Disturbed Right Ventricular Diastolic Function in Patients With Systemic Sclerosis: A Doppler Tissue Imaging Study

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Disturbed Right Ventricular Diastolic Function in Patients With Systemic Sclerosis*

A Doppler Tissue Imaging Study

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Background: **Cardiopulmonary involvement in patients with systemic sclerosis (SSc) carries a poor prognosis, mainly due to pulmonary hypertension and right-heart failure. To date, right ventricular (RV) involvement has not been studied in detail. We therefore assessed RV function in patients with SSc and related the findings to the clinical features of the disease.**

Method: **Twenty-six consecutive patients (21 women) with SSc (mean age, 56 ± 15 years [± SD]) and 25 healthy, age-matched control subjects (21 women) were studied. Doppler echocardiography including Doppler tissue imaging was used to evaluate cardiac function. Pulmonary function was also studied.**

Results: **Compared with control subjects, RV free wall thickness (5.8 ± 1.7 mm vs 3.7 ± 1.1 mm, $p < 0.001$) and right atrial (RA) systolic area (15.9 ± 3.7 cm^2 vs 13.0 ± 2.3 cm^2, $p < 0.01$) were increased in patients with SSc, while the global early diastolic/atrial component velocity ratio was reduced (1.2 ± 0.4 vs 1.7 ± 0.6, $p < 0.01$). The global isovolumic relaxation time (IVRT) [64 ± 23 ms vs 39 ± 13 ms, $p < 0.001$] and regional IVRT (83 ± 40 ms vs 46 ± 24 ms, $p < 0.001$) were prolonged in patients vs control subjects, whereas the RV global filling time was reduced (454 ± 122 ms vs 548 ± 104 ms, $p < 0.01$). RV systolic function and pulmonary pressures at rest were similar in the two groups, but the pulmonary artery acceleration time was reduced (119 ± 34 ms vs 141 ± 29 ms, $p < 0.05$) in patients compared to control subjects. Left ventricular function did not differ between the two groups.**

Conclusion: **Patients with SSc exhibit altered RV diastolic function together with an increase in RV wall thickness and RA area. These findings appear to be early markers of RV disturbance, probably in response to intermittent pulmonary arterial hypertension.**

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Key words: diastolic function; Doppler tissue imaging; echocardiography; right ventricle; systemic sclerosis

Abbreviations: ACE = angiotensin-converting enzyme; DLCO = diffusion capacity of the lung for carbon monoxide; DTI = Doppler tissue imaging; E/A ratio = early diastolic/atrial component velocity ratio; HRCT = high-resolution CT; IVCT = isovolumic contraction time; IVCv = isovolumic contraction velocity; IVRT = isovolumic relaxation time; LV = left ventricle/ventricular; MCTD = mixed connective tissue disease; PA = pulmonary artery; RA = right atrial; RV = right ventricle/ventricular; RVOT = right ventricular outflow tract; SSc = systemic sclerosis; TF = tricuspid flow

Systemic sclerosis (SSc) is a systemic disease characterized by inflammation with involvement of the endothelium and fibroblasts leading to fibrosis.[1] Visceral involvement is well recognized and can result in renal, cardiac, and pulmonary disease with associated worsening of the prognosis.[2] Cardiac complications in SSc include congestive heart failure, arrhythmias, and sudden death,[3–6] but the pathogenesis of cardiac involvement is not yet fully understood.[3] Increased fibroblast activity and collagen deposition,[7] with the development of myocardial fibrosis that may affect both ventricles, are possible etiologic mechanisms.[5] Previously, we reported that left ventricular (LV) hypertrophy[8] and diastolic dysfunction[9] were common in patients with SSc, while systolic function was normal or only slightly impaired.[10] Although there have been reports[11,12] on global right ventricular (RV) diastolic function in SSc, detailed investigations by using Doppler tissue imaging (DTI) have not been performed to date.

