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Fragmented QRS complex as a marker of myocardial fibrosis in patients with coronary artery disease

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Abstract

Aim – to analyze the relationship between fQRS and myocardial fibrosis in CAD patients using SPECT.

Material and methods. Retrospectively, we have analyzed the anamnesis and examinations of 116 patients with suspected coronary heart disease. The fQRS was assessed according to the criteria of Das M. et al., 2006, along with the presence of a pathological Q wave and a slow increase in the amplitude of the R wave. We analysed the transient myocardial ischemia and/or myocardial scarring using stress/rest SPECT with technetium-99m.

Results. fQRS was significantly more frequently detected in patients with stable and partially reversible perfusion defects – 44.1% and 52.2%, respectively, versus 13.0% and 5.5% in patients without perfusion defects or with reversible perfusion defects, $p < 0.05$. Among 28 patients with QRS fragmentation and myocardial fibrosis, 19 (67.8%) had classical signs of fibrosis on the ECG, 9 (32.1%) had no ECG-registered fibrosis but fQRS was detected. The sensitivity of fQRS marker in detecting myocardial fibrosis reached 84.4%, the specificity was 63.3%.

Conclusion. fQRS complex is an informative marker for detecting myocardial scarring in patients with coronary artery disease. Analysis of fQRS in daily clinical practice may increase the diagnostic value of electrocardiography in the detection of fibrosis.

Keyworlds: myocardial fibrosis, fQRS, fragmented QRS, CAD, ECG.

Conflict of interest: nothing to disclose.

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Limitations of the study: a small number of patients examined by SPECT in groups with different characteristics of perfusion defects and the retrospective nature of the study, the absence of indexed indicators in the evaluation of ECG.

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Фрагментация QRS-комплекса как маркер фиброза миокарда у пациентов с ишемической болезнью сердца

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Аннотация

Цель – проанализировать взаимосвязь fQRS с наличием рубцовых изменений миокарда, выявленных с помощью ОФЭКТ у пациентов с ишемической болезнью сердца (ИБС).

Материал и методы. Ретроспективно были проанализированы данные анамнеза и обследований 116 пациентов с подозрением на ИБС. Оценивалась fQRS по критериям M. Das и соавт. (2006), также оценивались наличие патологического зубца Q и замедленное нарастание амплитуды волны R. Изучалось наличие переходящей ишемии миокарда и/или рубцовых изменений миокарда с помощью перфузионной ОФЭКТ с 99м Тс-технетрилом на фоне пробы с физической нагрузкой или фармакологической пробы и в покое.

Результаты. Достоверно чаще fQRS выявлялась у пациентов со стабильными и частично-обратимыми дефектами перфузии (44,1% и 52,2% по сравнению с 13,0% и 5,5% у пациентов без дефектов перфузии или с обратимыми дефектами перфузии, $p<0.05$). Из 28 пациентов с фрагментацией QRS и рубцовыми изменениями миокарда 19 (67,8%) имели классические признаки рубцовых из-

менений миокарда на ЭКГ, а еще 9 (32,1%) не имели, однако у них регистрировалась fQRS. Чувствительность fQRS в выявлении фиброза миокарда составила 84,4%, специфичность 63,3%.

Выводы. Фрагментация синусового QRS-комплекса является информативным показателем для выявления рубцовых изменений миокарда у пациентов с ИБС. Анализ fQRS в рутинной клинической практике при интерпретации ЭКГ позволит увеличить диагностическое значение метода электрокардиографии в выявлении фиброза.

Ключевые слова: фиброз, фрагментация QRS, fQRS, ИБС, ЭКГ.

