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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

The presence of fragmented QRS on 12-lead ECG in patients with coronary slow flow

Hale Yilmaz[1], Baris Gungor[1], Tugba Kemaloglu[1], Nurten Sayar[1], Betul Erer[1], Mehmet Yilmaz[2], Nazmiye Cakmak[1], Ufuk Gurkan[1], Dilaver Oz[1], Osman Bolca[1]

[1]Departments of Cardiology, Siyami Ersek Thoracic and Cardiovascular Surgery Centre, Istanbul, Turkey
[2]Departments of Cardiovascular Surgery, Siyami Ersek Thoracic and Cardiovascular Surgery Centre, Istanbul, Turkey

Abstract

Background: Coronary slow flow (CSF) is characterised by delayed opacification of coronary arteries in the absence of epicardial occlusive disease. It has been reported that CSF may cause angina, myocardial ischaemia, and infarction. Fragmentation of QRS complex (fQRS) is an easily evaluated non-invasive electrocardiographic parameter. It has been associated with alternation of myocardial activation due to myocardial scar and/or ischaemia. Whether CSF is associated with fQRS is unknown. The presence of fQRS on ECG may be an indicator of myocardial damage in patients with CSF.

Aim: To investigate the presence of fQRS in patients with CSF.

Methods: Sixty patients (mean age 55.5 ± 10.5 years) with CSF and 44 patients with normal coronary arteries without associated CSF (mean age 53 ± 8.4 years) were included in this study. The fQRS was defined as the presence of an additional R wave or notching of R or S wave or the presence of fragmentation in two contiguous leads corresponding to a major coronary artery territory.

Results: The presence of fQRS was higher in the CSF group than in the controls ($p = 0.005$). Hypertension was significantly more common in the CSF group ($p < 0.001$). There was no significant association between the presence of fQRS and an increasing number of vessel involvements. Logistic regression analysis demonstrated that the presence of CSF was the independent determinant of fQRS (OR = 10.848; 95% CI 2.385–49.347; $p = 0.002$).

Conclusions: Fragmented QRS, indicating increased risk for arrhythmias and cardiovascular mortality, was found to be significantly higher in patients with CSF. We have not found an association between the presence of fragmented QRS and the degree of CSF. Further prospective studies are needed to establish the significance as a possible new risk factor in patients with CSF.

Key words: fragmented QRS, coronary slow flow, coronary artery disease

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INTRODUCTION

Coronary slow flow (CSF) is an angiographic finding characterised by delayed opacification of coronary arteries in the absence of epicardial occlusive disease. CSF is not a rare finding in patients undergoing routine coronary angiography, and its prevalence has been reported as 5.5% [1]. Several studies have shown that CSF may cause angina, myocardial ischaemia, and infarction [2–4]. Fragmented QRS (fQRS) complexes are novel electrocardiographic signals which reflect altered ventricular conduction around regions of a myocardial scar. The fQRS is defined as the presence of slurred QRS complexes with various RSR′ patterns without typical bundle branch block in two contiguous leads corresponding to a major coronary artery territory [5]. The detection of fQRS complexes in a routine 12-lead ECG is a marker for abnormal cardiac depolarisation. It has been demonstrated that the presence of fQRS in patients with coronary artery disease (CAD) has been related to regional myocardial damage, increased adverse cardiac events, and decreased event-free survival [6–8]. Hence fQRS may be a reliable indicator of past myocardial ischaemia in the absence of Q waves. In addition, fQRS has been related to arrhythmic events in patients with Brugada syndrome [9], and non-ischaemic cardiomyopathy [10].

Address for correspondence:
Hale Yilmaz, MD, Barbaros Mah. Zambak Sokak, Kentplus Sitesi D2 blok D: 37 Batiatasehir, Istanbul 34746, Turkey, tel: +90 (216) 688 0188, fax: +90 (216) 418 9649, e-mail: haleyilmaz@tnn.net
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To the best of our knowledge, fQRS has not been investigated in patients with CSF. Whether this pattern of flow is associated with fQRS is unknown. The presence of fQRS on ECG may be indicator of myocardial damage in patients with CSF. Therefore, this study was designed to investigate whether CSF results in fragmented QRS on ECG compared to normal coronary flow.

