Arch Cardiovasc Imaging. 2014 August; 2(3): e20735. DOI: 10.5812/acvi.20735

Published online 2014 August 5. **Research Article**

Right Ventricular Strain and Strain Rate in Patients With Systemic Sclerosis Without Pulmonary Hypertension

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Received: May 27, 2014; **Revised:** July 28, 2014; **Accepted:** August 3, 2014

Background: Cardiac involvement in Systemic Sclerosis (SSc) is a major risk factor for death. The aim of this study was to evaluate strain-based measures of the right ventricular (RV) systolic function in SSc patients without pulmonary hypertension.
Objectives: The aim of this study was to assess strain-based measures of the RV systolic function in patients with SSc without pulmonary hypertension.
Materials and Methods: Thirty-eight consecutive SSc patients (mean age = 48.1 ± 13 years) with normal pulmonary artery pressure and left ventricular ejection fraction and 27 healthy subjects (mean age = 53.2 ± 10 years) were investigated. The RV systolic strain and strain rate were assessed using standard echocardiography with tissue Doppler imaging (TDI) and compared with the results of the healthy subjects.
Results: In the SSc patients, the RV strain (-19 ± 10 vs. -25 ± 4 %; P = 0.004) and the systolic strain rate (-1.3 ± 0.5 vs. -1.5 ± 0.3, s-1; P = 0.03) were significantly lower than those in the control group.
Conclusions: This study indicated that the RV systolic strain and strain rate can be used to detect early RV systolic dysfunction in SSc patients without pulmonary hypertension. These parameters may be useful for the provision of a more adequate management of SSc patients.

*Keywords:*Right Ventricle; Strain; Systemic Sclerosis

1. Background

Systemic Sclerosis (SSc) is a rare connective tissue disease characterized by microvasculopathy, immune abnormalities, and tissue fibrosis (1). Myocardial fibrosis has been reported in 50-80% of cases in histological studies, yet it is often clinically unrecognized (2). Accordingly, the early detection of cardiac involvement in SSc patients facilitates early medical intervention. Until recently, the left ventricular function was mainly assessed in patients with SSc (3, 4), while the right ventricular (RV) function was often overlooked due to its complex geometry and lack of easily derived and objective functional methods (5, 6). Previous studies showed that subclinical RV involvement in SSc patients was more common than was predicted (7, 8). Tissue Doppler echocardiography with strain and strain rate imaging is a new noninvasive technique for a comprehensive assessment of the RV function, and the spectrum of its potential clinical applications is very extensive. Strain and strain rate data have useful diagnostic and therapeutic applications and can detect myocardial dysfunction at its early sub-clinical stage (8). In patients with pulmonary hypertension, the RV systolic strain and strain rate can predict pulmonary vascular resistance, future right heart failure, and mortality (5, 9). The measurement of strain is a valuable tool for detecting myocardial involvement caused by SSc (10).

2. Objectives

The aim of this study was to assess strain-based measures of the RV systolic function in patients with SSc without pulmonary hypertension.

3. Patients and Methods

Thirty-eight asymptomatic patients with SSc (age > 20 years) without pulmonary hypertension from the Reference Centre for Scleroderma in Shiraz, Iran, according to the American College of Rheumatology criteria and/or LeRoy's classification criteria for SSc (11) and 27 healthy subjects with normal findings of echocardiography were enrolled in this case-control study with informed consent. Noninvasive measurement of the pulmonary artery pressure (PAP) was assessed using echocardiography with the measurement of the tricuspid regurgitation (TR) or pulmonary regurgitation (PR) gradient and adding theright atrial pressure via the measurement of theinferior vena cava collapsibility as recommended by the American Society of Echocardiography guideline. In persons with no TR or PR, the pulmonary acceleration

time (PAT) was measured by placing the pulse Doppler sample volume at the pulmonic valve, and the mean PAP was calculated with the following formula:

Mean PAP = 80-(PAT/2)

Pulmonary hypertension was defined as systolic PAP more than 35 mmHg and mean PAP more than 25 mmHg (1, 2). The Ethics Committee of Shiraz University of Medical Sciences approved the protocol.

3.1. Standard Echocardiography

Standard echocardiography was performed in the left decubitus position using an ultrasound system (General Electric Vivid E 9, equipped with tissue Doppler and strain imaging technique). The RV images were obtained from the apical four-chamber view.

3.2. Right Ventricular Strain and Strain Rate

A three-beat, two-dimensional, digital clip of the apical four-chamber view of the RV (with a frame rate greater than 100 frames per second [fps]) was stored for the offline analysis of the systolic strain and strain rate. The strain and strain rate data were measured by placing the sample volume (2 mm) at the basal segment of the RVfree wall (Figures 1 and 2). Negative strain values indicate tissue shortening/contraction.

