European Journal of Internal Medicine 20 (2009) 378–382

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original article

# Systolic and diastolic function in patients with systemic sclerosis

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ARTICLE INFO

*Article history:*
Received 12 June 2008
Received in revised form 22 September 2008
Accepted 24 October 2008
Available online 29 November 2008

*Keywords:*
Systemic sclerosis
Tissue Doppler
Cardiac function

ABSTRACT

*Background:* Clinical and epidemiological findings indicate that symptomatic heart disease in patients with systemic sclerosis (SSc) predicts poor prognosis, but cardiac involvement may occur years before clinical manifestation. The aim of this study was to evaluate the cardiac function in patients with SSc and to correlate the echocardiographic parameters with others that quantify the diseases' severity.

*Methods:* Twenty consecutive patients with SSc were investigated with transthoracic echocardiography (TTE). Two dimensional, pulsed Doppler and pulsed tissue Doppler imaging (TDI) techniques were used, in all the patients, to assess the systolic and diastolic function for left ventricle (LV). Correlations were made between echocardiographic measurements and some clinical and serological features of the patients.

*Results:* None of the patients had any clinical signs of cardiac involvement, nor ECG or TTE systolic function impairment; there are significant differences between systemic sclerosis patients and control group for peak *A* velocity ($0.75 \pm 0.22$ vs $0.57 \pm 0.32$, $P = 0.05$), $E/A$ ratio ($1.14 \pm 0.22$ vs $1.48 \pm 0.26$, $P = 0.01$), $E$/Ea ratio ($8.25 \pm 1.57$ vs $7 \pm 2.2$, $P = 0.05$), which account for filling impairment of LV. There are also significant correlations between some other parameters, like the mean duration of Raynaud's phenomenon and $E$/Ea ratio ($r = 0.48$, $P < 0.05$).

*Conclusions:* The analysis of SSc heart disease, mainly at a preclinical level, is important in all the cases as an asymptomatic patient may have diastolic dysfunction which can be treated and should be closely observed.



## 1. Introduction

Systemic sclerosis is a connective tissue disorder of unknown etiology that affects multiple organs. It is characterized by fibrosis of the skin and other visceral organs such as heart, kidneys and lungs.

The pathogenesis of the heart involvement is not yet fully understood, but its complications usually include heart failure, arrhythmias and sudden cardiac death. Symptoms and signs of the heart involvement appear through the course of the disease, but one should not wait for their appearance to diagnose and treat these conditions. The early detection of cardiopulmonary involvement in SSc is clearly desirable, both for optimal treatment and for implementation of preventive measures in the early stages of the disease.

Previous echocardiographic studies in patients with SSc have reported a variable incidence of left ventricular hypertrophy with an uncertain relationship to hypertension [1]. Armstrong et al. then showed that in SSc subclinical changes occur in the myocardium even as early as the onset of the Raynaud's phenomenon [2]. Since then, there is increasing evidence that subclinical diastolic dysfunction, involving both left and right ventricles, occurs in various stages of the disease, often without clinically evident myocardial disease [3,4], but there is still little evidence showing that the diastolic dysfunction could be an early marker of myocardial involvement in patients with SSc.

Autopsy studies showed patchy myocardial fibrosis in both ventricles despite the absence of serious coronary artery lesions [5]. Diastolic dysfunction is related with myocardial fibrosis which starts mainly in subendocardium and correlates with longitudinal myofibrils function [6].

Our study was designed to find correlations between the degree of cardiac involvement and the parameters that quantify the disease severity. We used Doppler echocardiography along with Tissue Doppler imaging (TDI). This is a modern and noninvasive ultrasound technique, easy to use, which allows the measurement of tissue velocities [7]. To be sure that the cardiac involvement was not due to other conditions we excluded from the study the patients with conditions that would affect the heart function such as diabetes mellitus, hypertension, renal involvement and any other systemic disease.

## 2. Materials and methods

### 2.1. Study population

#### 2.1.1. Patients with systemic sclerosis

Twenty consecutive patients (18 women and 2 men) with systemic sclerosis (SSc) according to the previously defined criteria for SSc (2, 3) were studied, according to the following inclusion criteria: age <65 years;

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doi:10.1016/j.ejim.2008.10.011

normal chest radiographs and normal left ventricular systolic function at echocardiography. In all cases, rest ECG was normal.

Exclusion criteria: chronic renal failure, diabetes, malignancy, pregnancy, high blood pressure, ischemic or rheumatic heart disease, cardiomyopathy or congenital heart disease, and any other systemic diseases which could affect the heart. Myositis was also excluded because it may associate CPK elevation which can mimic a heart condition.

Five of the patients fulfilled the criteria for limited disease, and 15 patients fulfilled the criteria for diffuse cutaneous SSc. Mean age (±SD) of the 20 patients with SSc was 52.1 years (±10.4), and the disease had been diagnosed for 46.5±55.7 months. The extent of skin involvement was assessed according to the modified Rodnan model C with eight unilateral sites and a maximum of 16 points [8]. All patients had Raynaud's phenomenon and fifteen patients had sclerodactyly.

The treatment in SSc group included prednisone in small doses, angiotensin-converting enzyme inhibitor, calcium-channel blockers.

### 2.1.2. Controls

For comparison, 15 healthy subjects (12 women and 3 men), with a mean age of 48±12.8 years ($P=0.30$), age-matched and sex-matched, were used as control subjects.