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. Unfortu-

nately, patients acquire symptoms and signs in the evolution of the disorder; hence, cardiopulmonary investigations should not await their appearance. In regard to the assessment of pulmonary artery (PA) pressure, use of the tricuspid regurgitation peak gradient, the standard noninvasive method, is technically not possible in all cases.[13–15] Furthermore, it may underestimate the true PA pressure.[16] In the present echocardiographic study, we have applied the technique of DTI in order to identify both global and regional myocardial markers of early diastolic disturbance in RV function in patients with SSc.

Materials and Methods

Study Population

Twenty-six consecutive patients (21 women) with SSc according to the previously defined criteria for SSc[17] were studied. Eighteen of the patients fulfilled the criteria for limited disease, and 2 patients fulfilled the criteria for diffuse cutaneous SSc.[18] Six patients with high titers of ribonucleoprotein antibodies also fulfilled the criteria for mixed connective tissue disease (MCTD).[19] Mean age (± SD) of the 26 patients with SSc was 56 ± 15 years (range, 26 to 78 years), and the disease had been recognized for 11.8 ± 8.7 years (range, 1 to 35 years). The extent of skin involvement was assessed according to the modified Rodnan model C with eight unilateral sites and a maximum of 16 points.[20] All patients except one had Raynaud phenomenon.[21] Seven patients were severely affected with digital pitting scars or ulcers, and two patients had had fingers amputated. Six patients were receiving angiotensin-converting enzyme (ACE) inhibitors and/or β-blockers.

For comparison, 25 healthy subjects (21 women) with a mean age of 56 ± 16 years (range, 25 to 76 years) were used as control subjects. All patients and control subjects gave consent to participate in the study, which was approved by the local ethics committee. Seven of the patients and five control subjects were smokers.

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Echocardiography

Echocardiography was performed using ultrasound (Acuson 128 XP; Acuson; Mountain View, CA) equipped with a 2.5- to 4.0-MHz (V4c; Acuson) transducer and DTI technology. The examination was performed with the subject in the left lateral decubitus position with normal breathing. Tracings were recorded at the end-expiratory phase. Standard two-dimensional parasternal and apical projections were obtained.[22,23] All recordings were performed with a simultaneous superimposed phonocardiogram to detect the pulmonary component of the second heart sound (S_2). All images were recorded at sweep speeds of 50 mm/s and 100 mm/s. From M-mode echocardiography recordings, the following measurements were made on consecutive three beats, according to recommendations of the American Society of Echocardiography.[22] Internal LV end-diastolic and end-systolic diameters, and ventricular septal and posterior wall thickness at end-diastole were all measured. LV fractional shortening was calculated as the difference between diastolic and systolic diameters divided by diastolic dimension. The LV volume was measured and ejection fraction calculated according to the modified Simpson rule using apical four- and two-chamber views.[23]

From RV outflow tract (RVOT), fractional shortening was calculated as the percentage fall in RVOT diameter in systole with respect to that in diastole, as previously described.[24] From the same view position, RV anterior free wall systolic motion and end-diastolic wall thickness were measured. The RV long-axis function was recorded from the apical four-chamber view with the M-mode cursor positioned at the free wall angle of the tricuspid valve annulus.[11] The left atrial (LA) and right atrial (RA) areas were traced manually and measured at end-systole from the two-dimensional apical four-chamber view.

Conventional Doppler Echocardiography Assessment of Global Function

Mitral and tricuspid flow (TF) velocities were obtained with the sample volume placed at the tip of the mitral and tricuspid valve leaflets, respectively. The presence of valvular regurgitation was determined by color Doppler echocardiography. Transtricuspid peak retrograde velocities were recorded using the continuous-wave Doppler technique, and a modified Bernoulli equation was used to estimate the RA-RV peak pressure gradient.[25] PA flow velocity was recorded from the parasternal short-axis view with the sample volume placed at the central position. From the mitral and TF velocity profiles, the following measurements were made according to the recommendations of the American Society of Echocardiography[11,25] (Fig 1): (1) early diastolic/atrial component velocity ratio (E/A ratio); (2) E-wave deceleration time; (3) isovolumic relaxation time (IVRT), measured as the time interval from S_2 to the onset of the E-wave; and (4) mitral and tricuspid filling times, measured as the time intervals from the onset of E-velocity to the cessation of A-velocity. Tricuspid peak retrograde velocities were detected by color Doppler echocardiography and recorded using the continuous-wave Doppler technique. The RA-RV peak pressure gradient was estimated using a modified Bernoulli equation from three consecutive beats. From the pulmonary valve flow recording, we measured acceleration time as the interval between the onset to its peak velocity point, while pre-ejection was measured as the time from the onset of the Q wave on an ECG to the onset of ejection. The ejection time was measured from the onset to the end of ejection flow.

