

The importance of fragmented QRS in the early detection of cardiac involvement in patients with systemic sclerosis

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ABSTRACT

Objective: Systemic sclerosis (SSc) is an autoimmune connective tissue disorder characterized by fibrosis. The prognosis of the disease is bad when clinically symptomatic cardiac dysfunction is occurred, therefore early detection of cardiac dysfunction is important in patients with SSc. The aim of this study was to investigate the frequency of fQRS in superficial electrocardiography in cardiacally asymptomatic patients with SSc and its relation to the systolic pulmonary artery pressure (sPAP).

Methods: This study included 31 cardiacally asymptomatic patients with SSc (23 females, 40.4±9.2 years) and 41 healthy volunteers as the control (31 females, 38.2±11.8 years). The ECGs with 12 derivations and transthoracic echocardiographies of the patients were evaluated. The presence of fQRS in the superficial ECG, and its relation to systolic pulmonary artery pressure (sPAP) were investigated.

Results: The mean sPAP value in the SSc group was observed to be higher than that of the control group (26 mm Hg and 20 mm Hg, respectively, $p<0.001$). The presence of fQRS in the SSc group was more frequent than the control group (55% and 10%, respectively, $p<0.001$). In SSc patients presence of fQRS become relevant with ≥ 24 mm Hg sPAP by 88% sensitivity and 79% specificity.

Conclusion: In our study, the presence of fQRS in SSc patients, were more frequent than in the normal population. Since pulmonary hypertension is the primary cause of mortality in patients with SSc, the correlation of fQRS with sPAP should also be considered.

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Keywords: systemic sclerosis, fragmented QRS, pulmonary hypertension, electrocardiography

Introduction

Systemic sclerosis (SSc) is a chronic autoimmune disorder that leads to diffuse micro-vascular damage and fibrosis in the skin and organs (1). Myocardial fibrosis is the main finding of cardiac involvement in patients with SSc, and is responsible for the majority of the cardiac findings (2). Detection of myocardial fibrosis before the onset of the clinical findings is important for the prevention of life-threatening complications. Delayed enhanced (DE) cardiac magnetic resonance imaging (MRI) may help to determine the patients at high risk of life-threatening arrhythmias by enabling early detection of myocardial fibrosis (3). However, the high cost and difficult access of cardiac MRI limit its usage.

It has been reported in recent studies that the presence of fragmented QRS complexes (fQRS) in the superficial ECG was related to scar and fibrosis (4-8). This study was planned in

order to investigate the importance of fQRS presence in the early detection of myocardial fibrosis in patients with SSc and evaluate the correlation to pulmonary HT which is the primary reason of mortality.

Methods

Healthy control group and patients' group who were directed for cardiac routine control by Antalya Training and Research Hospital, rheumatology clinic were included in this study. Patients with diabetes mellitus, hypertension or ischemic heart disease, or those who smoke were excluded. Patients who have evidence that suggestive of coronary artery disease be slow to take offense to the study. Patients who arrhythmic on the surface ECG findings and had pathological findings in transthoracic echocardiographic examination were excluded from the study. Superficial ECGs with 12 derivations were obtained from the

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patients (filtering range: 0.15-100 Hz, AC filtering 60 Hz, 25 mm/s and 10 mm/mV). fQRS presence was investigated in the superficial ECGs. The presence of fragmented QRS was said in the presence of different RSR' patterns with or without Q waves in two neighbouring derivations (QRS time<120 ms), in the presence of an additional R wave (R' wave) or notching within the S wave, or in the presence of more than 1 R waves without typical bundle branch block (Fig. 1) (9). Estimated systolic pulmonary artery pressure (sPAP) was determined upon echocardiographic tricuspid insufficiency.