## 2.2. Study protocol

### 2.2.1. Echocardiographic methods

Transthoracic echocardiography was carried out using an ALOKA alpha Premiere device with a 2.5/3.5 MHz transducer, with patients in the left lateral decubitus position. All imaging was carried out by the same ultrasonographer, with standardized machine settings, and in similar conditions, after the patients had rested for 15 min.

Left ventricular diameters (EDD: left ventricular end diastolic diameter, ESD: left ventricular end systolic diameter), end diastolic septal thickness and posterior wall thickness were measured in the parasternal long axis view, according to the criteria of the American Society of Echocardiography [9]. Left ventricular ejection fraction (EF) was calculated with modified Simpson formula from apical two and four chambers views.

Pulsed Doppler transmitral and transtricuspid flow velocity profile was obtained from the apical four chamber view, and the sample volume was positioned at the tip of the mitral/tricuspid valve leaflets. The following parameters were evaluated for diastolic function: peak *E* (peak transvalvular flow velocity in early diastole); peak *A* (peak transvalvular flow velocity in late diastole); *E*/*A* ratio. *E*/*A* ratio 1–2 was defined as normal [10].

Myocardial systolic and diastolic velocities were recorded using the pulsed-wave tissue Doppler imaging technique. Velocities were obtained from the apical four-chamber view. The sample volume was placed at basal level of LV free (lateral) wall, within the mitral annulus, which measures the lateral annulus velocity and the global function of longitudinal cardiac motion (Fig. 1) [11]. Two major negative velocities were recorded with the movement of the annulus toward the base of the heart during diastole: one during the early phase of diastolic myocardial velocity (Ea) (normal range=), and another during the late phase of diastolic myocardial velocity (late diastolic velocity of the mitral annulus [Aa]. We calculated *E*/Ea ratio (normal value was considered under 8) [10]. A major positive systolic velocity was recorded with the movement of the annulus toward the cardiac apex during systole (Sa). All velocities were recorded for five consecutive cardiac cycles, and the results were averaged.

### 2.2.2. Statistical analysis

Continuous variables were expressed as mean (SD). Differences were tested for significance by unpaired Student's *t* test. Upper and lower 95% confidence limits for each variable were calculated from the two tails of the Student's *t* test distribution. We compared the results with control group. A $P$ value <0.05 was considered significant.

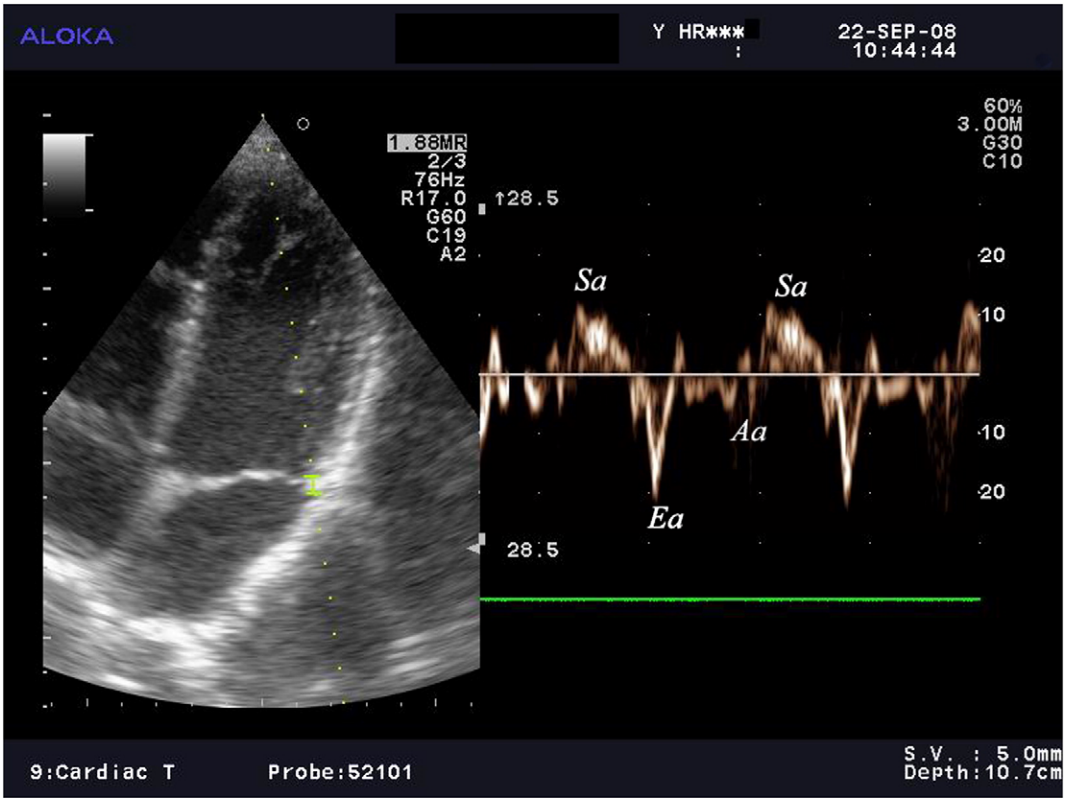


**Fig. 1.** Tissue Doppler imaging technique. Sample placed within mitral annulus. Ea = early diastolic velocity (annular); Aa = late diastolic velocity (annular); Sa = systolic velocity (annular).