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ИБС – ишемическая болезнь сердца; ВСС – внезапная сердечная смерть, ЖНР – желудочковые нарушения ритма; ИМ – инфаркт миокарда; ОИМ – острый инфаркт миокарда; ОФЭКТ – однофотонная эмиссионная компьютерная томография; ЭКГ – электрокардиография; ГКМП – гипертрофическая кардиомиопатия; fQRS – фрагментация QRS-комплекса; ДКМП – дилатационная кардиомиопатия; МРТ – магнитно-резонансная томография; ЭХО-КГ – эхокардиография; ЧКВ – чрескожное вмешательство; АКШ – аортокоронарное шунтирование; ХСН – хроническая сердечная недостаточность; ЛЖ – левый желудочек; ФВ – фракция выброса; Ф.к. – функциональный класс; КДО – конечный диастолический объем; КСО – конечный систолический объем; МЖП – межжелудочковая перегородка; ПМЖА – передняя межжелудочковая артерия; ПКА – правая коронарная артерия, ЛКА – левая коронарная артерия, ОА – огибающая артерия, ЗМЖВ – задняя межжелудочковая ветвь; КАГ – коронароангиография; ПСЛЖ – передняя стенка левого желудочка, БСЛЖ – боковая стенка левого желудочка; НСЛЖ – нижняя стенка левого желудочка; ЗСЛЖ – задняя стенка левого желудочка; ВЛЖ – верхушка левого желудочка; ПИКС – постинфарктный кардиосклероз; ППЦ – положительная прогностическая ценность; ОПЦ – отрицательная прогностическая ценность.

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BACKGROUND

Coronary artery disease (CAD) is one of the most common diseases of the cardiovascular system and ranks first among the causes of sudden cardiac death (SCD), whereas the mechanism of SCD is most often caused by ventricular arrhythmias (VAs) [1]. Myocardial fibrosis is critical to VA genesis against CAD [2, 3].

In chronic CAD, short episodes of ischemia lead to interstitial and perimuscular fibrosis, which activate profibrotic processes in the myocardium. Against the progression of ischemia, aggravated by the development of fibrosis, interstitial and perimuscular fibrosis can subsequently transform into focal fibrosis [4, 5, 6, 7].

Replacement and reactive fibrosis are typical of myocardial infarction (MI). In replacement fibrosis, a fibrous scar is formed in place of cardiomyocytes that have died because of ischemia [8, 9]. Reactive fibrosis after MI develops under the influence of mechanical and humoral factors in the peri-infarction zone and even in areas of intact myocardium away from the infarction [10, 11].

The relationship between fibrosis and arrhythmias has been studied in several experimental studies. The inducibility of Vas is nearly linearly related to the degree of fibrosis [12]. With myocardial fibrosis, conditions are created both for the development of VA by the reentry mechanism and for arrhythmogenesis with abnormal automaticity or trigger activity due to early and late postdepolarization [13, 14, 15].

Thus, identifying myocardial fibrosis in the early stages can have a significant effect on further management and treatment. Cardiac imaging techniques such as magnetic resonance imaging and single-photon emission computed tomography (SPECT) have the highest sensitivity and specificity in detecting fibrotic, including cicatricial, changes in the myocardium [16, 17, 18, 19]. However, these diagnostic procedures are not widely available; therefore, the search for markers of myocardial fibrosis using screening technologies, such as electrocardiography (ECG), remains relevant.

ECG is currently the most common method for examining patients with cardiac problems and is often performed at the first visit to a doctor. Traditional ECG signs of myocardial fibrosis, namely, a slow increase in the R wave amplitude or a pathological Q wave, do not contain sufficient information. Thus, the sensitivity and specificity of the latter in detecting postinfarction myocardial scars are 48.8%–66% and 75%–85%, respectively [20, 21, 22]. Konno et al. [23] showed that in patients with hypertrophic cardiomyopathy, the sensitivity, specificity, and accuracy of the pathological Q wave in detecting fibrosis were 7%, 97%, and 60%, respectively. Numerous studies have assessed the diagnostic accuracy of ECG criteria such as a slow increase in the R wave amplitude as a marker of structural changes in the myocardium. According to some data, this ECG sign has high sensitivity and specificity in diagnosing MI (85%–87.2% and 60.9%–75%, respectively) [24, 25]. However, in a population study that included 20,739 people, the positive predictive result for identifying patients

with pathology of the cardiovascular system was only 7.3% [26].

Thus, new electrocardiographic markers of cicatricial changes in the myocardium are needed. One of the possible ECG signs of myocardial fibrosis is QRS complex fragmentation (fQRS). This ECG phenomenon was described in 2006 by Das et al. [27]. This indicates an impairment of the processes of myocardial depolarization against structural changes (scar and fibrosis) and ischemia. Studies have compared ECG data and cardiac imaging methods for identifying myocardial fibrosis (**Table 1**).