Statistical analysis

Data were analyzed with the SPSS software version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as frequency and percentage. The χ^2 test and Fisher's exact test were used to compare categorical variables. The Kolmogorov-Smirnov test was used to assess the distribution of continuous variables. Student's t-test was used for variables with normal distribution and the values were presented as mean±SD. Continuous variables without normal distribution were analyzed using Mann-Whitney U test and obtained values were presented as median (50th) values and interquartile ranges (25th and 75th). Multivariate logistic regression analysis was used to evaluate the independent associates of the risk of systemic sclerosis. Parameters with a p value of less than 0.1 in univariate analysis were included in the model. Receiver operating characteristics (ROC) analysis was used to determine the cut-off value and the sensitivity/specificity of PAP. The odds ratios (OR) and 95% confidence intervals (CI) were calculated. A two-tailed p value of <0.05 was considered statistically significant.

Results

This study included 31 cardiacallly asymptomatic patients with SSc (23 females, 40.4±9.2 years) and 41 healthy volunteers as the control (31 females, 38.2±11.8 years). The echocardiographic parameters and fQRS frequencies in superficial ECGs of both groups were compare (Table 1). No significant difference was observed between groups regarding age, gender, left ventricular ejection fraction (EF), left atrium, left ventricle, right atrium and right ventricle diameter (p>0.05). The mean sPAP value of the patients in the SSc group was detected to be higher than that of the control group (26 mm Hg and 20 mm Hg, respectively, p<0.001). All of the participants were in sinus rhythm. The presence of fQRS in the SSc group was more than that of the control group (55% and 10%, respectively, p<0.001) (Table 1). Significant difference was observed between the groups with and without fQRS regarding the sPAP value in the SSc group (32 mm Hg and 20 mm Hg, respectively, p<0.001) (Table 2). In SSc patients presence of fQRS become relevant with ≥24 mm Hg sPAP by the 88% sensitivity and 79% specificity (Fig. 2).

A significant correlation was found in univariate logistic regression analysis (OR, 11; 95% CI, 3-39; p<0.001) and multivariate analysis (OR, 5.8; 95% CI, 1.4-23.2; p=0.014) between the

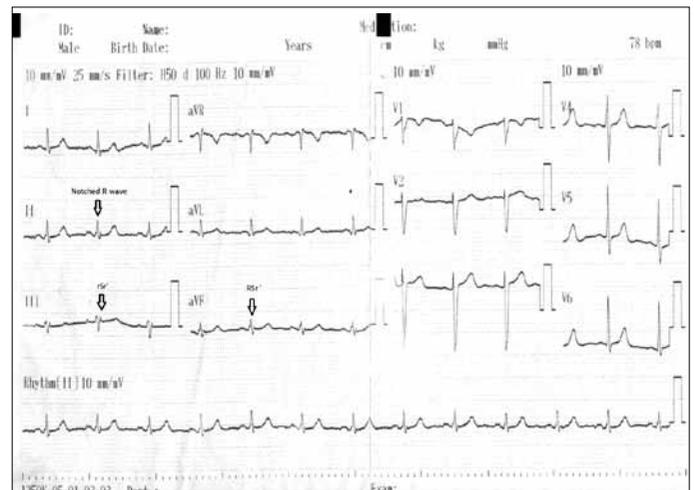


Figure 1. The fQRS on 12-lead ECG was defined by the presence of fragmented QRS, notched R or S wave, or RSR' pattern without any bundle branch block, in at least 2 contiguous leads in one of the coronary artery territories (LAD- lead V₁ to V₆, LCx- lead I, aVL and V₆, and RCA-lead II, III and aVF)

LAD - left anterior descending coronary artery; LC - circumflex coronary artery; RCA - right coronary artery

