

Fragmentation of the QRS complex in patients with acute coronary syndrome treated invasively

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Abstract

Background: Previous studies showed that the presence of fragmented QRS (f-QRS) in patients with acute coronary syndrome (ACS), who underwent complete revascularisation, is associated with worse prognosis and the possibility of arrhythmia occurrence.

Aim: To assess the prognostic value of f-QRS in patients with ACS and complete revascularisation, in the context of cardiac arrhythmias.

Methods: We analysed 124 consecutive patients (66.1% males; mean age 62.38 ± 11.0 years) with ACS (STEMI 49%) treated invasively. Based on electrocardiogram (ECG) record, performed during the admission to the clinic, after the complete revascularisation (TIMI = 3) and during discharging from hospital (4th–5th days after ACS), we classified QRS as f-QRS based on generally accepted criteria (QRS < 120 ms, which included an additional R wave [R'] or notching in the nadir of the S wave, or > 1 R' (fragmentation) in two contiguous leads, corresponding to a major coronary artery territory. 24-h Holter ECG recording was performed on the fifth day after ACS to assess the frequency of conduction disturbances and others arrhythmias.

Results: There were no statistically significant differences between patients with and without f-QRS during hospitalisation. In the patients with f-QRS there were no statistically significant conduction disturbances and other arrhythmias compared to patients without f-QRS at discharge.

Conclusions: In the patients with ACS, who underwent successful revascularisation (TIMI = 3), the presence of f-QRS is not correlated with a higher incidence of arrhythmias compared to patients without f-QRS in short-term follow-up.

Key words: fragmented QRS complexes, arrhythmias, acute coronary syndrome

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INTRODUCTION

Cardiac arrhythmias are frequent complications among patients after acute coronary syndrome (ACS) and are one of the reasons for the need to monitor all patients with ACS. Arrhythmias of the worst prognosis that occur in this group of patients are sustained with ventricular fibrillation (VF) and rapid ventricular tachycardia (VT), which represent a direct threat to life. On the other hand, supraventricular arrhythmias, mainly atrial fibrillation (AF) and atrial flutter (AFL), are an unfavourable prognostic predictor of long-term forecast despite the fact that they are not directly life-threatening arrhythmias. The most effective method of dealing with arrhythmias during the peri-infarction period is an early and complete revascularisation [1]. Recommended by the

European Society of Cardiology, percutaneous coronary intervention (PCI) as a method of ACS treatment significantly reduced the morbidity (remove number of cardio-vascular diseases) and mortality in this group of patients [2]. Research continues on a non-invasive method that would allow the rapid stratification of the risk of life-threatening arrhythmias in patients with ACS. In recent years, numerous studies have indicated that such a marker of life-threatening rhythms in the course of ACS may be the presence of fragmentation within the QRS (f-QRS) in the electrocardiogram (ECG) ACS [1]. According to many researchers, f-QRS is considered to be a predictor for recurrence of severe cardiac events and high mortality, and is an indicator of early intervention treatment for patients [3]. No one has previously analysed the presence

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Table 1. Comparison of Holter examination in patients with acute coronary syndrome (ACS) depending on fragmented QRS (f-QRS) occurrence

	ACS with f-QRS (n = 62)		ACS without f-QRS (n = 62)		P
HR average [bpm]	69 ± 10		69 ± 9		0.33
HR min [bpm]	57 ± 9		57 ± 9		0.29
Supraventricular extrasystole	14	22.5%	10	16%	0.36
Ventricular extrasystole	53	85%	50	80%	0.47
Bradycardia	12	19%	14	22.5%	0.66
Pause	3	5%	4	6.5%	0.69
Atrial fibrillation	5	8%	9	14.5%	0.26
Atrial flutter	26	42%	23	37%	0.58
Second- or third-degree AVB	1	1.6%	0	0%	0.31

P values are given for the differences between the groups. HR — heart rate; AVB — atrioventricular block

of f-QRS in patients after myocardial infarction (MI) and complete revascularisation [4, 5]. In turn, the rapid restoration of coronary artery patency and the flow of the microcirculation are the basis of minimising serious complications after MI [3, 6, 7]. Therefore, the aim of this study is to assess the relationship between the frequency of f-QRS and the occurrence of arrhythmias in patients with ACS, who underwent successful revascularisation, in a short-term observation.