DTI Assessment of Regional Myocardial RV Function

Myocardial systolic and diastolic velocities were recorded using the pulsed-wave DTI technique. Velocities were obtained from

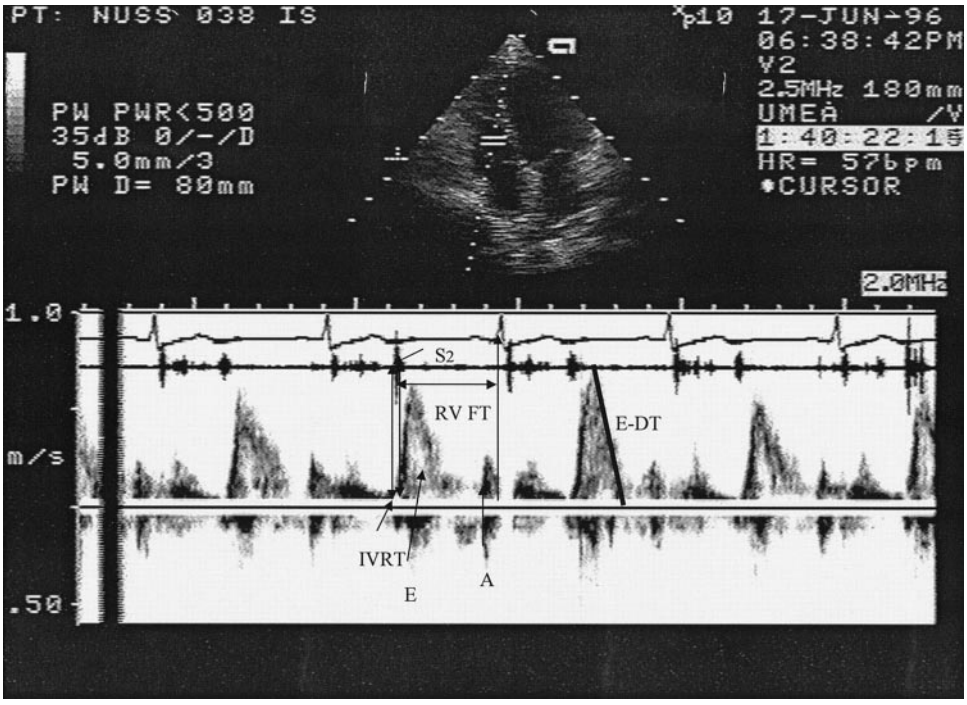

FIGURE 1. Global RV diastolic velocities and timings. E = early diastolic velocity; A = late atrial diastolic velocity; E-DT = E-wave deceleration time; S_2 = second heart sound; RVFT = RV filling time.

the apical four-chamber view. The sample volume was placed at the basal level of the RV free wall. DTI was used to measure myocardial velocities and time intervals, as previously described.[26] From DTI recordings (Fig 2, *left*), the following measurements were made: (1) peak isovolumic contraction velocity (IVCv); (2) peak systolic velocity; (3) peak early and atrial diastolic velocities (and the E/A ratio); (4) isovolumic contraction time (IVCT), the time interval from the end of atrial to the onset of systolic flow components; and (5) IVRT, the time interval from pulmonary component of S_2 to the onset of early diastolic velocity. All measurements were taken from three beats, and the mean value was used. One investigator (E.K.) coded all the patients and control subjects, and another investigator (P.L.) blindly analyzed the echocardiographic data.