Table 1. Demographic characteristics with and without systemic sclerosis

	All (n=72)	SSc (-) (n=41)	SSc (+) (n=31)	P
Age, years	39±11	38±12	40±9	0.403
Male gender, n (%)	18 (25%)	10 (24%)	8 (26%)	0.891
sPAP, mm Hg	22 (19-28)	20 (18-24)	26 (20-36)	<0.001
LVEF, %	65 (60-66)	65 (60-66)	65 (60-65)	0.561
fQRS present	21 (29%)	4 (10%)	17 (55%)	<0.001
Which show a normal distribution mean±SD, not show a normal distribution median (25 th and 75 th percentile)				
LVEF - left ventricular ejection fraction; sPAP - systolic pulmonary arter pressure				

presence of SSc and presence of fQRS. A significant correlation was found in univariate logistic regression analysis (OR, 1.2; 95% CI, 1.1-1.3; p=0.001) and multivariate analysis (OR, 1.1; 95% CI, 0.9-1.2; p=0.083) between the presence of SSc and sPAP increase (per mm Hg).

Discussion

Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disorder characterized by microvascular dysfunction and fibrosis (1). fQRS may be observed in the ECG in situations causing non-homogeneous depolarization such as fibrosis, scar or ischemia in the myocardium (4-8). In our study, fQRS was detected in 55% of the superficial ECGs of the patients with SSc, which was 10% in the control group. Furthermore, the presence of fQRS was determined to be related to the increase in sPAP. Therefore, it was concluded that the early detection of myocardial fibrosis may be possible by investigating the presence of fQRS in the superficial ECG before the onset of clinical findings in cardiacallly asymptomatic patients with SSc.

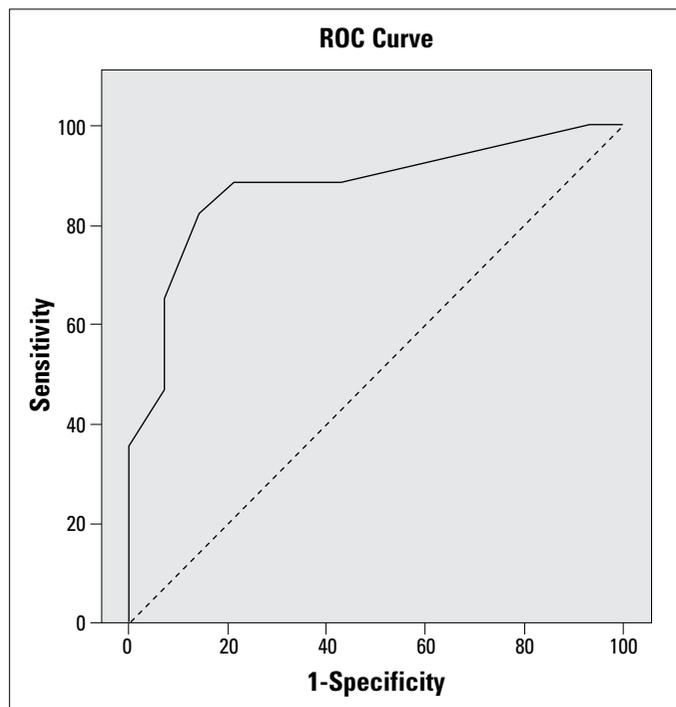


Figure 2. In SSc patients presence of fQRS become relevant with ≥ 24 mm Hg sPAP by the 88% sensitivity and 79% specificity (Area under the curve=0.874, $p < .001$)

Table 2. Significant difference was observed between the groups with and without fQRS regarding the mean sPAP value in the SSc group

SSc patients	All (n=31)	fQRS (-) (n=14)	fQRS (+) (n=17)	P
sPAP, mm Hg	26 (20-36)	20 (20-23)	32 (26-40)	<0.001

sPAP - systolic pulmonary arter pressure

The cardiac findings are observed in 15-35% of the patients with SSc (10, 11). Whole layers of the heart may be affected; pericardial effusion, arrhythmia, transmission defect, myocardial ischemia, myocardial hypertrophy, cardiac failure and rarely valve defects may be observed (2). However, most of the cardiac findings are subclinical, and if these findings become evident, the prognosis of the disease bad and response to the treatment is limited. Therefore, early detection of cardiac involvement is important (12). It has been reported that cardiac MRI or tissue Doppler echocardiography (TDI) may be used for the early detection of cardiac dysfunction in SSc (13, 14). In our study, the presence of fQRS were more frequent on the surface ECG, although transthoracic echocardiography findings were within normal limits.