METHODS

The study comprised a group of 124 patients with ACS (including 66.1% men, mean age 62.38 ± 11.0 years), who were admitted to hospital. The study included patients who met the following criteria: each subject was fully effectively revascularised (reached Thrombolysis in Myocardial Infarction [TIMI] = 3) and had in the ECG narrow (< 120 ms) QRS complex. We analysed 12-lead ECGs, which were performed during the admission procedure, after a full and effective revascularisation, and finally at discharge. The study did not include patients' ECGs performed before an episode of ACS, due to the unavailability of the research results. Patients were divided into two groups according to the presence or the absence of f-QRS. On the basis of the adopted criteria (QRS < 120 ms, present at least in two contiguous leads, which included an additional R wave [R'] or notching in the nadir of the S wave, or the presence of > 1 R'), the presence of fragmentation within the QRS complex was assessed. In addition, on the fifth day of hospitalisation (on average) patients underwent 24-h digital Holter monitoring. Based on 24-h Holter ECG recording, each group was analysed for the presence of conduction disturbances and other arrhythmias (i.e. supraventricular extrasystole [SVE] and ventricular extrasystole [VE] or premature ventricular contractions, bradycardia, pause, AF, AFL, and also the presence of second- or third-degree atrioventricular block; Table 1). The study of transthoracic echocardiography results allowed us to assess left ventricular ejection fraction (LVEF) in both groups (Table 2).

Statistical analysis

The statistical analysis was performed with Statistica software (version 10). Student's t-test and Mann-Whitney U test were used for variables with normal distribution and the values were presented as an average ± standard deviation. The χ^2 test was used to compare categorical variables. In order to check the collocations between the variables, Spearman's correlation was used. $P \leq 0.05$ was considered statistically significant.

RESULTS

Table 2 shows the results of the comparison of clinical parameters in relation to the f-QRS presence. The prevalence of hypertension, diabetes, and glucose intolerance in both groups were similar. In both groups, the median value of body mass index was calculated, which for patients with existing f-QRS in ECG recording was 28.9 kg/m^2 and for patients with no f-QRS was 28.5 kg/m^2 . Myocardial infarction with ST segment elevation (STEMI) was diagnosed in 60 (48%) patients, and myocardial infarction without ST elevation (NSTEMI) in 64 (52%). The incidence of STEMI and NSTEMI were comparable in both groups (NS) (Table 2). The analysis of therapeutic procedure showed no statistically significant differences between the two groups (Table 3).

Among all the patients included in the analysis half (n = 62) were found to have f-QRS. QRS fragmentation was found in the ECG in 43 (69%) patients on admission, in 64% (n = 40) after full revascularisation, and in 71% (n = 44) in the ECG done at discharge from the clinic (Table 4). Among 35.5% (n = 22) of patients f-QRS occurred in all three ECG recordings. In 27.5% (n = 17) of patients f-QRS were observed in two ECG recordings, and in a single recording in 37% (n = 23) of patients. Analysis based on the 24-h Holter monitoring revealed no statistically significant differences in the incidence of conduction disturbances and other arrhythmias between the two groups (Table 1). The most common arrhythmia in patients with f-QRS as well as without f-QRS was VE, followed by AFL (Table 1). The second or third degree of atrioventricular block

Table 2. Clinical characteristics

	ACS with f-QRS (n = 62)		ACS without f-QRS (n = 62)		P
STEMI	32	52%	28	45%	0.47
NSTEMI	30	48%	34	55%	0.47
QRS width	101 ± 18		98 ± 19		0.06
Sinus rhythm	56	90%	54	88%	0.57
Hypertension	49	79%	51	82%	0.65
Diabetes mellitus type 2	19	30%	17	27%	0.69
Glucose intolerance	4	6%	4	6%	1.00
Left ventricular ejection fraction < 35%	13	21%	4	6%	0.03
Maximum troponin [ng/mL]	1.66 ± 2.06		0.73 ± 0.69		0.71
Maximum CK-MB [IU/mL]	154.24 ± 169.68		102.94 ± 128.94		0.008
Fasting plasma glucose	6.37 ± 1.78		6.08 ± 1.71		0.47
HGB admission [mg/dL]	9.03 ± 0.96		8.93 ± 1.08		0.76
HGB last designation [mg/dL]	8.29 ± 1.13		7.93 ± 1.22		0.15
Haematocrit admission [%]	41.46 ± 4.61		41.41 ± 3.54		0.78
Haematocrit last designation [%]	38.09 ± 5.53		39.57 ± 4.86		0.11
Maximum creatinine [mmol/L]	92.82 ± 26.47		89.18 ± 24.82		0.34
Duration of chest pain on admission [min]	16 ± 31		22 ± 41		0.14