The results obtained were contradictory; therefore, we cannot draw definite conclusions about the reliability of using fQRS in clinical practice; however, studies have indicated the high sensitivity of this marker.

In addition, some studies have shown the risk-stratification significance of this ECG sign. Thus, in patients with CAD, fQRS was a predictor of the development of ventricular tachyarrhythmias and SCD [36, 37, 38, 39].

AIM

This study aimed to analyze the relationship between fQRS and the presence of cicatricial changes in the myocardium, identified using cardiac imaging techniques (perfusion SPECT) in patients with CAD.

MATERIAL AND METHODS

We retrospectively analyzed the medical history and examination data of 116 patients with suspected CAD who were examined at the VA Almazov National Medical Research Center. Their anamnesis and results of echocardiography (ECHO-CG) and coronary angiography (if available) were analyzed.

fQRS was assessed according to the criteria of Das et al. (2006) in narrow and wide complexes, according to which fQRS should be considered in the presence of an additional wave or notch on the R or S wave in at least two adjacent leads (corresponding to one zone of blood supply) for narrow complexes and in the presence of a distance between two notches of >40 ms or more than two additional waves or notches for wide complexes (>120 ms). When performing an ECG, fQRS was assessed in 12 conventional leads with standard settings (12-channel ECG recording, high-pass filter 0.05–20 Hz, low-pass filter 100–150 Hz, paper speed 25–50 mm/s, and voltage 10 mm/mV). We also assessed other ECG parameters that may indicate myocardial fibrosis, namely, the pathological Q wave and slow increase in the R wave amplitude.

The presence of transient myocardial ischemia and/or cicatricial changes in the myocardium was studied using perfusion SPECT with 99m Tc-technetril during an exercise tolerance test or a pharmacological test and at rest, performed at the Research Laboratory of Nuclear Medicine of the VA Almazov National Medical Research Center of the Russian Ministry of Health. The distribution of radiopharmaceutical agents in the myocardium, indices of myocardial perfusion impairment at rest and during physical activity, general perfusion deficit, area, and reversibility of perfusion defects were assessed.

The severity of perfusion defects was assessed on a five-point scale, where 0 is normal; 1, questionable hypoperfusion; 2, moderate hypoperfusion; 3–4, severe hypoperfusion; and 5, aperfusion. In accordance with this system, the state of perfusion in each segment is assessed at rest and during an exercise tolerance test. The index of perfusion impairment at rest (summary rest score, SRS) and the index of perfusion impairment during the exercise tolerance test (summary stress score SSS) were identified.

ECHO-CG was performed using a VIVID 7 Dimension device (General Electric, USA) according to a standardized protocol and in accordance with the recommendations of the European Society of Echocardiography.

Statistical data analysis was performed using STATISTICA 10 (StatSoft, USA, Tulsa, OK) and SPSS Statistics 17.0 (SPSS Inc., Chicago, USA).

Because the distribution of quantitative indicators was different from normal, the nonparametric Mann–Whitney U test was used to analyze them and compare

Authors	Year	Number of patients	Pathology	Results
M. Das et al.	2006 2008	479 879	CAD	fQRS is a more sensitive method for identifying cicatricial tissue compared with the Q wave [27, 28].
D. Wang et al.	2010 2014	460 248	CAD	No advantage in the presence of fQRS was noted compared with the Q wave for detecting myocardial fibrosis [29, 30].
L. Lorgis et al.	2014	209	AMI	fQRS is associated with the MI zone size, impaired myocardial perfusion, and a decrease in LV ejection fraction [31].
T. Tancharoen et al.	2013	250	CAD and non-CAD	fQRS is an independent predictor of cicatricial changes in the myocardium [32].
M. Ahn et al.	2013	86	DCMP of nonischemic origin	No relationship was revealed between fQRS and structural changes in the myocardium according to MRI data [33].
R. Sadeghi et al.	2015	2560	Meta-analysis of studies in patients with CAD/MI	fQRS has higher sensitivity and lower specificity than the Q wave [34].
S. Ozdemir et al.	2013	261	CAD	fQRS has high sensitivity and specificity as a marker for detecting ischemia and MI [35].