Pulmonary Function Tests

Of the 26 patients, 22 patients (15 with limited-type SSc, 5 with MCTD, and 2 with diffuse-type SSc) underwent lung function testing within period of 6 months before and 2 months after the echocardiography examination. Of these 22 patients, none were being treated for pulmonary disease. It was assumed that major

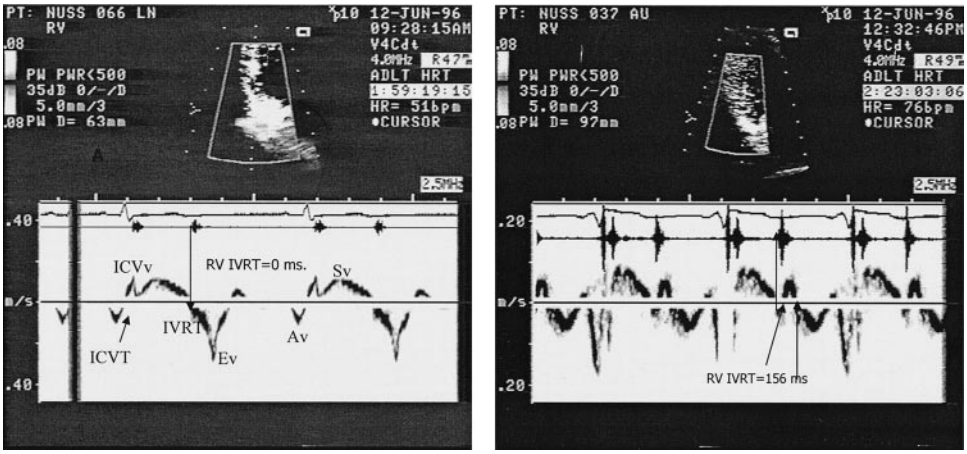

FIGURE 2. Regional RV diastolic velocities and timings in a healthy subject (*left panel*) and a patient with SSc (*right panel*). Note the prolonged IVRT in the SSc patient. Ev = peak early diastolic velocity; Av = peak atrial diastolic velocity; Sv = systolic velocity.

changes in pulmonary function between the two examinations were not likely to be present. Pulmonary function testing was performed (Jaeger Masterlab, Body Box 10151, Transfer 10154; Jaeger; Wuerzburg, Germany) according to the recommendations of the American Thoracic Society.[27] Values are presented as a percentage of the predicted value. High-resolution CT (HRCT) was performed in all but four of the patients (Philips Tomoscan LX; Philips; Eindhoven, the Netherlands). Scans were performed at full inspiration in the supine position with 120 kV and 175 mA, including continuous scans through the lungs with 10-mm thickness followed by scans with 1.5-mm thickness with a slice spacing of 30 mm. The classification of lung involvement by SSc was made according to Devenyi and Czirjak.[28]

Statistics

A commercially available statistical program (SPSS 10.1; SPSS; Chicago, IL) was used. All data are presented as mean ± SD. An unpaired Student *t* test was used to compare data from patients and control subjects. Mann-Whitney nonparametric test was used in small samples, *eg*, comparisons within the patient group. Pearson correlations were used to compare associations between indexes. The intraobserver and interobserver variability is expressed as the coefficient of variation (SD of difference divided by the mean of two observations); $p < 0.05$ was considered statistically significant.

Results

General Characteristics and Hemodynamic Data

Age, BP, creatinine clearance, height, weight, and body surface area did not differ between patients and control subjects. However, heart rate was significantly higher among patients (Table 1). All patients were in sinus rhythm.

