Original Article

Exploring the Impact of Fragmented QRS on Ejection Fraction and Other Echocardiographic Parameters in Systemic Sclerosis Patients: A Retrospective Cohort Study

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Highlights

- FQRS has no significant effect on EF and other echocardiographic parameters over at least a three-year interval in SSc patients.

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ABSTRACT

Background: Systemic sclerosis (SSc) is an autoimmune connective tissue disorder that leads to fibrosis of the skin and internal organs. Fragmented QRS (fQRS) is an important electrocardiographic (ECG) finding related to myocardial fibrosis. This study aimed to evaluate the effect of fQRS on ejection fraction (EF) and other echocardiographic parameters in individuals diagnosed with SSc.

Methods: This was a retrospective cohort study consisting of 52 patients with fQRS as the case group and 60 patients without fQRS as the control group. The characteristics and echocardiographic parameters of the patients from a minimum of a 3-year interval were recorded. All data were compared between the two groups using SPSS software, version 20.0 (IBM Corp).

Results: There were no significant differences in demographics, paraclinical results, and echocardiographic parameters, including average EF, pulmonary hypertension, and tricuspid regurgitation velocity, between cases and controls at the beginning and end of the follow-up.

Conclusion: Based on our results, fQRS had no significant effect on EF and other echocardiographic parameters over at least a 3-year interval in SSc patients. However, additional research with longer follow-up periods and larger sample sizes is needed to characterize the association fully.

Keywords: Fragmented QRS; FQRS; Ejection Fraction; Systemic Sclerosis; Scleroderma; Pulmonary Hypertension

Introduction

Systemic sclerosis (SSc) is an autoimmune connective tissue disorder that leads to microvascular and macrovascular damage, as well as fibrosis of the skin and internal organs.[1]

Cardiac involvement is one of the common manifestations of SSc, with a prevalence rate of 15% to 35% and a mortality rate of 20% to 30%.[2-4] SSc can affect various parts of the heart, including the myocardium, pericardium, and endocardium. These involvements may result in systolic and diastolic dysfunction, leading to low ejection fraction (EF), along with the development of arrhythmias and valvulopathies.[5-7]

Fragmented QRS (fQRS) is an important electrocardiographic (ECG) finding defined by an additional R wave (R') or notching within the QRS complex.[8] It can be related to myocardial fibrosis, ischemic changes, and conduction defects.[9,10] The presence of fQRS in people with suspected or known coronary artery disease significantly elevates the risk of cardiac events and all-cause mortality.[9]

Previous studies have shown that fQRS is more prevalent in patients with SSc than in healthy populations.[11] Considering this fact and the association between fQRS and cardiac fibrosis, individuals with SSc are more likely to develop myocardial scarring.[12] These fibrotic changes may have the potential to decrease EF and lead to ventricular dysfunction.[9,10,13] Nonetheless, there is a lack of research investigating the effect of fQRS on EF in an SSc population. Accordingly, the objective of this study was to evaluate the effect of fQRS on EF and other echocardiographic parameters in individuals diagnosed with SSc.

Materials and Methods

Study Design and Population

This retrospective cohort study, based on Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, enrolled a total of 112 patients with SSc.[14] The STROBE checklist is provided in Supplementary File 1. The included participants were patients with SSc who were referred to the rheumatology clinic at Shariati Hospital and had been under observation for a minimum of 3 years. The case group comprised 52 patients with fQRS, and the control group involved 60 patients without fQRS. The patients' diagnoses were based on the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) systemic sclerosis classification criteria.[15] They had normal Framingham risk scores, no history of previous atherosclerotic cardiovascular diseases or arrhythmias, and normal baseline EFs. All individuals underwent ECG and echocardiography every 6 to 12 months. Participants exhibiting regional wall motion abnormality (RWMA) on their echocardiography underwent either computed tomography angiography (CTA) or single-photon emission computed tomography (SPECT). After ischemic events were ruled out, cardiovascular magnetic resonance imaging (CMR) was conducted for further assessment.

Procedures

Twelve-lead ECGs were obtained using the same instrument with the record set at 25 mm/s and a voltage calibration of 1 mV/cm and were analyzed by a single experienced cardiologist. The fQRS is characterized as a narrow QRS complex (<120 ms) with a notch between the Q wave and the S wave in at least two contiguous leads, provided that bundle branch blocks (BBBs) were excluded.[8]

The same cardiologist performed echocardiography with the GE Vivid S5 ultrasound system. Data acquisition was performed with a 3.5-MHz transducer at a depth of 16 cm in the parasternal and apical views (standard parasternal short-axis from the midventricular level, apical long-axis, two-chamber, and four-chamber images).

CMR was conducted by a second cardiologist with the Philips Ingenia 1.5 Tesla MRI system. The protocol included cine imaging for cardiac function assessment, late gadolinium enhancement for tissue characterization, and flow imaging for blood flow dynamics. The patient was positioned supine, and ECG gating ensured precise synchronization with the cardiac cycle. Cine images were acquired in standard views, and late gadolinium enhancement imaging featured an adjusted

inversion time. The comprehensive examination provided detailed information on cardiac structure and function.