3.3. Offline Analysis

All the images were stored digitally for offline analysis (EchoPac PC Dimension, GE Vingmed). B-Mode images of the RVfree wall were used to measure the strain and strain rate in the basal and mid segments of the RVfree wall. The TDI strain and strain rate in each segment were

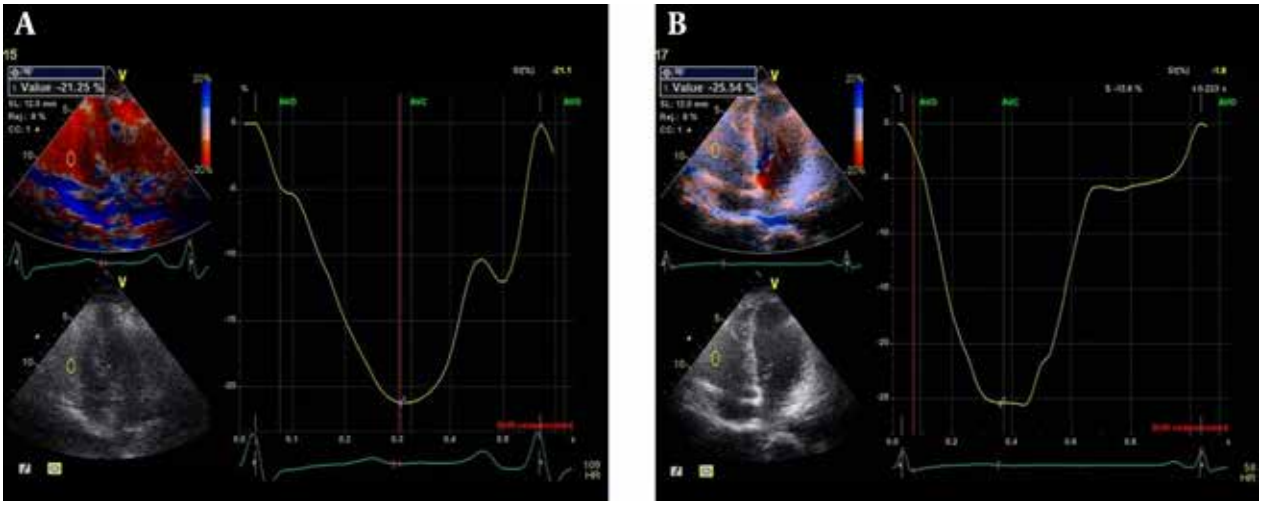

Figure 1. Right Ventricular Longitudinal Systolic Strain In a Patient With SSc (A) And a Normal Subject (B)

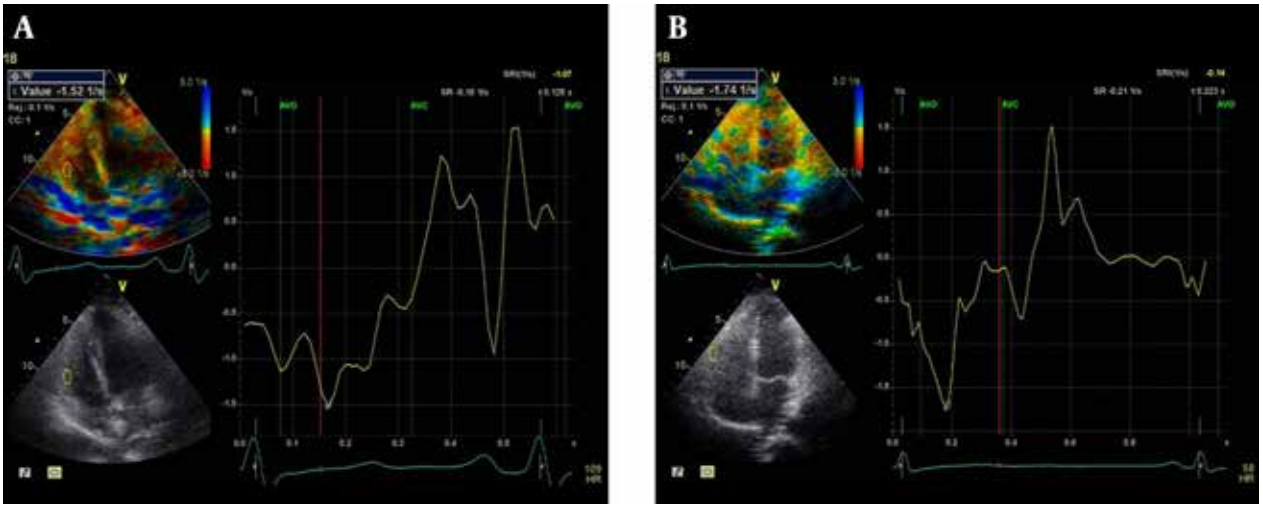

Figure 2. Right Ventricular Longitudinal Systolic Strain Rate In a Patient With SSc (A) And a Normal Subject (B)