METHODS

Study population

This study included 60 patients (mean age 55.5 ± 10.5 years; 56.6% men) with angiographically proven normal coronary arteries and CSF in at least one of the major coronary arteries, and 44 patients with angiographically proven normal coronary arteries without associated CSF (mean age 53 ± 8.4 years; 50% men). We prospectively enrolled 121 patients who underwent coronary angiography under the discretion of their attending physician. Patients with a history of cardiomyopathy and myocardial infarction (MI), left ventricular hypertrophy (LVH), pathological Q wave on ECG, typical left bundle block or right bundle block, incomplete right bundle block and paced rhythm on ECG, were excluded from the study. In all subjects, echocardiographic examinations were performed. LVH was excluded by using echocardiography. MI and necrosis were evaluated by using history, ECG, echocardiography and left ventriculography. Patients who were taking medications that could affect the ECG such as antiarrhythmics, beta-blockers, and calcium antagonists were also excluded from the study. The final study population included 60 patients with CSF and 44 controls. 41 patients with CSF had CCS class I angina, and 19 patients with CSF had CCS class II angina. 14 CSF patients had ischaemic findings in myocardial perfusion scintigraphy, and 37 patients had a positive treadmill test. All subjects consented to participate in the study, which was approved by the local Ethics Committee.

Electrocardiogram

The resting surface 12-lead ECG (40 Hz, 25 mm/s, 10 mm/mV, Cardiofax GEM; Nihon Kohden Corp., Tokyo, Japan) was analysed by two independent clinicians who were blinded to angiographic data. There was 99.9% concordance for ECG sign of fQRS. The fQRS was defined as the presence of an additional R wave (R′) or notching of R or S wave or the presence of fragmentation (more than one R′) in two contiguous leads corresponding to a major coronary artery territory. The fQRS was defined when it was present in at least two contiguous leads of those representing anterior (V_1 to V_5), lateral (I, aVL and V_5, V_6), inferior (II, III, aVF), or posterior (V_1, V_2) myocardial segments [5]. The fQRS was seen in more than one myocardial segment in some patients. An example of an ECG of a patient who had SCF and fQRS is shown in Figure 1.

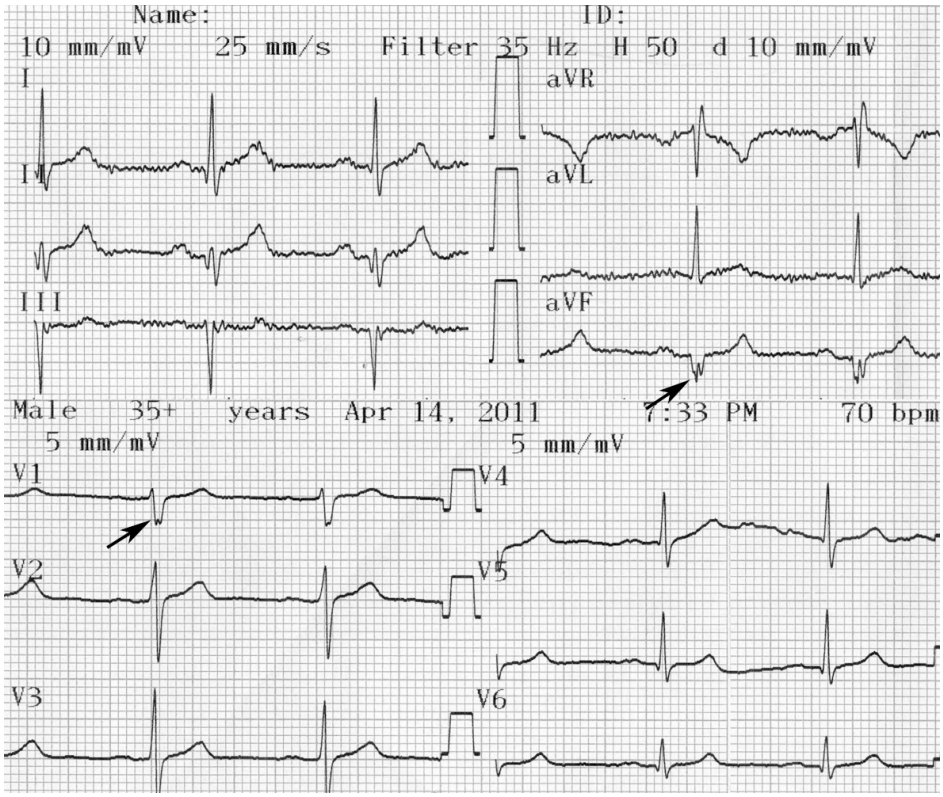

Figure 1. Example of ECG — a patient who had coronary slow flow and fragmented QRS