Pulmonary Function Tests, Blood Gases, and HRCT

Among patients, arterial blood gases (Po_2, 11.7 ± 1.4 kPa; Pco_2, 5.2 ± 0.7 kPa; and saturation, 96.2 ± 1.2%) and lung volumes were found to be within the normal ranges. However, the mean value for diffusing capacity of the lung for carbon monoxide (Dlco) for the whole group was reduced (75% of predicted). Thirteen patients (59%) [2 patients with diffuse-type SSc, 3 patients with MCTD, and 8 patients with limited-type SSc] had a Dlco < 80% of the predicted value. Six of the patients showed signs of fibrosis on the HRCT scan. One patient had ground-glass appearances confined to the lower parts of both lungs, one patient had reticular-pattern fibrosis with mild honeycombing in the lower portions of both lower lobes, three patients had fibrosis in the lower portions of both lower lobes, and one patients showed reticular-pattern fibrosis in the lower portions of both lower lobes.

Table 1—*General Characteristics of the Study Population

Characteristics	Control Subjects (n = 25)	Patients (n = 26)	p Value
Age, yr	56 ± 16	56 ± 15	0.99
Female/male gender, No.	21/4	21/5	0.77
Systolic BP, mm Hg	135 ± 21	142 ± 26	0.29
Diastolic BP, mm Hg	79 ± 11	79 ± 14	0.99
Height, m	167 ± 0.09	1.66 ± 0.08	0.70
Weight, kg	69 ± 14	68 ± 11	0.79
Creatinine clearance, mL/min	82 ± 15	84 ± 32	0.77
Body surface area, m^2	1.8 ± 0.2	1.8 ± 0.2	0.77
Heart rate, beats/min	63 ± 8	72 ± 13	< 0.05

*Data are presented as mean ± SD unless otherwise indicated.

LA and LV Dimensions and Function

There were no significant differences in LV dimensions and wall thickness, or LA end-systolic area, between patients and control subjects. LV systolic function measured either from M-mode or two-dimensional (Simpson modified rule) recordings was similar in both groups. In addition, traditional measurements of diastolic function were normal among the patients, whereas mitral flow filling time was shortened compared with control subjects (433 ± 117 ms vs 497 ± 109 ms, $p < 0.05$). However, this difference between the two groups disappeared when heart rate was taken into account (Table 2).

RV and RA Dimensions

RA end-systolic area and RVOT wall thickness (15.9 ± 3.7 cm^2 vs 13.0 ± 2.6 cm^2 [$p < 0.01$] and 5.8 ± 1.7 mm vs 3.7 ± 1.1 mm [$p < 0.001$], respectively) were increased among patients compared to control subjects, whereas RV end-diastolic diameters are similar (Table 3).

RV Systolic Function

RV systolic function measured in both inflow and outflow tracts was similar in the two groups, regardless of whether it was determined from M-mode or conventional Doppler or DTI recordings. However, the PA acceleration time was reduced among the SSc patients (119 ± 34 ms vs 141 ± 29 ms, $p < 0.01$) [Table 4].

RV Diastolic Function

RV isovolumic relaxation and filling times in SSc patients differed significantly from control subjects (Table 5). Global IVRT (64 ± 23 ms vs 39 ± 13 ms, $p < 0.001$) and regional IVRT (83 ± 40 ms vs 46 ± 24 ms, $p < 0.001$) were prolonged and TF late atrial filling velocity was increased in patients vs

Table 2—*LV Function

Variables	Control Subjects (n = 25)	Patients (n = 26)	p Value
Two-dimensional and M-mode echocardiographic measurements			
LV end-diastolic dimension, mm	47.1 ± 4.5	48.2 ± 4.6	0.39
LV end-systolic dimension, mm	28.3 ± 4.0	28.0 ± 5.8	0.81
LV fractional shortening, %	40 ± 5	42 ± 10	0.38
Septal end-diastolic thickness, mm	11.0 ± 2.4	10.9 ± 1.9	0.93
Posterior wall end-diastolic thickness, mm	9.9 ± 2.4	9.9 ± 2.1	0.99
LV ejection fraction, %	58.2 ± 6.7	57.2 ± 10.3	0.70
LA end-systolic area, cm^2	16.0 ± 4.5	18.2 ± 5.1	0.12
Conventional Doppler echocardiographic measurements (global function)			
Mitral R-R interval, ms	960 ± 131	841 ± 199	< 0.05
Mitral E velocity, cm/s	56 ± 19	67 ± 22	0.06
Mitral A velocity, cm/s	58 ± 16	59 ± 17	0.91
Mitral E/A ratio	1.1 ± 0.6	1.2 ± 0.5	0.43
Mitral E-deceleration, ms	180 ± 59	180 ± 49	0.99
Mitral IVRT, ms	88 ± 21	94 ± 28	0.40
Mitral filling time, ms	497 ± 109	433 ± 117	< 0.05
Mitral filling time/R-R interval, %	51.0 ± 6.9	49.2 ± 8.2	0.51