Table 1. Right Ventricular Strain And Systolic Strain Rate

	SSc Patients	Control	P Value
Systolic Strain, %	-19 ± 10	-25 ± 4	0.004
Systolic Strain Rate, s^{-1}	-1.3 ± 0.5	-1.5 ± 0.3	0.03

averaged over three consecutive cardiac cycles, and the averages of the basal and mid-segment data were considered as the RV strain and strain rate.

3.4. Inter-and Intra-Observer Variability Analysis

Two echocardiographers, blinded to the clinical data, separately measured the RV strain values from 10 random subjects (5 patients and 5 controls) for inter-observer variability analysis. Intra-observer variability analysis was calculated through the measurement of the strain values twice on two consecutive days by one observer.

3.5. statistical Analysis

The analyses were performed through SPSS 16 for Windows, (SPSS Inc., Chicago, Illinois). The data were tested for normal distribution with the Kolmogorov-Smirnov test. The independent t-test was used to compare the data from the patients and the control subjects. The intra-class correlation coefficient was employed to calculate inter- and intra-observer variability. All the results are presented as mean ± standard deviation (SD). Differences were considered statistically significant if the P value was less than 0.05.

4. Results

The mean ages of the SSc patients and the control group were 48.1 ± 13 and 53.2 ± 11 years, respectively (P = 0.2). In TDI, the RV systolic strain and strain rate were decreased significantly in the patients with SSc (-19.02 ± 8.9% and -1.3 ± 0.5/sec, respectively) compared to those in the control group (-24.6 ± 4.4% and -1.5 ± 0.3/sec, respectively) (Table 1).

The inter-observer variability for the RV strain and strain rate was good with an intra-class correlation coefficient of 0.95 (CI 0.81-0.98) and 0.99 (CI 0.99-1), respectively. The intra-observer variability for the RV strain and strain rate was 0.94 (CI 0.79-0.98) and 0.99 (CI 0.98-0.99), respectively.

5. Discussion

The results of this study indicated that the RV systolic strain and strain rate were significantly decreased in SSc patients without pulmonary hypertension. This finding confirms the primary RV involvement in SSc, independent of pulmonary hypertension, which is in accordance with several studies (7, 12,13). The prognosis of SSc correlates highly with pulmonary hypertension, but primary cardiac involvement is another poor prognostic factor (6). This is why many investigators have evaluated cardiac involvement in SSc patients. For these patients, the RV involvement, even though subclinical, is more common than was previously expected and is associated with worse outcomes of the disease (6). RV dysfunction is a strong predictor of the outcome in patients with SSc (14). A sensitive marker for the detection of early RV dysfunction in patients with connective tissue disease is the RV myocardial deformation (15, 16). Recent reports have shown that thestrain rate and strain measurements are feasible for the identification and quantification of normal and abnormal systemic ventricle regional function (17). The strain rate is a strong index of the myocardium contractility. Matias et al. showed that the strain rate is valuable for detecting early RV function changes in SSc patients with a normal PAP (16). In agreement with our findings, lower systolic and diastolic strain rates than those in controls were detected in SSc patients (4). D'Andrea et al. likewise found that the peak systolic strain rate and strain were both decreased in the basal, middle, and apical RV lateral walls in SSc patients (10). As was stated in prior non-SSc studies, there is a relation between myocardial fibrosis, circulating markers of fibrosis, and reduced myocardial strains (18, 19); therefore, strain measurements may be a valuable tool to identify preclinical myocardial involvement in SSc patients (15). The high prevalence of RV systolic dysfunction in early SSc patients with a normal PAP may be due to intrinsic myocardial involvement (20). In conclusion, noninvasive assessment of the RV systolic strain and strain rate is a cost-effective and safe method to detect the early stages of cardiac involvement in SSc patients without pulmonary hypertension. However, prospective studies are needed for the prognostic implications of these changes.

Acknowledgements

The present article was financially supported by Shiraz University of Medical Sciences with grant No 3222.

Author's Contributions

Alireza Moaref: Study concept and design, Critical revision, Study supervision. Firuzeh Abtahi, Acquisition of data. Shahnaz Shekarforoush: Analysis and interpretation of data, Drafting of the manuscript. Kamran Aghasadeghi; Drafting of the manuscript, Critical revision and Statistical analysis.

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