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Regional myocardial dysfunction assessed by two-dimensional speckle tracking echocardiography in systemic sclerosis patients with fragmented QRS complexes

Kursat Tigen, MD,[a] Murat Sunbul, MD,[a,*] Gulsen Ozen, MD,[b] Erdal Durmus, MD,[a] Tarik Kivrak, MD,[a] Altug Cincin, MD,[a] Beste Ozben, MD,[a] Halil Atas, MD,[a] Haner Direskeneli, MD,[b] Yelda Basaran, MD[a]

[a] *Marmara University Faculty of Medicine, Department of Cardiology, Istanbul, Turkey*
[b] *Marmara University Faculty of Medicine, Department of Rheumatology, Istanbul, Turkey*

Abstract

Background: The aim of the study was to explore the relation between regional myocardial dysfunction and fragmented QRS (fQRS) complexes in systemic sclerosis (SSc).
Methods: Fifty-three SSc patients and 26 controls were included. All subjects underwent speckle tracking echocardiography for evaluation of left ventricular (LV) function and ECG to check for fQRS complexes.
Results: SSc patients had significantly lower LV global longitudinal, radial and circumferential strain and twist compared to controls. Thirteen SSc patients had fQRS (DII, DIII, aVF leads in eleven patients and V1 to V5 leads in two patients) and they had significantly lower global longitudinal and circumferencial strain compared to SSc patients with normal QRS. The SSc patients with fQRS in DII, DIII, and aVF leads had impaired longitudinal strain and delay in time to peak longitudinal strain in inferior LV segments compared to those with normal QRS.
Conclusion: fQRS is associated with lower strain measures in SSc patients indicating impairment in LV function.

Keywords: Fragmented QRS; Speckle tracking echocardiography; Systemic sclerosis

Introduction

Systemic sclerosis (SSc) is a connective tissue disease characterized by vascular dysfunction and excessive fibrosis involving the skin and visceral organs [1]. Cardiac manifestations are common in SSc, with an estimated clinical prevalence of 15%–35% and when clinically evident, are often associated with mortality [2,3]. However, in the majority of SSc patients, cardiac manifestations may remain subclinical [4–6]. Thus, monitoring of myocardial involvement represents an important aspect of the disease management [7]. Two-dimensional (2D) speckle-tracking echocardiography (STE) has been proposed as a sensitive method for the evaluation of myocardial involvement in SSc patients [8,9]. Spethmann et al. [10] showed that left ventricular (LV) deformation analysis by STE was a sensitive method to detect early LV systolic impairment primarily in the basal segments in patients with SSc having preserved LV ejection fraction (EF).

Cardiac involvement in SSc does not only involve the myocardium but also the conduction system [11]. Ventricular late potentials were proposed to be used as an early index of myocardial fibrosis in SSc [12]. Morelli et al. [13] explored the role of late ventricular potentials in detecting early myocardial involvement in SSc patients and reported that signal averaged electrocardiography (ECG) was a sensitive and inexpensive technique in the clinical assessment and follow up of patients with SSc. While fragmented QRS (fQRS) is shown to be associated with regional myocardial damage and increased cardiovascular morbidity and mortality in patients with coronary artery disease [14,15], the association between fQRS and regional myocardial dysfunction has not been studied in SSc patients.

The aim of this study was to evaluate deformation analyses derived from 2D STE for early detection of LV regional myocardial dysfunction in patients with SSc and to explore a relation between myocardial function and fQRS complexes present in surface ECG of SSc patients.

* Corresponding author at: Fevzi Cakmak Mahallesi, Mimar Sinan Caddesi, No: 41, Ustkaynarca, Pendik, İstanbul, Turkey.
E-mail address: drsunbul@yahoo.com.tr

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Materials and methods

The investigation complies with the principles outlined in the Declaration of Helsinki. The study was approved by the Local Ethics Committee and all participants gave written informed consent before participating.

Sixty-two consecutive patients with SSc who were followed by the Department of Rheumatology were enrolled to the study. The diagnosis of SSc was based on the American Rheumatism Association criteria [16]. After the exclusion of the patients with coronary artery disease, valvular heart disease, cardiomyopathy, arrhythmias or conduction disorders, LV systolic dysfunction (LV EF < 55%), and diabetes mellitus, peripheral arterial disease, and chronic obstructive pulmonary disease, the remaining 53 SSc patients were included in the study. Twenty-six healthy subjects were included into the study as control group.