P values are given for the differences between the groups. ACS — acute coronary syndrome; CK-MB — creatinine kinase-myocardial band; f-QRS — fragmented QRS; HGB — haemoglobin; NSTEMI — non-ST segment elevation myocardial infarction; STEMI — ST segment elevation myocardial infarction

Table 3. Medical treatment

Drugs	N (%)
Acetylsalicylic acid	123 (99%)
Beta-blockers	116 (93.5%)
ACE-I/ARBs	116 (93.5%)
Statin	121 (97.5%)
Diuretic	44 (35%)
Aldosterone antagonist	26 (21%)
Thienopyridine	92 (74%)
Insulin	11 (9%)
Oral antidiabetic drugs:	23 (18.5%)
Metformin	10 (8%)
Other	19 (15%)

ACE-I — angiotensin-converting-enzyme inhibitor; ARBs — angiotensin receptor blockers

occurred in one patient in the group of f-QRS. Spearman's correlation analysis showed that at a statistically significant level ($p < 0.05$) there is a poor positive correlation ($r = 0.27$) between the presence of f-QRS complex in the recording ECG on admission to hospital and the number of VE in 24-h Holter monitoring. A similar relationship was noticed with regard to the presence of f-QRS complex in all three of the ECG recordings ($r = 0.23$) (Table 4). This indicates a higher daily number of VE in patients with f-QRS in comparison to patients without

f-QRS, which proves to be a significant factor that distinguishes between the two groups of patients ($p < 0.05$; Fig. 1). There was no possible relationship between other arrhythmias and conduction. The analysis of the results of echocardiography revealed that LVEF < 35% was significantly more common in patients with f-QRS (Table 2).

DISCUSSION

Ventricular depolarisation (QRS complex) and ventricular repolarisation (ST segment and T wave) in patients with acute MI can be monitored on the basis of the analysis of 12-lead ECG. It is a cheap and noninvasive screening examination that allows identification of a group of patients with acute ischaemia quickly due to emerging characteristic changes in the ECG. Aggressive medical therapy, the use of thrombolytic agents and early coronary revascularisation led to a decrease (from 66.6% to 37.5%) in the rate of pathological Q wave ECG in patients with MI and all over rate of distortion of the QRS complex [8], which is associated with the search for new markers of infarct scars on ECG.

The results obtained in this study confirmed that the presence of f-QRS in the ECG after PCI is a frequently observed phenomenon that affects 69% of patients at the time of admission to hospital.

Fragmented QRS complex presented in the ECG is a non-invasive parameter, gaining more and more importance in the diagnosis and prognosis of cardiovascular diseases. Fragmenta-

Table 4. Fragmented QRS (f-QRS)

	N = 62	R Spearman	
		VE	SVE
f-QRS on admission	43 (69%)	0.27*	-0.02**
f-QRS after PCI	40 (64%)	0.22*	0.06**
f-QRS at discharge	44 (71%)	0.17**	0.01**
f-QRS in any one ECG	62 (100%)	0.19*	0.05**
f-QRS in one ECG records of one patient	23 (37%)	-0.16**	0.02**
f-QRS in two ECG records of one patient	17 (27.5%)	0.15**	-0.05**
f-QRS in three ECG records of one patient	22 (35.5%)	0.23*	0.06**

*p < 0.05; **p > 0.05; PCI — percutaneous coronary intervention; SVE — supraventricular extrasystole; VE — ventricular extrasystole