Data Collection and Outcomes

The characteristics of the patients, including age, sex, SSc subtype, and disease duration, were documented. Disease duration was calculated from the development of the Raynaud phenomenon to the time of the study. Additional factors, such as the presence of interstitial lung disease based on high-resolution CT, forced vital capacity assessed via spirometry, and plasma hemoglobin, were recorded. The echocardiographic parameters from at least a 3-year interval, including EF, systolic pulmonary arterial pressure (sPAP), tricuspid regurgitation velocity (TRV), RWMA, diastolic dysfunction, and pericardial effusion, were also recorded. Pulmonary hypertension (PHTN) and high TRV were defined as an sPAP of more than 40 mm Hg and a TRV exceeding 2.8 m/s, respectively.[16,17]

Statistical Analysis

All demographic, paraclinical, and echocardiographic parameters were compared between cases and controls using SPSS software version 20.0 for Windows (IBM). Continuous data are reported as mean (SD) and were compared using the independent samples t test. Categorical data are reported as frequencies and were compared using the χ^2 test. A P value of less than 0.05 was considered statistically significant.

Results

The study followed up 52 cases and 60 controls for at least 3 years. During this period, no patients converted from a negative fQRS status to a positive one, and none developed new-onset arrhythmias. The median follow-up was 5.1 years (95% CI, 3.00 to 8.73). As shown in (Table 1), there were no significant differences in age and sex distributions, disease characteristics, or paraclinical results between the two groups.

Table 1. The demographics and most recent paraclinical results of the studied patients

	Cases (n=52)[1]	Controls (n=60)[1]	P[2]
Female	45 (86.5%)	56 (93.3%)	0.341
Mean age, y	51.6 (10.3)	50.7 (13.0)	0.700
Disease duration, y	16.4* (7.9)	15.9** (7.3)	0.777
Follow-up, y	5.2 (1.6)	5.2 (1.9)	0.851
SSc subtype			
lSSc	17 (32.7%)	21 (35.0%)	0.843
dSSc	35 (67.3%)	39 (65.0%)	
Mean FVC, %	74.4*** (17.9)	74.8**** (19.7)	0.906
Mean Hb, g/dL	12.8 (1.4)	12.9 (1.5)	0.661
ILD	29/51 (56.9%)	32/58 (55.2%)	1.000

[1] Mean (SD); n (%)
[2] The Welch two-sample *t* test; the Fisher exact test
* n=44 ** n=55 *** n=50 **** n=58
dSSc: diffuse systemic sclerosis; FVC: forced vital capacity; Hb: hemoglobin; ILD: interstitial lung disease; lSSc: limited systemic sclerosis; SSc: systemic sclerosis

The comparison of the echocardiographic outcomes between the two groups at baseline and the 3-year follow-up is demonstrated in (Table 2). There were no significant differences in average EF and the number of patients with PHTN, high TRV, diastolic dysfunction, or pericardial effusion between cases and controls at the beginning and end of the follow-up.

Table 2. The comparison of the echocardiographic parameters at baseline and follow-up between cases and controls

	Cases at Baseline[1] (n=52)	Controls at Baseline[1] (n=60)	P[2]	Cases at Follow-Up[1] (n=52)	Controls at Follow-Up[1] (n=60)	P[2]
Mean EF, %	56.2 (2.6)	55.8 (2.6)	0.402	53.9 (5.7)	53.6 (3.6)	0.777
PHTN	1 (1.9)	3 (5.0)	0.622	3 (5.8)	10 (16.7)	0.084
High TRV	6/31 (19.4)	6/27 (22.2)	1.000	7/34 (20.6)	8/20 (40.0)	0.207
RWMA	0 (0.0)	0 (0.0)	-	6 (11.5)	0 (0.0)	0.009
DD	4 (7.7)	3 (5.0)	0.703	3 (5.8)	5 (8.3)	0.722
PE	1 (1.9)	3 (5.0)	0.622	1 (1.9)	0 (0.0)	0.464

[1] Mean (SD); n (%)

[2] The Welch two-sample *t* test; the Fisher exact test

EF: ejection fraction; PHTN: pulmonary hypertension; TRV: tricuspid regurgitation velocity; RWMA: regional wall motion abnormality; DD: diastolic dysfunction; PE: pericardial effusion

According to echocardiography, six patients with RWMA at the follow-up echocardiography underwent CMR, and their results are presented in Table 3. All were fQRS-positive females with a mean age of 49.2 ± 6.5 years. Half of them had diffuse SSc, while the other half had limited SSc. Two of them had abnormal EFs (<55%), and one had developed PHTN at the 3-year echocardiography compared with their baseline results.[16,18]

Table 3. The demographics, follow-up echocardiographic parameters, and CMR results of patients with RWMA