*Data are presented as mean ± SD.

control subjects (36 ± 13 cm/s vs 26 ± 8 cm/s, $p < 0.001$) [Fig 2]. Furthermore, TF filling times (454 ± 122 ms vs 548 ± 104 ms, $p < 0.01$) and wall distensibility (1.2 ± 0.4 vs 1.7 ± 0.6, $p < 0.01$), as measured by conventional Doppler E/A ratio, were reduced. These differences in diastolic indexes between the two groups remained statistically significant even after adjustments for heart rate (Table 5).

Relationships Between RV Diastolic Function and Clinical Features

The extent of RV diastolic dysfunction was not related to the duration of the disease or to the SSc skin score. There was no difference in RV diastolic function comparing those with (n = 6) or without (n = 16) CT signs of pulmonary fibrosis, or when comparing those with (n = 13) or without (n = 9) impaired DLCO (< 80% of predicted).

Relationships Between RV Diastolic Function and Pulmonary Function

We did not find any relationships between vital capacity, total lung capacity, or DLCO and indexes of RV diastolic function (regional or global IVRT or E/A ratio), RV wall thickness, or RA area. However, a significant correlation was found between vital capacity/DLCO and DTI-derived IVRT/R-R time interval ($r = 0.44$, $p < 0.05$)

Influence of β-Blocker and ACE Inhibitor Treatment on LV and RV Function

Data were compared for patients receiving ACE inhibitors (n = 5) and/or β-blockers (n = 4) vs patients not receiving drug therapy (n = 19). None of the indexes recorded differed significantly between the two groups.

Interobserver and Intraobserver Variability

Parameters, which differed significantly between patients and control subjects, were checked for their interobserver and intraobserver variability. Ten randomly selected tracings were analyzed independently by two different observers and by the same observer on two different occasions. The coefficient of variation varied between 3% and

Table 3—*RA and RV Dimensions

Variables	Controls Subjects (n = 25)	Patients (n = 26)	p Value
Two-dimensional and M-mode echocardiographic measurements			
RA end-systolic area, cm^2	13.0 ± 2.3	15.9 ± 3.7	< 0.01
RV end-diastolic dimension, mm	20.4 ± 6.9	21.1 ± 7.8	0.74
RVOT free wall thickness, mm	3.7 ± 1.1	5.8 ± 1.7	< 0.001

*Data are presented as mean ± SD.

Table 4—*RV Systolic Function

Variables	Control Subjects (n = 25)	Patients (n = 26)	p Value
M-mode echocardiographic measurements			
RVOT fractional shortening, %	53 ± 18	50 ± 18	0.49
RVOT systolic amplitude, mm	7.8 ± 4.0	6.2 ± 4.5	0.20
RV inflow tract, mm	23.4 ± 5.7	21.8 ± 6.6	0.39
Conventional Doppler echocardiographic measurements (global function)			
PA R-R interval, ms	934 ± 126	870 ± 124	0.08
PA acceleration time, ms	141 ± 29	119 ± 34	< 0.05
PA pre-ejection period, ms	91 ± 18	92 ± 16	0.79
PA ejection time, ms	310 ± 39	307 ± 42	0.75
RV-RA gradient, mm Hg	18.9 ± 6.2	22.1 ± 5.8	0.10
DTI (regional function)			
Systolic velocity, cm/s	13.2 ± 3.0	13.5 ± 2.8	0.67
IVCv, cm/s	10.7 ± 3.9	9.8 ± 3.6	0.41
IVCT, ms	84 ± 21	85 ± 21	0.82

*Data are presented as mean ± SD.