Table 1. *Comparison of ECG data (fQRS, Q wave) and cardioimaging methods of examination in the detection of myocardial fibrosis*
Таблица 1. *Работы по сопоставлению данных ЭКГ (fQRS, зубца Q) и кардиовизуализирующих методов обследования в выявлении фиброза миокарда*

the groups. Group characteristics are described using medians and quartiles.

Comparison of groups according to qualitative indicators was performed using the chi-square method with p calculated using Fisher's exact test.

Exploratory analysis of the set of indicators was performed using principal component analysis and cluster analysis for indicators and patients.

Groups were compared based on a set of quantitative indicators using linear discriminant analysis with step-by-step exclusion of the least informative indicators.

When analyzing the associations of markers with classifying indicators, their information characteristics (sensitivity, specificity, predictive value of positive and negative results, and diagnostic accuracy), kappa criterion, and significance of the relationship (according to Fisher's exact test) were calculated.

RESULTS

Clinical characteristics of the patients

The study included 116 patients with suspected CAD (68.9% men, age 61 years (median), quartiles 53–66). Approximately one-third of the patients (35.4%) had a history of myocardial revascularization [percutaneous intervention (PCI) or coronary artery bypass grafting (CABG)]. Less than half of the patients (37.1%) had a typical presentation of effort angina, with symptoms at the grade II level most often noted. Hypertensive disease was diagnosed in most patients (87.1%).

Manifestations of chronic heart failure (CHF) were detected in 2/3 of patients (66.4%) and were more often registered at the grade II level. According to ECHO-CG, most patients had preserved left ventricular (LV) function, namely, ejection fraction (EF) of 55% (median), with quartiles of 35 and 62. No significant LV dilatation was noted, with an end-diastolic volume of 96.5 (median), with quartiles of 84 and 142, and end-systolic volume of 31 (median), with quartiles of 28 and 64.5.

In 17 patients (14.6%) after SPECT, PCI was performed according to the indications, and CABG was performed in 6 (5.2%) patients.

The clinical characteristics of the study groups are presented for a general description of the included patients. In this study, fQRS was considered a marker of myocardial fibrosis in CAD, and no clinical manifestations of CAD were noted. Therefore, comparisons between groups based on clinical characteristics were beyond the scope of the study.

Total	n (%) or median (quartiles)
N	116
Male sex	79 (68,9%)
Age	61 (53; 66)
History of MI	59 (50,9%)
History of ГБ	111 (87,1%)
Angina clinical pattern	
Grade I	1 (0,9%)
Grade II	36 (31,0%)
Grade III	6 (5,2%)
Grade IV	0 (0%)
CHF grade	
Grade I	11 (9,5%)
Grade II	64 (55,2%)
Grade III	2 (1,7%)
Grade IV	0
ECHO-CG	
EF	55 (35;61,5)
End-diastolic volume	96,5 (84;142)
End-systolic volume	31 (28; 64,5)
Interventricular septum	11 (10;12)
History of CABG, total	9 (7,8%)
History of PCI, total	32 (27,6%)
Anterior interventricular artery	16 (50,0%%)
RCA	7 (21,9%)
LCA trunk	3 (9,4%)
CA	2 (6,3%)
Posterior interventricular artery	3 (9,4%)
SPECT	
No perfusion defects	36 (31,0%)
Reversible perfusion defects	23 (19,8%)
Partially reversible perfusion defects	23 (19,8%)
Stable perfusion defects	34 (29,3%)
ECG	
QRS duration	100 (92;111)
Pathological Q	36 (31,0%)
Slow increase in the R wave amplitude	9 (7,8%)
QRS fragmentation	32 (27,6%)
Coronary angiography, total (after SPECT)	50 (43,1%)
Hemodynamically significant stenoses according to the results of coronary angiography	23 (46%)
Anterior interventricular artery	9 (39,1%)
RCA	3 (13,0%)
LCA trunk	1 (4,3%)
CA	5 (21,7%)
Posterior interventricular artery	1 (4,3%)
Multivessel disease	6 (26,1%)
CABG, total (after SPECT)	6 (5,2%)
Assessment of the CHF grade according to the NYHA; assessment of the angina grade according to the Canadian Heart Association classification	