FQRS	Sex	Age (y)	Disease Duration (y)	SSc Subtype	EF (%)	sPAP (mm Hg)	TRV (m/s)	DD	PE	CMR Result
Present	F	52	20	dSSc	55	34	2.7	No	No	Diffuse myocardial edema
Present	F	45	14	dSSc	35	35	2.3	No	No	Patchy subepicardial and interstitial fibrosis
Present	F	43	22	lSSc	55	44	2.8	No	No	Subepicardial to midwall pattern of fibrosis
Present	F	60	40	lSSc	55	36	2.8	No	No	Global silicon enhancement ratio of myocardium over skeletal muscle
Present	F	51	N/A	lSSc	45	36	2.4	Yes	No	Subendocardial enhancement in the basal inferolateral segments
Present	F	44	24	dSSc	55	25	1.1	No	No	No myocardial fibrosis

fQRS: fragmented QRS; CMR: cardiovascular magnetic resonance imaging; RWMA: regional wall motion abnormality; SSc: systemic sclerosis; EF: ejection fraction; sPAP: systolic pulmonary arterial pressure; TRV: tricuspid regurgitation velocity; dSSc: diffuse systemic sclerosis; lSSc: limited systemic sclerosis; F: female; N/A: not available; DD: diastolic dysfunction; PE: pericardial effusion

Discussion

According to existing literature, the prevalence of fQRS is higher in patients with SSc compared with healthy individuals.[11] Further, fQRS is associated with myocardial fibrosis and ischemic changes and may lead to ventricular dysfunction.[9,10] Nevertheless, in two case-control studies of healthy individuals with preserved EF, there was no significant difference in EF between groups with and without fQRS, whereas the positive fQRS group exhibited a significantly lower global longitudinal strain (GLS) compared with the negative fQRS group.[19,20]

The principal finding of the present study was that fQRS was not associated with EF on echocardiography in patients with SSc for at least 3 years. This is consistent with results from a study

by Tigen et al,[12] who also reported that the presence of fQRS did not have a significant effect on EF among patients with SSc with fQRS, those with SSc without fQRS, and healthy individuals.[12]

Based on our findings, there were no significant differences in the number of patients with PHTN, high TRV, diastolic dysfunction, or pericardial effusion between cases and controls. Tigen et al[12] likewise found that systolic pulmonary artery pressure was not significantly associated with fQRS in individuals with SSc. In contrast, Bayar et al[21] reported that mean systolic pulmonary artery pressure was higher in patients with fQRS than in those without fQRS.

The absence of significant differences in EF and other echocardiographic parameters between the two groups suggests that although fQRS may be associated with myocardial fibrosis, it does not necessarily correlate with changes in cardiac function.

Our results indicate that over at least a 3-year period, the average EF in both groups, as well as the incidence of diastolic dysfunction in cases and pericardial effusion in controls, decreased compared with other factors, including the number of patients with PHTN, high TRV, and RWMA. This reduction may be attributable to the treatments, such as vasodilators, administered during this period. Further investigation with larger sample sizes is needed to fully elucidate these alterations and their potential mechanisms.

Similar investigations have been conducted in other populations. For example, GLS values have been shown to be lower in individuals with positive fQRS compared with those with negative fQRS among patients with Behçet disease and subclinical hyperthyroidism.[22,23] In another study, the myocardial perfusion index was significantly higher in patients with subclinical hypothyroidism and positive fQRS than in those without fQRS, and ejection time was longer in individuals with negative fQRS.[24] Additionally, among patients with type 2 diabetes mellitus, a statistically significant difference in left ventricular GLS was identified between fQRS-negative and fQRS-positive groups.[25]

We performed CMR in six patients with RWMA on echocardiography, all of whom were fQRS-positive females. The majority had some degree of fibrosis in either the epicardium or myocardium. However, only two individuals exhibited abnormal EF, and only one developed PHTN after 3 years. Consequently, although the CMR results indicate a relationship between fQRS and cardiac fibrosis, fQRS does not appear to have a significant effect on EF in a population with scleroderma.

Considering the existing literature, no association has been identified between fQRS and decreased EF in patients with SSc to date.[12] Our study, likewise, demonstrated that there were no significant changes in EF, no differences in the number of individuals with PHTN or high TRV, and no emergence of arrhythmias during a minimum 3-year follow-up among the enrolled participants. Thus, the presence of fQRS alone does not appear to be a significant concern for cardiac dysfunction in individuals with SSc, at least over a 3-year period.

The present study has several limitations that should be acknowledged. First, the follow-up duration and limited sample size may constrain the conclusiveness of our findings. Second, because of restricted resources, we were unable to perform CMR for all participants to assess the extent of myocardial fibrosis and limited CMR evaluation to patients who demonstrated RWMA on echocardiography.

Conclusion

In conclusion, fQRS appears to have no significant effect on EF or other echocardiographic parameters over at least a 3-year interval in patients with SSc. However, additional research with longer follow-up periods and larger sample sizes is needed to fully characterize this association.

Declarations:

Ethical Approval

This study was approved by the Administration Committee of the Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran (approval No. IR.TUMS.SHARIATI.REC.1402.144).

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Conflict of Interest

The authors report no conflict of interest.

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