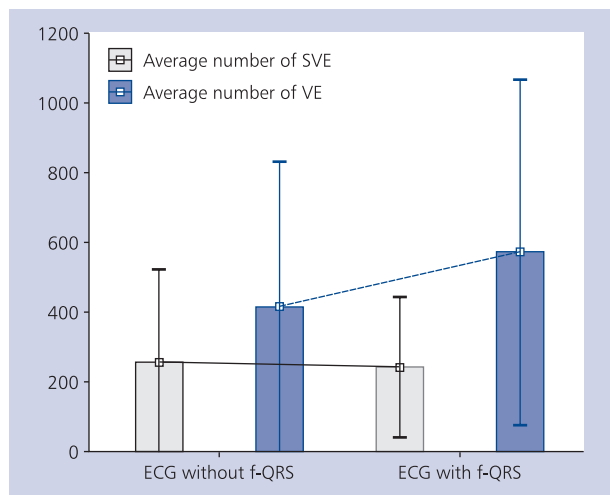


Figure 1. Comparison of average values of ventricular extrasystole (VE) and supraventricular extrasystole (SVE) registered in 24-h Holter electrocardiogram (ECG) recording in patients with and without fragmented QRS (f-QRS) in ECG

tion of narrow QRS (< 120 ms) is defined as an additional R (R') wave or an incision within the S wave or the presence of at least 2 R-waves in two contiguous leads corresponding to the area by the relevant vasculature coronary artery [9]. The presence of f-QRS ECG was associated with a heterogeneous, "zig-zag" scar formed around the conduction within the myocardium [3]. Earlier studies have shown that f-QRS is a valuable predictor of MI, malignant cardiac arrhythmias, left ventricular dysfunction, and coronary artery ectasia [9, 10].

Additionally f-QRS is used as a marker for diseases such as Chagas disease, Fallot's disease, sarcoidosis, Brugada syndrome, and long QT syndrome. In earlier studies it was observed that the f-QRS is not associated with the location of MI, creatinine kinase-MB, acute thrombosis, MI, re-hospital, flow TIMI 3 after PCI, or a patient using a stent. It has been shown, however, that this parameter compared with QRS duration was set to poorer prognosis in this group of patients. The work

on f-QRS, often appearing in the application, was associated with a higher risk of VT/VF in patients with acute MI, including those with primary PCI [11]. One of the studies of f-QRS has shown that in the short-term follow-up of patients after ACS, who underwent PCI and were f-QRS-negative, no statistically significant differences were found in the growth of malignant cardiac arrhythmias compared with the patients who underwent PCI and their fragmentation was presented [3]. This study did not indicate, however, whether PCI was completed to fully restore the flow.

Our study included a group of patients in whom PCI has always resulted in complete revascularisation (TIMI = 3), and significant differences were not noticed in the incidence of serious disturbances of ventricular and supraventricular rhythm in relation to the presence or absence of fragmentation within the QRS complex. The same applied to conduction disturbances. In contrast, Ari et al. [3] demonstrated that the presence of f-QRS in 48-h ACS is an important marker of severe cardiac events in patients with acute MI, who were subjected to primary PCI [4]. It was one of the first studies that took the effective PCI into account, but included only a small group of STEMI patients. The lack of standardised criteria for research, and small research groups are likely to be the cause of receiving conflicting results which make f-QRS predictive value in relation to arrhythmias controversial. The presence or absence of f-QRS in patients with MI in the ECG before and after PCI was previously studied. It was noted that the f-QRS may be useful in identifying patients with a higher risk of ischaemic areas or myocardial necrosis [12, 13].

In our study, we did not notice major differences in the number of patients with f-QRS before and after PCI, and at the end of hospitalisation. As we can see (Table 1), the proportion of patients with fragmentation is reduced from 69% to 64%, but it increases again to 71% at discharge, which may be indicative of the instantaneous local improvement of MI. Based on the results of the study, we noticed that a reduced LVEF below 35% combined with the presence of f-QRS has a value of bad prognosis, which confirmed earlier studies [14]. In the

present study, the wall motion score index (WMSI), which is an alternative to LVEF, was analysed to check the possible relationship between those parameters. Interestingly, WMSI was significantly associated with the f-QRS presence. What is more, both parameters (WMSI and LVEF) were strictly associated with impaired left ventricular systolic function and severe myocardial damage. That is why f-QRS presence in patients after MI might be a marker of severe left ventricular dysfunction [15]. However, in a larger population, with LVEF \leq 35%, who received implantable cardioverter defibrillator (ICD) for sudden cardiac death primary prevention, f-QRS was not associated with a higher risk of arrhythmic mortality [16]. According to current guidelines, impaired left ventricular systolic function and ventricular arrhythmias are one of the indications for ICD implantation [17]. Reduced LVEF and VT/VF, as has already been mentioned, often correlate with poor prognosis in patients with f-QRS. One study demonstrated that patients with f-QRS and ICD received an appropriate treatment with an ICD five times more often than patients without f-QRS [18].