14% for intraobserver variability and between 3% and 15% for interobserver variability of different parameters.

Discussion

We were able to demonstrate that in the present group of patients with SSc, LV function was normal, RV systolic function was preserved, but RV diastolic function was disturbed. This was evidenced by abnormal relaxation and filling properties, together with RV hypertrophy and RA dilatation in the absence of Doppler indications of pulmonary arterial hypertension estimated from the RV-RA drop gradient. These abnormalities were defined using state-of-the-art global (conventional Doppler echocardiography) and regional myocardial function techniques (DTI).

It is well accepted that age affects RV diastolic function.[29] Accordingly, we took particular care to age match our control subjects with the SSc patients in the present study. Another possibility to consider is activation of the sympathetic nervous system in the SSc patients,[30] as suggested by the increased heart rate in the patients vs control subjects. However, when the diastolic measurements were corrected for cardiac

Table 5—*RV Diastolic Function*

Variables	Control Subjects (n = 25)	SSc Patients (n = 26)	p Value
M-mode echocardiography			
RV E slope, cm/s	8.5 ± 3.7	7.4 ± 3.1	0.52
RV A slope, cm/s	8.2 ± 2.7	8.8 ± 2.3	0.44
Conventional Doppler measurements (global function)			
TF R-R interval, ms	949 ± 126	870 ± 141	< 0.05
TF filling time, ms	548 ± 104	454 ± 122	< 0.01
TF filling time/R-R interval, %	58 ± 7	52 ± 7	< 0.01
IVRT, ms	39 ± 13	64 ± 23	< 0.001
IVRT/R-R interval, %	4.2 ± 1.7	7.5 ± 2.8	< 0.001
E velocity, cm/s	40.2 ± 9.8	41.9 ± 11.6	0.58
A velocity, cm/s	25.9 ± 7.5	36.0 ± 12.7	< 0.001
E/A ratio	1.7 ± 0.6	1.2 ± 0.4	< 0.01
Deceleration time, ms	187 ± 60	188 ± 52	0.96
DTI (regional function)			
RV R-R interval, ms	941 ± 127	871 ± 117	< 0.05
E velocity, cm/s	12.9 ± 4.8	12.1 ± 3.2	0.52
A velocity, cm/s	13.9 ± 5.0	15.0 ± 3.9	0.43
E/A ratio	1.0 ± 0.6	0.9 ± 0.6	0.41
IVRT, ms	46 ± 24	83 ± 40	< 0.001
IVRT/R-R interval, %	5.0 ± 2.7	9.6 ± 4.4	< 0.001

*Data are presented as mean ± SD. See Figure 1 legend for expansion of abbreviations.

cycle length, the abnormalities remained. Accordingly, neither age nor heart rate are likely to explain the measured RV diastolic dysfunction. Moreover, RV diastolic dysfunction was not related to renal function, skin involvement, or duration of disease.

The hallmarks of SSc heart disease are myocardial fibrosis and ischemia. We and others[31] have demonstrated that intermittent coronary vasospasm, *ie*, Raynaud phenomenon, is prevalent in patients with SSc. The pattern of RV diastolic disturbance seen in the present study could therefore be related to myocardial fibrosis and/or ischemia, both of which are known to affect ventricular relaxation and filling and are characterized by reduced E-wave velocity.[32,33] However as LV function was unaffected, it is difficult to ascribe the abnormalities of RV function to myocardial fibrosis or ischemia alone.