Table 1. Clinical and laboratory findings of the subjects

	Control (n = 44)	Coronary slow flow (n = 60)	P
Age[b] [years]	53.2 ± 8.5	55.7 ± 10.7	0.206
Gender[c] (males)	22 (50.0%)	34 (56.7%)	0.635
Body mass index[b] [m²]	29.2 ± 4.9	30.5 ± 5.1	0.165
Diabetes mellitus[c]	6 (13.6%)	15 (25.4%)	0.222
Hypertension[c]	14 (31.8%)	41 (68.3%)	0.001*
Smoking[c]	12 (27.3%)	11 (18.3%)	0.397
Family history[c]	12 (27.3%)	16 (26.7%)	1.000
Total cholesterol[b] [mg/dL]	190.2 ± 42.3	186.9 ± 53.6	0.735
Triglycerides[a] [mg/dL] (median)	149.3 ± 58.7 (127.0)	168.8 ± 102.3 (155.0)	0.576
HDL[b] [mg/dL]	44.2 ± 10.4	43.1 ± 13.7	0.662
LDL[b] [mg/dL]	115.1 ± 35	123.1 ± 45.5	0.334
VLDL[a] [mg/dL] (median)	30.2 ± 12.2 (25.50)	33.4 ± 20.7 (30.0)	0.787
Fragmented QRS[c]	3 (6.8%)	19 (31.7%)	0.005*

[a]Mann Whitney U Test; [b]Independent Samples Test; [c]Yates Continuity Correction; *p < 0.01

Angiographic data and frame counting

Coronary angiography was performed using the standard Judkins technique. CSF was defined according to the TIMI frame count (TFC) method, and the subjects with a TFC greater than two standard deviations (SD) from the normal range were accepted as having CSF. Determination of frame counts was carried out by the method of Gibson et al. [11]. All angiograms were filmed at 15 f/s. We used a conversion factor of two to convert the frame rate values to adjust for the 30 f/s acquisition speed used in the original cine angiographic studies.

Statistical analysis

The NCSS (Number Cruncher Statistical System) 2007 and PASS 2008 Statistical Software (Kaysville, UT, USA) program was used for the statistical analysis. During the evaluation of the data obtained from the study, descriptive statistical methods of mean, SD, frequency and ratio values were used in the tables. All continuous variables were given as mean ± SD; categorical variables were defined as percentages. Categorical data was compared with the χ^2 test, Yates Continuity Correction and Fisher's Exact test. Mean values of continuous variables were compared between groups using the Student-t test or Mann-Whitney U test. A Multivariate Enter Logistic Regression analysis was used to identify significant determinants of fQRS. P values of less than 0.05 were considered significant.

RESULTS

Clinical and laboratory findings of the subjects are shown in Table 1. The two groups were similar in terms of age, sex, body mass index, diabetes mellitus, family history of CAD, and smoking status (p > 0.05). Also there was no significant difference in terms of lipid profile, total cholesterol, LDL, HDL, VLDL, and triglyceride levels between two groups (p > 0.05). Hypertension was significantly more common in the CSF group than those in the normal coronary artery group (p < 0.001).

Table 2. Angiographic data for subjects with coronary slow flow (n = 60)

Left anterior descending artery		37 (61.7%)
Circumflex artery		28 (46.7%)
Right coronary artery		36 (60.0%)
Vessel involvement:	1-vessel	32 (53.3%)
	2-vessel	15 (25.0%)
	3-vessel	13 (21.7%)

CSF was significantly related with the presence of fQRS. The presence of fQRS was higher in the CSF group than in the normal coronary artery group (31.7% vs. 6.8%, p = 0.005). There was no significant difference in terms of QRS duration between the CSF and control groups (92.6 ± 13.2 vs. 90.9 ± 9.6; p = 0.501).

In the CSF group, single-vessel, two-vessel and three-vessel involvements and distribution of left anterior descending artery (LAD), circumflex artery (Cx), and right coronary artery (RCA) are shown in Table 2. TFC of the subjects are presented in Table 3. In the CSF group, there was no significant association between TFC of involved vessels and the presence of fQRS (for LAD: p = 0.324, for Cx: p = 0.422, for RCA: p = 0.932). Also there were no statistical significances in single-, two-, three-vessel involvements between patients with and without fQRS (p = 0.786).