Table 2. *Characteristics of patients included in the study*
Таблица 2. *Характеристика пациентов, включенных в исследование*

Analysis of SPECT results

Based on the SPECT results, the patients were divided into groups depending on the nature of the detected perfusion defects. The number of patients without scintigraphic signs of perfusion defects both at rest and during the exercise tolerance test (n = 36) was approximately equal to the number of patients with stable perfusion defects (n = 34). Slightly fewer patients had reversible (n = 23) and partially reversible (n = 23) perfusion defects. The presence of stable and partially reversible defects was considered an indirect sign of cicatricial changes in the myocardium. Detailed characteristics of the patients are presented in **Table 2**.

The fQRS was recorded in 32 patients, whereas this ECG indicator was significantly more often recorded in patients with stable and partially reversible perfusion defects (44.1% and 52.2% vs. 13.0% and 5.5% in patients without defects of perfusion or with reversible perfusion defects, $p < 0.05$). Classic ECG signs of cicatricial changes in the myocardium, namely, pathological Q wave and slow increase in the R wave amplitude, were registered in 42 patients and were more often recorded in the same groups (**Table 3**).

In patients with stable and partially reversible perfusion defects, fQRS was more often recorded in leads corresponding to the LV anterior wall (46.7% and 50%, respectively) and in groups without

Group	fQRS, n (%)	Traditional ECG signs of cicatricial changes in the myocardium (pathological Q wave and/or slow increase in the R wave amplitude), n (%)
Patients with stable perfusion defects *(n = 34)*	15 (44,1%)	25 (73,5%)
Patients with partially reversible perfusion defects *(n = 23)*	12 (52,2%)	12 (52,2%)
Patients with reversible perfusion defects *(n = 23)*	3 (13,0%)	4 (17,5%)
Patients without perfusion defects *(n = 36)*	2 (5,5%)	1 (2,8%)

Table 3. *The frequency of depolarization abnormalities (fQRS, pathological Q wave, poor R wave progression) according to ECG results in patients with suspected/confirmed CAD compared with SPECT results*
Таблица 3*. Встречаемость нарушений деполяризации (fQRS, патологический зубец Q, замедленное нарастание амплитуды волны R) по результатам ЭКГ у пациентов с предполагаемой/подтвержденной ИБС при сопоставлении с результатами ОФЭКТ*

Patient group	Patient group		
	LVAW (V1–V5), n (%)	Lateral LV wall (I, avL, V6), n (%)	LVIW (II, III, avF),
1 (with stable perfusion defects)	7 (46,7)	5 (33,3)	3 (20)
2 (with partially reversible perfusion defects)	6 (50)	1 (8,3)	5 (41,7)
3 (with reversible perfusion defects)	0	0	3 (100)
4 (no perfusion defects)	0	0	2 (100)

Table 4. *Leads with fragmentation of the QRS complex in patients with suspected/confirmed CAD*
Таблица 4. *Отведения, в которых регистрировалась фрагментация QRS-комплекса у пациентов с предполагаемой/подтвержденной ИБС*

cicatricial changes in the myocardium (with reversible defects or without perfusion defects) in leads corresponding to the LV inferior wall (**Table 4**).

Figure 1 presents an ECG of patient P., 80 years old, with a history of postinfarction cardiosclerosis, in whom SPECT revealed partially reversible perfusion defects (index of perfusion disturbances during exercise of 7, total perfusion deficit of 9% of the LV volume, index of perfusion impairment at rest of 2, index of stress-induced perfusion impairment of 5, total perfusion deficit at rest of 5% of the left ventricular volume, total stress-induced perfusion deficit of 4% of the LV volume). The detected changes in perfusion correspond to a moderate degree of disturbance in the blood supply to the myocardium. The ECG registers fragmentation of the wide QRS complex in the form of notches in the leads, corresponding to the lateral and posterior LV walls (II, III, avR, avL, and aVF), multinotches are recorded, and in some cases, the distance between the notches is >40 ms.

fQRS was recorded in two patients without perfusion defects (5.5%) according to SPECT in leads II, III, and avF, corresponding to the inferior LV wall. In these patients, according to ECHO-CG data, the ejection fraction was within normal values, and no impairment of regional contractility was detected.

fQRS was detected in three patients with reversible perfusion defects (13%), and ECG patterns were recorded in leads corresponding to the inferior LV wall (leads II, III, and avF). During the exercise tolerance test, SPECT in these patients revealed perfusion defects in the inferior LV wall (n = 2) and the inferior and lateral LV walls (n = 1).