Pulmonary involvement is one of the leading causes of death in SSc patients. Whereas pulmonary arterial hypertension is commonly seen in the long-standing limited type of SSc, interstitial pulmonary fibrosis, caused by alveolitis, is more common in the diffuse type. It is clearly important to separate these two types of pulmonary involvement as they differ regarding their pathogenesis, clinical associations, predictive factors, and treatment.[34] The limited type comprised 70% of the patients in the present study. A decreased DLCO is an excellent predictor of the subsequent development of pulmonary hypertension in the limited type. The DLCO may be reduced for many years prior to the diagnosis of pulmonary hypertension.[2] In fact, 59% of our patients displayed a reduced DLCO without any evidence of pulmonary hypertension. In spite of the fact that PA systolic pressure as estimated by echocardiography at rest was normal, abnormalities in PA pressure in these patients cannot be excluded. It must be remembered that Doppler echocardiography may underestimate RV pulmonary pressure when obtained from the tricuspid regurgitation peak gradient.[16,35,36] Our data relating to PA pressure were obtained from a single measurement and during rest.

Consequently, mild or early intermittent pulmonary hypertension cannot be excluded in our patients, and Raynaud phenomenon within the lung is a possibility.[37] The shortened acceleration time in pulmonary flow, which is a variable thought to reflect pulmonary resistance or impedance, supports the probability of an increased RV afterload. So too does the finding of increased RV wall thickness. In the event of increased afterload, diastolic dysfunction may be demonstrated at an earlier stage than systolic dysfunction.[38] This may explain why RV systolic function was found to be normal in our patients.

In contrast to our previous findings in another cohort of SSc patients,[8,9] we noted that LV diastolic function was normal in the present study. This discrepancy could be explained by the absence of gross pulmonary arterial hypertension, LV hypertrophy, systemic hypertension, and renal insufficiency, conditions that are likely to affect LV diastolic function in patients with SSc.[39] Furthermore, our previous material predominantly comprised patients with diffuse SSc as opposed to the predominantly limited type in the present study population.

RV diastolic dysfunction in patients with SSc has previously been reported but only in the presence of pulmonary hypertension and LV systolic and diastolic dysfunction.[11,12] The present study is the first one that in detail investigated RV function by using DTI. It also shows that RV diastolic disturbances could be detected when systolic and diastolic LV function is normal. Chamber interaction is therefore unlikely to be a major reason for the RV diastolic dysfunction.

The early detection of RV dysfunction may be important in clinical practice when assessing the prognosis and optimizing expensive treatment in pulmonary hypertension. However, this is not easy to achieve because the anatomic and functional features of the RV are complex. The longitudinal motion of the atrioventricular plane has been used as a measurement of the RV function of the inflow tract.[11] Recently, we proposed a simple echocardiographic method for the evaluation of systolic function of the RVOT.[24] DTI is a relatively new method that permits the characterization of regional myocardial velocities throughout the cardiac cycle. This new technique was found to be useful in assessing RV function in heart failure,[40] ischemic heart disease,[41] and hypertrophic cardiomyopathy.[42] To our knowledge, RV function in patients with SSc has so far not been extensively studied using DTI. Our present results confirm a previous report[12] using traditional echocardiographic methods.

Study Limitations

We were not able to perform right-heart catheterization to verify diastolic function and PA pressures. However, some of the echocardiographic parameters used in the present study have been validated.[43] Direct evidence of myocardial fibrosis can only be verified by myocardial biopsy, but an investigation of this kind was not justified ethically in this group of patients. The relatively small sample of patients reduced the possibility to stratify accurately the findings.

CONCLUSIONS

We have demonstrated alternations in RV diastolic function together with an increase in RV wall thick-

ness and RA area in patients with SSc. A primary myocardial defect due to fibrosis or ischemia seems an unlikely explanation since LV function was normal. Pulmonary fibrosis alone is unlikely, as no relationship was found between the degree of fibrosis and RV diastolic disturbance. The most probable cause is mild or early intermittent pulmonary arterial hypertension. Detection of abnormalities in RV diastolic function might provide a means of identifying patients at risk for progressive heart failure. Another important clinical implication of the present study is that RV function should be studied in detail in patients with SSc. This may be useful for initiation of treatment and follow-up.

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