The myocardial involvement may either be primary in the patients with SSc or secondary to the pulmonary or systemic hypertension. The main cardiac finding of the disease is myocardial fibrosis (2, 15-17). Myocardial fibrosis may either have a linear or a patch-like pattern, both ventricles are affected, primarily diastolic relaxation is impaired. In this period when the systolic function is maintained, early myocardial dysfunction may be evaluated via TDI or MRI. In a study by Tzelepis, et al. (3),

myocardial fibrosis was detected in 66% of the patients by DE-MRI. In that study, late enhancement (LE), which is the finding of fibrosis, was detected typically within the basal and median segments of the left ventricle, subendocardium and epicardium, and generally with a linear pattern. No significant difference was observed between the limited SSc and diffuse type SSc regarding the grade of fibrosis. It was reported that abnormal findings in Holter ECG were more frequent in those with LE (3). In our study, the fQRS frequency, which was accepted as the predictor of fibrosis in patients with SSc was 54.8%, this rate was similar to the rate of myocardial fibrosis reported in the study above.

Foci of fibrosis are ideal substrates for ventricular arrhythmias in patients with SSc. Therefore, annual Holter ECG is recommended for the early detection of arrhythmias. The most common arrhythmic finding observed in the Holter ECG is premature ventricular contractions (PVC). It has been reported that patients with frequent PVCs had higher risk of sudden death than those without PVC (18). In the study of Plastiras et al. (19) PVC (67%), atrial fibrillation and supraventricular tachycardia (20-30%), discontinuous ventricular tachycardia (7-13%) were detected in patients with SSc. Similarly, increases in the P wave dispersion which is an independent predictor of atrial fibrillation and interatrial electro-mechanical delay were reported (20). It has been reported in another study that ventricular late potentials were more frequent in the ECGs with signal mean, and these regions might be substrates for malignant arrhythmias in patients with SSc (21). In our study, the relationship of the presence of fQRS with arrhythmias could not be assessed, because they were all asymptomatic and there were no cardiac Holter ECG recordings.

The main pulmonary complications observed in patients with SSc are pulmonary fibrosis and pulmonary hypertension (22, 23). Pulmonary hypertension may be observed not only due to pulmonary arterial hypertension in SSc, but also as a result of interstitial AC disease or cardiac involvement (24-27). Early detection of the pulmonary arterial hypertension and interstitial pulmonary disease which are the most frequent causes of death in SSc, is also important for the prevention of secondary damage to the heart. For this reason, the patients are recommended echocardiographic sPAP measurement, pulmonary vascular resistance measurement, TAPSE (post-systolic tricuspid annular movement) measurement and respiratory function test (28). In our study, systolic pulmonary artery pressure estimated by Doppler echocardiography was normal, though it was higher than control group. The sPAP level was over 24 mm Hg in the majority of the patients with fQRS detection. This may be advisory for a closer follow-up of these patients with regard to pulmonary hypertension.

It has been reported in recent studies that, fQRS in superficial ECG was more frequent among patients with rheumatoid arthritis and ankylosing spondylitis compared to the normal population and suggested that it may be used in the early detection of cardiac involvement in these patients (29, 30).

Study limitations

Since the study did not include the follow-up of the cases, the effect of fQRS on the prognosis could not be evaluated. In evaluation of cardiac fibrosis, cardiac MR is not to be in use for not being present.

Conclusion

The presence of fQRS in SSc patients, were more frequent than in the normal population. Since pulmonary hypertension is the primary cause of mortality in patients with SSc, the correlation of fQRS with sPAP should also be considered.

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