More often, fQRS was detected in patients with stable perfusion defects located in the area of the LV anterior wall (LVAW) (80%), LV inferior wall (LVIW) (60%), and interventricular septum (IVS) (60%).

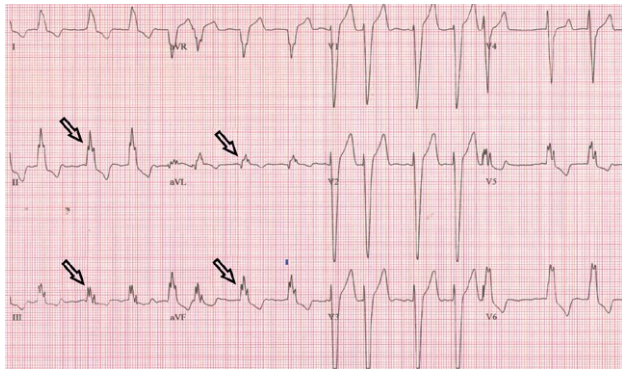
Statistically significant differences were observed in the characteristics of perfusion defects in patients with fQRS. In these patients, the index of perfusion defects at rest was 1.5 times higher than that in patients without fQRS (16.7 and 10.9, $p < 0.05$). The overall perfusion deficit at rest in the fQRS group was approximately two times greater than that in patients without fQRS (25.2 and 13.8, respectively, $p < 0.05$). The area of perfusion defects at rest was also larger in patients with fQRS (28.5 and 21.1, $p < 0.05$) (**Table 5, Fig. 2**).

Thus, fQRS may indicate not only the presence of myocardial fibrosis but also an association with the volume of fibrous tissue, thus being a marker of a high risk of life-threatening arrhythmias.

Most often, fQRS was recorded in the group with partially reversible perfusion defects, where perfusion defects were more often detected in the IVS (66.7% at rest and 58.3% under load), LVAW (50% at rest and 75% at load), and LV posterior wall (LVPW) (66.7% at rest and 25.0% under load (**Table 6**).

No significant differences were found between the characteristics of perfusion defects in patients with and without fQRS with partially reversible perfusion defects (**Fig. 3**).

Traditional signs of fibrosis (cicatricial changes) according to ECG (pathological Q wave and slow increase in the R wave amplitude) were most often recorded in patients with stable perfusion defects (73.5%) and less often recorded in patients with partially reversible (52.2%) and reversible (17.5%) perfusion defects (**Table 3**).



Note. The arrow indicates fragmented-wide QRS complexes (ECG recording speed 25 mm/s).
Рисунок 1. *Пример ЭКГ пациентки П., 80 лет с фрагментацией широкого QRS-комплекса на фоне постинфарктного кардиосклероза, подтвержденного данными ОФЭКТ.*
Figure 1. *ECG of 80 years old patient with scar after myocardial infarction detected by SPECT with fragmented wide QRS complex.*

	N	Localization of the stable perfusion defect					
		IVS, n (%)	LVAW, n (%)	Lateral LV wall, n (%)	LVPW, n (%)	LVIW, n (%)	Left ventricular apex, n (%)
Patients with fQRS	15	9 (60)	12 (80)	4 (26,7)	6 (40)	9 (60)	5 (33,3)
Patients without fQRS	19	9 (47,4)	11 (57,9)	6 (31,6)	6 (31,6)	5 (26,3)	8 (42,1)

Note. Statistical significance of differences was calculated using the Mann–Whitney U test, $p < 0.05$.
Table 5. *Characteristics of perfusion defects in patients with stable perfusion defects according to SPECT*
Таблица 5. *Характеристика дефектов перфузии у пациентов со стабильными дефектами перфузии по данным ОФЭКТ*

