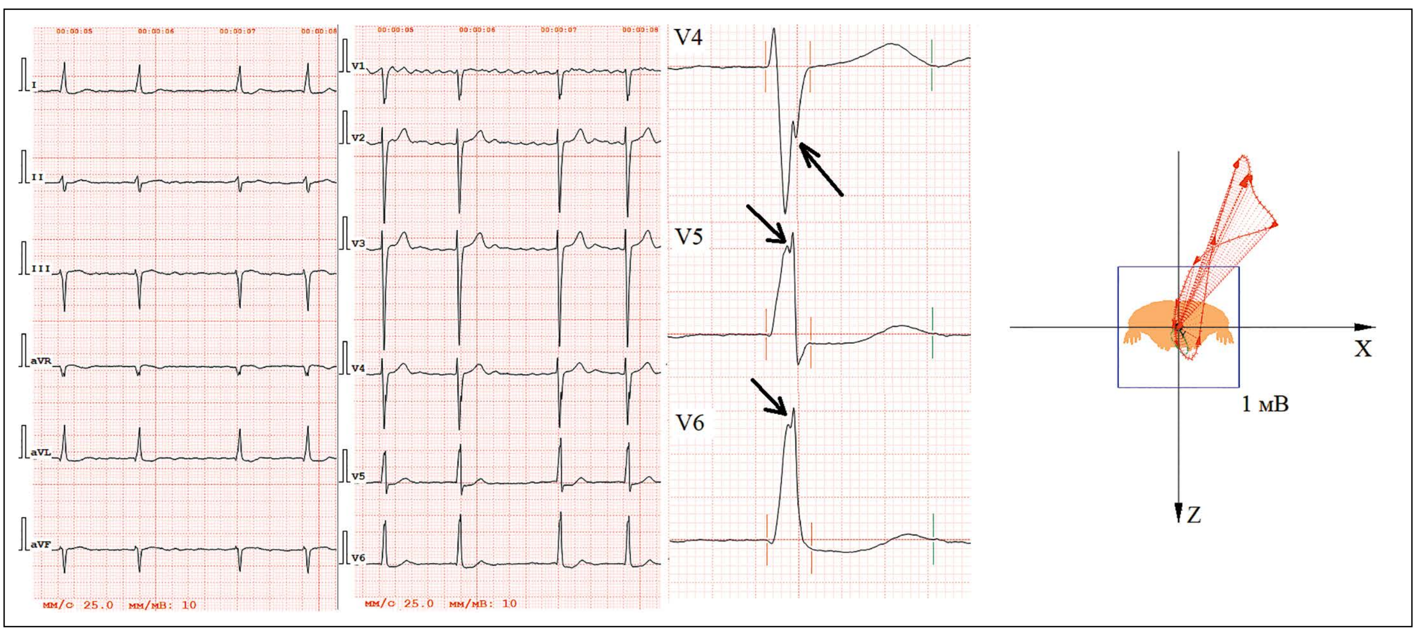


Figure 3. ECG and VCG of a 68-year-old patient with DCM. QRS fragmentation is shown by arrows. QRSd 104 ms, fQRS-Ta 152°, sQRS-Ta 154°, P/S 44 %



study, the QRS loop planarity index was correlated with LV volumes and myocardial work indices.

Gotsman I. [13] showed in a large cohort of CHF patients that baseline fQRS-Ta increased as LVEF decreased and was a predictor of all-cause death. In the study by Gleeson S. [14], higher sQRS-Ta was associated in patients with LVEF 31–40% with increased LVEDV, LVESV, reduced LVEF; more than 3-fold risk of serious arrhythmic events and all-cause mortality; more than 4-fold risk of hospitalizations for CHF. In our study, sQRS-Ta and fQRS-Ta were correlated with GLS and myocardial work. Our study has several limitations. Only patients with reduced LVEF were included in the study. If CHF patients with preserved LVEF, patients without CHF, and healthy individuals were also included in the study, the correlations of the indicators of interest could have been stronger. We did not address in our study the possibility of using the indicators of interest to predict treatment response and their changes during treatment. Those may be the subject of further research.

Conclusion

In this study, ECG parameters were compared with echocardiographic parameters characterizing

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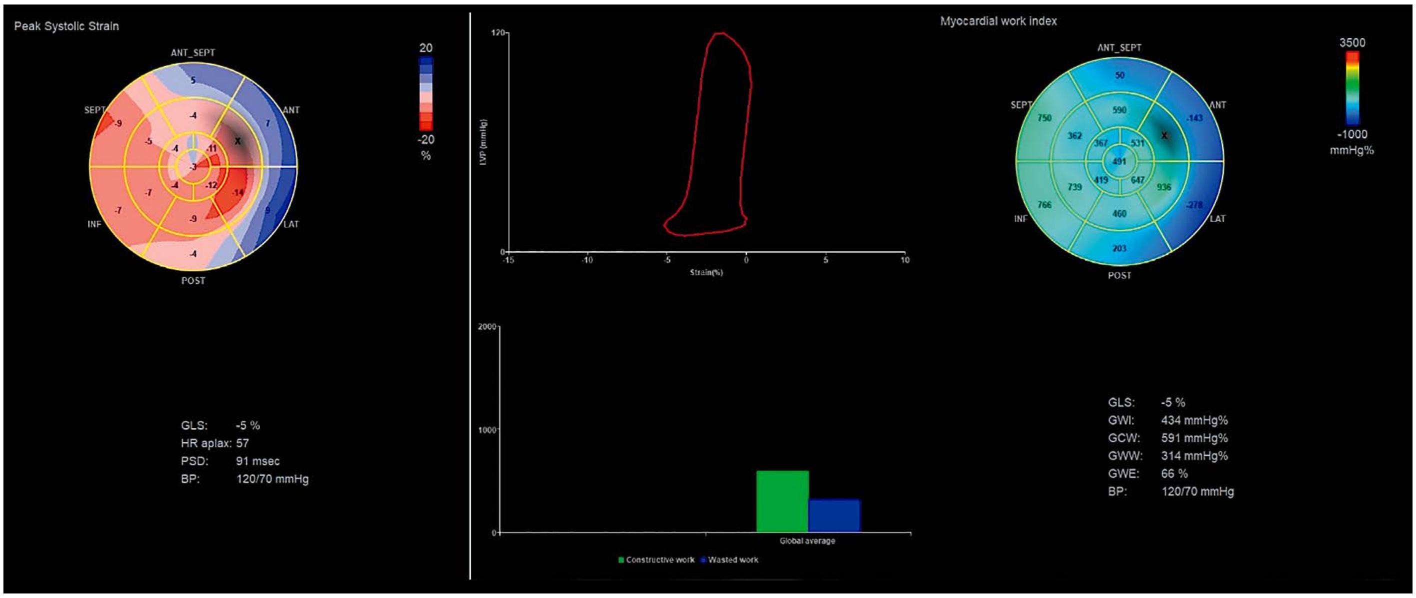
Figure 4. LVGLS (bovine eye), pressure-strain loop, and myocardial work of a 68-year-old patient. GLS 5 %, GWI 434 mm Hg %, GCW 591 mm Hg %, GWW 314 mm Hg %,GWE 66 %, BP 120/70 mm Hg



LV contractility in the group of patients with CHF class II–III with reduced LVEF and AF. The presence of QRS fragmentation was associated with worse GLS, higher GWW values, and lower GWE. Several weak yet significant correlations of the indicators of interest were identified. Further study of these parameters can be promising for assessing the severity of changes in the structural and functional state of the myocardium in the presence of various cardiovascular pathologies.

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No conflict of interest is reported.

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