Table 3. TIMI frame counts of coronary arteries

	Control group (n = 44)	CSF group (n = 60)	P*
Left anterior descending artery	19.8 ± 2.0	28.4 ± 9.3	0.001
Circumflex artery	20.7 ± 3.5	29.9 ± 9.3	0.001
Right coronary artery	19.2 ± 2.3	30.3 ± 9.8	0.001

Independent Samples Test; *p < 0.01; CSF — coronary slow flow

Table 4. TIMI frame counts of vessels in coronary slow flow group according to with and without fQRS

Artery involvement	fQRS (+) (n = 19)	fQRS (–) (n = 41)	P*
Left anterior descending artery	26.9 ± 6.3	29 ± 10.4	0.324
Circumflex artery	28.6 ± 8.2	30.6 ± 9.7	0.422
Right coronary artery	30.1 ± 11.2	30.3 ± 9.2	0.932

*Independent Samples Test; fQRS — fragmented QRS

Table 5. Relation between fragmented QRS and clinical characteristics

	Odds ratio	95% confidence interval		P
		Lower	Upper	
Coronary slow flow	10.848	2.385	49.347	0.002
Hypertension	0.268	0.068	1.057	0.06
Smoking	0.357	0.076	1.689	0.194
Gender	3.241	0.984	10.672	0.063
Age	1.053	0.993	1.116	0.084

In other words, there was no relation between the presence of fQRS and an increasing number of vessel involvements.

In the CSF group, 11 patients with hypertension also had fQRS simultaneously. There was no hypertensive patient with fQRS in the control group. The presence of both hypertension and fQRS was significantly more common in the CSF group (p = 0.002). Multivariate Enter Logistic Regression analysis demonstrated that the presence of CSF was an independent determinant of fQRS (OR = 10.848; 95% CI 2.385–49.347; p = 0.002) (Table 5).

DISCUSSION

This study showed that the CSF phenomenon is associated with the presence of fQRS complexes on routine 12-lead ECG and hypertension. We have not found an association between the presence of fQRS and the degree of CSF.

CSF in epicardial coronary arteries is a unique angiographic finding which reveals various clinical presentations such as unstable angina, acute MI, ventricular tachycardia, and microvascular angina [12, 13]. Although the mechanisms of CSF are not clear, some reports have suggested that CSF might be caused by atherosclerotic changes in the coronary artery microvasculature, high small vessel resistance and increased microvascular tone [14–17]. Also, it has been reported that patients with CSF had higher adrenalin and noradrenalin levels and that TFC was found positively correlated with adrenalin and noradrenalin levels [18]. These findings suggest that adrenergic hyperactivity may have an impact on CSF pathogenesis.

Fragmentation of QRS complex is an easily evaluated non-invasive electrocardiographic parameter. It has been associated with inhomogeneous activation of the ventricles and myocardial conduction delays due to myocardial scar and/or ischaemia, which could predict arrhythmic events as well as death.

It has been demonstrated that fQRS predicts myocardial scar detected by myocardial single-photon emission computed tomography imaging in patients with known or suspected CAD [6]. Myocardial scar is a substrate for reentrant ventricular arrhythmias and is associated with poor prognosis. Das et al. [10] found that event-free survival for an arrhythmic event was significantly lower in the fQRS group than in the non-fQRS group in patients with CAD and dilated cardiomyopathy. fQRS was an independent predictor of an arrhythmic event. In addition, the presence of fQRS was found to predict an increased mortality and recurrent cardiac events than either Q wave alone or resolved Q wave without QRS fragmentation [10, 19].

It has been shown that CSF can be the cause of transient myocardial hypoperfusion in patients with angina and normal coronary arteries [17]. QT dispersion, indicating increased

risk for ventricular arrhythmias and cardiovascular mortality, has been found to be significantly higher in patients with CSF. Whether CSF is associated with fQRS is unknown. In our study, the frequency of fQRS complexes was higher in patients with CSF (31.7% vs. 6.8%). Additionally, the presence of CSF was found to be an independent determinant of fQRS. Fragmented QRS may be derived from the effects of myocardial ischaemia or scar on myocardial electricity at the cellular level in patients with CSF. A poor myocardial perfusion may not protect against ischaemia and the occurrence of micro infarcts. Thus, CSF may be responsible for depolarisation abnormalities in these patients.

In previous reports, diffuse intimal thickening of the coronary arteries and carotid intima-media thickness were positively correlated with TFC in patients with CSF [14, 20]. These studies reported that the degree of atherosclerosis is a determining factor of CSF. In our study, there was no significant association between TFC of involved vessels and the presence of fQRS. Additionally, we have not found a relation between the presence of fQRS and an increasing number of vessel involvements. It seems that the presence of fQRS is not affected by the degree of flow rate of the coronary artery.