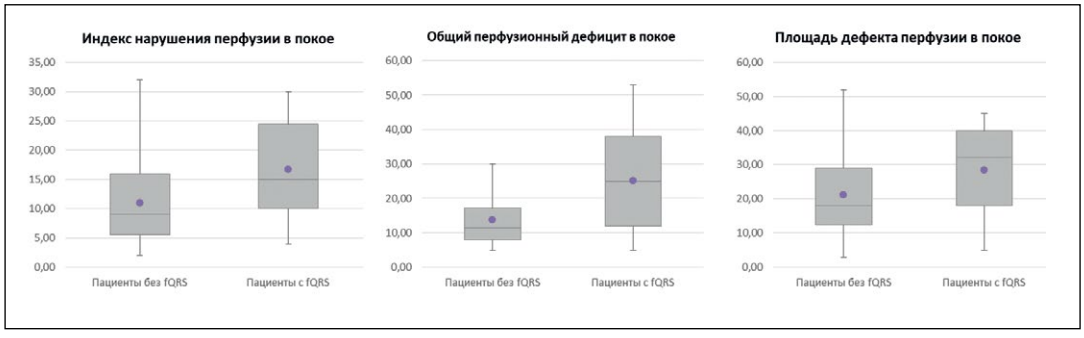


Рисунок 2. *Объем стабильных дефектов перфузии.*
Figure 2. *Volume of stable perfusion defects.*

		Localization of the perfusion defects					
		IVS, n (%)	LVAW, n (%)	Lateral LV wall, n (%)	LVPW, n (%)	LVIW, n (%)	Left ventricular apex, n (%)
Patients with fQRS *(n = 12)*	At rest	8 (66,7)	6 (50,0)	3 (25,0)	8 (66,7)	4 (33,3)	7 (58,3)
	On load	7 (58,3)	9 (75,0)	5 (41,7)	3 (25,0)	7 (58,3)	6 (50,0)
Patients without fQRS *(n = 11)*	At rest	2 (18,2)	5 (45,4)	3 (27,3)	2 (18,2)	7 (63,3)	3 (27,3)
	On load	3 (27,3)	8 (72,7)	4 (36,3)	3 (27,3)	7 (63,3)	3 (27,3)

Table 6. *Characteristics of perfusion defects in patients with partially reversible perfusion defects according to SPECT*
Таблица 6. *Характеристика дефектов перфузии у пациентов с частично обратимыми дефектами перфузии по данным ОФЭКТ*

Using a full sample of patients (n = 116), the information content characteristics of fQRS as a marker of fibrotic changes in the myocardium according to SPECT data were assessed. fQRS is an informative marker for detecting fibrosis, with high sensitivity and positive predictive value (**Table 7**).

Moreover, 19 (67.8%) of the 28 patients with fQRS and cicatricial changes in the myocardium had classic signs of cicatricial changes in the myocardium on ECG, and another 9 (32.1%) patients did not have them; however, they had recorded fQRS (**Fig. 4**).

DISCUSSION

We examined fQRS in patients with suspected or confirmed CAD by comparing ECG data with SPECT results. In our study, fQRS was recorded significantly more often (44.1% and 52.2% vs 13.0% and 5.5%, $p < 0.05$) in patients with stable and partially reversible perfusion defects than in those without defects according to SPECT data, which corresponds to existing ideas about the pathogenesis of this ECG marker [40, 41]. Importantly, a third of patients (32.1%) with cicatricial changes in the myocardium confirmed by SPECT data, classical electrocardiographic signs of cicatricial changes, such as the Q wave and a slow increase in the amplitude of the R wave, were not detected; however, fQRS of narrow and wide complexes was recorded. This observation proves the importance of using this ECG marker in routine practice.