Several studies have related to the issue raised by us, i.e. the patients after PCI with f-QRS in the ECG [19–23]. The cited articles show a different point of view of the researchers. Probably this theme will be raised many times in future because there are high prognostic hopes of this parameter, which may facilitate the early diagnosis of patients.

CONCLUSIONS

Despite numerous studies, the predictive value of f-QRS in 12-lead ECG in patients after ACS is controversial. Research carried out in large groups of patients provides conflicting results, so there is a need to carry out a number of meta-analyses in order to draw the right conclusions. Our study did not confirm an increased incidence of arrhythmias in patients with ACS who underwent successful revascularisation (TIMI = 3), which were characterised by the presence of f-QRS ECG compared to patients without f-QRS.

Conflict of interest: Z. Kalarus: Consultant of Boehringer-Ingelheim and appearance fee for lecture Pfizer, Boehringer-Ingelheim, Abbott, Eli Lilly; B. Średniawa: Consultant of Medtronic Bakken Research Centre and appearance fee for speaking and meetings Boehringer-Ingelheim, Servier, MSD, Berlin-Chemie, Sandoz, Merc, Bayer.

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Fragmentacja zespołów QRS u pacjentów z ostrym zespołem wieńcowym leczonych inwazyjnie

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Streszczenie

Wstęp: Wcześniejsze badania wykazały, że obecność fragmentacji w obrębie zespołów QRS (f-QRS) u pacjentów z ostrym zespołem wieńcowym (ACS), którzy zostali poddani skutecznej, pełnej rewaskularyzacji, wiąże się z gorszym rokowaniem i możliwością występowania zaburzeń rytmu serca.

Cel: Celem pracy była ocena wartości prognostycznej f-QRS u pacjentów z ACS i skuteczną rewaskularyzacją, w kontekście zaburzeń rytmu serca.

Metody: Przeanalizowano przypadki 124 kolejnych chorych (66,1% mężczyzn, średni wiek $62,38 \pm 11,0$ lat) z ACS (STEMI 49%) leczonych inwazyjnie. Na podstawie badania elektrokardiograficznego (EKG), wykonanego w czasie przyjęcia do kliniki, po skutecznej rewaskularyzacji (TIMI = 3) i podczas wypisywania ze szpitala (w 4.–5. dniu po zawale serca) oceniono występowanie f-QRS na podstawie ogólnie przyjętych kryteriów: QRS < 120 ms, złożony z dodatkowego załamka R (R') lub ząbienie na ramieniu zstępującym załamka S, lub 1 R' (fragmentacji) w 2 odprowadzeniach, odpowiadających obszarowi unaczynienia przez główne tętnice wieńcowe. W celu oceny częstości zaburzeń przewodzenia i zaburzeń rytmu serca w 5. dniu po ACS wykonywano 24-godzinne EKG metodą Holtera.

Wyniki: W trakcie hospitalizacji nie stwierdzono istotnie statystycznych różnic między pacjentami z f-QRS oraz bez f-QRS. U osób z f-QRS nie istniały statystycznie istotne zaburzenia przewodzenia i inne zaburzenia rytmu w porównaniu z chorymi bez f-QRS przy wypisywaniu ze szpitala.

Wnioski: U chorych z ACS, poddanych skutecznej rewaskularyzacji (TIMI = 3), obecności f-QRS nie wiąże się z większą częstością występowania zaburzeń rytmu serca w porównaniu z pacjentami bez f-QRS w okresie krótkoterminowej obserwacji.

Słowa kluczowe: zaburzenia rytmu serca, fragmentacja zespołów QRS, ostry zespół wieńcowy

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