Because CSF is associated with coronary atherosclerosis, it can be influenced by cardiovascular risk factors. Several studies have reported that CSF is related to metabolic syndrome, current smoking, male sex and obesity [1, 21, 22]. In other reports, patients with CSF showed no significant differences in risk factors from the control group [12, 14]. In our study, hypertension was more common in the CSF group. However, no significant differences were observed for age, gender, diabetes mellitus, smoking, or lipid profile.

We have some limitations in this study. The overall sample size is small. Patients were not followed prospectively for arrhythmic episodes that may help to determine the significance of fQRS as a risk stratification tool.

CONCLUSIONS

Fragmented QRS, indicating increased risk for arrhythmias and cardiovascular mortality, was found to be significantly higher in patients with CSF. The presence of fQRS on ECG may be an indicator of myocardial damage in patients with CSF. Further long-term prospective studies are needed to establish its significance as a possible new risk factor in patients with CSF.

Conflict of interest: *none declared*

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Fragmentacja zespołu QRS w 12-odprowadzeniowym EKG u chorych ze zwolnionym przepływem wieńcowym

Hale Yilmaz[1], Baris Gungor[1], Tugba Kemaloglu[1], Nurten Sayar[1], Betul Erer[1], Mehmet Yilmaz[2], Nazmiye Cakmak[1], Ufuk Gurkan[1], Dilaver Oz[1], Osman Bolca[1]

[1]Departments of Cardiology, Siyami Ersek Thoracic and Cardiovascular Surgery Center, Istanbul, Turcja

[2]Departments of Cardiovascular Surgery, Siyami Ersek Thoracic and Cardiovascular Surgery Center, Istanbul, Turcja

Streszczenie

Wstęp: Zwolniony przepływ wieńcowy (CSF) cechuje się opóźnieniem opacyfikacji tętnic wieńcowych przy braku zwężeń w tętnicach nasierdziowych. Istnieją doniesienia, że CSF może powodować dławicę, niedokrwienie mięśnia sercowego i zawał serca. Fragmentacja zespołu QRS (fQRS) jest nieinwazyjnym, łatwym do oceny parametrem elektrokardiograficznym. Uważa się, że fQRS stanowi następstwo zmian aktywności mięśnia sercowego spowodowanych przez blizny i/lub niedokrwienie. Nie wiadomo, czy CSF wiąże się z obecnością fQRS. Stwierdzenie fQRS w badaniu EKG może być wskaźnikiem uszkodzenia miokardium u chorych z CSF.

Cel: Celem niniejszego badania była ocena występowania fQRS u chorych z CSF.

Metody: Do badania włączono 66 pacjentów (średnia wieku 55,5 ± 10,5 roku) z CSF i 44 osób z prawidłowymi tętnicami wieńcowymi, u których nie występowało zwolnienie przepływu wieńcowego (średnia wieku 53 ± 8,4 roku). Defragmentację zespołu QRS definiowano jako obecność dodatkowego załamka R, zawęźlenie załamka R lub S bądź obecność fragmentacji w dwóch sąsiadujących odprowadzeniach odpowiadających obszarowi unaczynienia tętnicy wieńcowej.

Wyniki: Obecność fQRS stwierdzano częściej w grupie chorych z CSF niż w grupie kontrolnej ($p = 0,005$). Nadciśnienie tętnicze występowało istotnie częściej u osób z CSF ($p < 0,001$). Nie wykazano istotnych zależności między obecnością fQRS a zwiększoną liczbą zajętych naczyń. Na podstawie analizy regresji logistycznej stwierdzono, że CSF była niezależnym czynnikiem determinującym występowanie fQRS (OR = 10,848; 95% CI 2,385–49,347; $p = 0,002$).

Wnioski: Wykazano, ze fQRS, świadcząca o zwiększonym ryzyku zaburzeń rytmu i zgonu z przyczyn sercowo-naczyniowych, występowała istotnie częściej u chorych z CSF. Autorzy nie stwierdzili zależności między występowaniem fQRS a zaawansowaniem CSF. Należy przeprowadzić dalsze prospektywne badania w celu określenia znaczenia fQRS jako potencjalnego nowego czynnika ryzyka u chorych z CSF.

Słowa kluczowe: fragmentacja QRS, zwolniony przepływ wieńcowy, choroba wieńcowa

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Adres do korespondencji:
Hale Yilmaz, MD, Barbaros Mah. Zambak Sokak, Kentplus Sitesi D2 blok D: 37 Batiatasehir, Istanbul 34746, Turkey, tel: +90 (216) 688 0188, faks: +90 (216) 418 9649, e-mail: haleyilmaz@tnn.net

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