Standard echocardiography and 2D speckle tracking echocardiography

All patients underwent a complete echocardiographic study with a commercially available echocardiography device (Vivid 7, GE Vingmed Ultrasound AS, Horten, Norway) by a single experienced cardiologist. 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 midventricular level, apical long-axis, two-chamber and four-chamber images). Standard M-mode, 2D and color coded TDI images were obtained during breath hold, stored in cine loop format from 3 consecutive beats and transferred to a workstation for further offline analysis (EchoPAC 6.1; GE Vingmed Ultrasound AS). Gain settings, filters, and pulse repetitive frequency were adjusted to optimize color saturation, and a color Doppler frame scanning rate of 100–140 Hz was used for color TDI images. Cardiac dimensions were measured according to the guidelines of the American Society of Echocardiography and LV EF was calculated by biplane Simpson's method [17].

Multidirectional analysis of LV strain (in the radial, circumferential, and longitudinal directions) was performed using 2D speckle-tracking imaging as previously described [18,19]. All of the images were recorded with a frame rate of at least 30 frames per seconds to allow for reliable operation of the software (EchoPac 6.1). The speckles, natural acoustic markers equally distributed within the myocardium, can be detected and tracked on the standard grayscale 2D images. Myocardial strain can be calculated by measuring the change of the position of the speckles within a myocardial segment along the cardiac cycle. The assessment of global radial strain (GRS) and global circumferential strain (GCS) was performed by applying 2D speckle-tracking imaging to the parasternal short-axis views of the LV. The midventricular short-axis of the LV was divided into six segments, and the values of GRS and GCS were derived from the average of the six segmental peak systolic strain values. The assessment of longitudinal peak systolic strain was performed by applying 2D speckle-tracking imaging to the apical two- and four-chamber views of the LV. The LV was divided into six segments in each apical view. The values of global longitudinal strain (GLS) were derived from the average of the six segmental peak systolic longitudinal strain values. For the measurement of timing, the onset of the aortic valve closure was used as the reference point which was estimated automatically by the software and adjusted by the user if needed. Time to peak longitudinal systolic strain was quantified and displayed automatically by the software as previously described [20].

A recent study [21] demonstrated LV peak systolic longitudinal strain value of 18.6% ± 0.1% as the average of nearly 250 volunteers without evidence of cardiovascular disease. We used this value as a cut-off point to indicate patients with reduced LV peak systolic longitudinal strain.

LV 'twist' was defined as the net difference of LV peak systolic 'rotation' between basal (clockwise) and apical (counterclockwise) short axis planes. The value was expressed in '°'. 'Untwist' was expressed as a diastolic angular motion of the LV, opposite to twist. 'Untwisting rate' [°/s] was defined as the peak twist rate during early diastole.

For the left atrial (LA) speckle tracking analysis, LA-focused images in apical four-chamber view were obtained. A minimum frame rate of 40 frames per second was required for the reliable operation of this program. For two dimensional speckle tracking strain analysis, a line was manually drawn along the LA endocardial border of the apical four chamber view after contraction, when the LA was at its minimum volume, using the point-and-click approach as previously described [18]. The software then automatically generated additional lines near the atrial epicardium and mid-myocardial line, with the narrowest region of interest (ROI). The ROI then included the entire LA myocardial wall, and a click feature increased or decreased the widths between endocardial and epicardial line for thicker or thinner walls, respectively. The software generated strain curves for each atrial segment. The value of peak early and late diastolic longitudinal strain were determined as left atrial reservoir (LA Res) and conduit (LA Con) function.

Electrocardiographic analysis

The resting 12-lead ECG (0.5 Hz to 150 Hz, 25 mm/s, 10 mm/mV) was analyzed by two independent clinicians who were blinded to echocardiographic data. There was a 97.5% concordance for ECG signs. In case of disagreement, the final diagnosis was achieved by mutual agreement. The fQRS included various RSR′ patterns and was defined by the presence of an additional R wave (R′), notching in the nadir of the S wave, notching of the R wave, or the presence of more than one R′ (fragmentation) in two contiguous leads corresponding to a major myocardial segment. The presence of fQRS in two or more contiguous V1 to V5 leads corresponded to anterior myocardial segments, the presence of two or more fQRS in leads DI, aVL and V5, V6 corresponded to the lateral myocardial segments, and the presence of two or more fQRS in leads DII, DIII and aVF corresponded to the inferior myocardial segments.

Statistical analysis

Statistical analyses were performed using SPSS 20.0 statistical package for Windows. Continuous data were