Previously, international studies have noted that fQRS is also more common in patients with hemodynamically significant stenoses of the coronary arteries than in healthy individuals [42, 43]. We also recorded a higher incidence of fQRS in patients with reversible myocardial perfusion defects than in those without perfusion defects. However, fQRS was generally determined less frequently in our study than in the works of Korkmaz et al. and Caliskan et al. (13.3%, 54.8%, and 70%, respectively). These differences

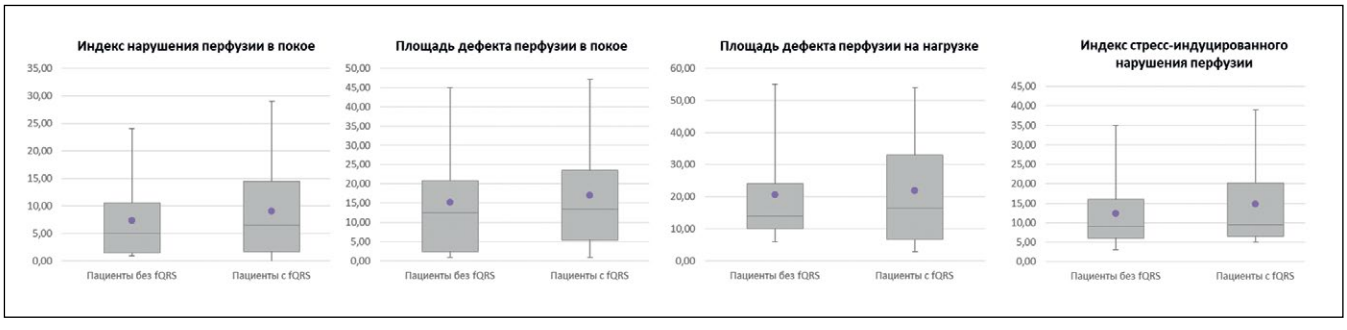


Figure 3. *Volume of partially reversible perfusion defects.*
Рисунок 3. *Объем частично обратимых дефектов перфузии.*

	Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %	Diagnostic accuracy, %
fQRS	84,4	64,3	81,3	65,5	69,8

Table 7. *Informative value of fQRS in the detection of myocardial fibrosis when compared with SPECT*
Таблица 7. *Информативность fQRS в выявлении фиброза миокарда при сопоставлении с данными ОФЭКТ*

Figure 4. *Comparison of ECG signs associated with fibrosis and the presence of fibrosis (scarring) of the myocardium according to SPECT data.*
Рисунок 4. *Сопоставление ЭКГ-признаков, ассоциированных с фиброзом, и наличия фиброза (рубцовых изменений) миокарда по данным ОФЭКТ.*

occur because these studies did not separately evaluate patients with partially reversible perfusion defects.

In patients with stable defects, fQRS was associated with larger perfusion defects. The volume of the myocardial cicatricial tissue is an important risk-stratification marker. Consequently, our case confirms the significance of fQRS as a marker of not only fibrosis but also an increased risk of developing life-threatening arrhythmias and SCD in patients with CAD.

Most often, according to our data, fQRS was recorded in patients with partially reversible perfusion defects, which indicate the presence of a scar and residual ischemia in the peri-infarction zone [44]. However, we did not find a relationship between fQRS and the area of perfusion defects in patients with partially reversible perfusion defects. However, unstable cicatricial zones of the myocardium but areas with alternating zones of healthy myocardium and fibrosis are the most unfavorable for the development of arrhythmias. It can be assumed that fQRS in this case reflects the pronounced structural heterogeneity of the myocardium, regardless of the defect size, and may indirectly imply a more unfavorable prognosis.

CONCLUSION

Fragmentation of the sinus QRS complex is an informative indicator for identifying cicatricial changes in the myocardium in patients with CAD (sensitivity of 84.4% and specificity of 63.3%).

fQRS not only indicates the presence of cicatricial tissue but is also associated with its volume and characteristics (presence of a "re-infarction" zone). Considering the known relationship between cicatricial tissue and the presence of malignant rhythm disturbances in the presence of CAD, the fQRS marker can be assumed to be significant for the risk stratification of this group of patients. This assumption will be confirmed in the ongoing prospective follow-up of patients.

Analysis of fQRS in routine clinical practice when interpreting ECG will increase the diagnostic value of ECG in detecting fibrosis.

Study limitations. The limitations of this study were the small number of patients with SPECT in groups with different characteristics of perfusion defects, retrospective nature of the study, and lack of indexed indicators when assessing ECHO-CG.

Conflict of interest. *The authors declare no conflict of interest.*

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