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Assessment of ventricular and left atrial mechanical functions, atrial electromechanical delay and P wave dispersion in patients with scleroderma

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Abstract

Background: *The aim of this study was to investigate ventricular functions and left atrial (LA) mechanical functions, atrial electromechanical coupling, and P wave dispersion in scleroderma patients.*

Methods: *Twenty-six patients with scleroderma and twenty-four controls were included. Left and right ventricular (LV and RV) functions were evaluated using conventional echocardiography and tissue Doppler imaging (TDI). LA volumes were measured using the biplane area-length method and LA mechanical function parameters were calculated. Inter-intraatrial electromechanical delays were measured by TDI. P wave dispersion was calculated by 12-lead electrocardiograms.*

Results: *LV myocardial performance indices (MPI) and RV MPI were higher in patients with scleroderma ($p = 0.000$, $p = 0.000$, respectively) while LA passive emptying fraction was decreased and LA active emptying fraction was increased ($p = 0.051$, $p = 0.000$, respectively). P wave dispersion and inter-intraatrial electromechanical delay were significantly higher in patients with scleroderma (25 [10–60]* vs *20 [0–30], $p = 0.000$, 16.50 [7.28–26.38]* vs *9.44 [3.79–15.78] and 11.33 [4.88–16.06]* vs *4.00 [0–12.90], $p < 0.05$, respectively). Interatrial electromechanical delay was negatively correlated with LV E wave, ($p = 0.018$). LV E wave was demonstrated to be a factor independent of the interatrial electromechanical delay ($R^2 = 0.270$, $\beta = -0.52$, $p = 0.013$).*

Conclusions: *This study showed that in scleroderma patients, global functions of LV, RV and mechanical functions of LA were impaired, intra-interatrial electromechanical delays were prolonged and P wave dispersion was higher. LV E wave was demonstrated to be a factor that is independent of the interatrial electromechanical delay. Reduced LV E wave may also give additional information on the process of risk stratification of atrial fibrillation.* (Cardiol J 2011; 18, 3: 261–269)

Key words: atrial functions, atrial electromechanical delay, scleroderma

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Introduction

Scleroderma is a systemic disease characterized by the involvement of the skin and visceral organs [1]. Cardiac involvement may be present asymptomatically and is observed in 30% of autopsies [1, 2]. It may be a result of the sclerosing inflammatory process. Previous studies have demonstrated diffuse myocardial fibrosis and conduction disturbances [2, 3]. Fibrosis due to collagen deposition leads to both right ventricular (RV) and left ventricular (LV) systolic and diastolic dysfunction, conduction disturbances, and atrial and ventricular arrhythmias [4]. Atrial arrhythmias have been reported in 10–20% of patients with scleroderma [5, 6]. The mechanisms that cause atrial fibrillation (AF) are not completely understood. Atrial inflammation might promote AF [7]. This inflammatory process may play a role that results in AF in scleroderma also.

Left atrial (LA) volume as a LA functional index has recently been identified as a potential indicator of cardiac disease and atrial arrhythmia. LA functions are important determinants of ventricular filling. Parameters of LA function may provide additional information about resistance before the filling of the ventricle. Additionally, the atrial emptying pattern is strongly affected by LV diastolic properties.

The prolongation of intraatrial and interatrial conduction time and P wave dispersion (Pd) are well known electrophysiological charecteristics of the AF prone atrium [8, 9]. Intraatrial and interatrial conduction time has been evaluated by Pd and tissue Doppler imaging (TDI) [10, 11].

Our aim was to investigate the functions of LV, RV and LA, atrial electromechanical coupling with TDI, and also to demonstrate Pd in patients with scleroderma.

Methods

Twenty-six patients with scleroderma (median age 48.5 [range 21–71] years; 24 female, two male) and twenty-four age-matched and gender-matched control subjects (median age 46.0 [22–56] years; 22 female, two male) were included. Patients with right bundle or left bundle branch block, pacemaker implantation, valvular heart disease, heart failure and taking beta-blockers, digitalis or antiarrhythmic drugs were excluded. All patients were observed to be in sinus rhythm and were asymptomatic in terms of heart failure and pulmonary hypertension.

The study protocol was approved by the Local Ethics Committee and written informed consent was obtained from each patient.

Echocardiography

In all patients, two-dimensional, M-mode, pulsed and color flow Doppler echocardiographic examinations (Vivid 7 Pro, GE, Horten, Norway, 2–4 Mhz phased-array transducer) were performed by one cardiologist. During echocardiography, a single lead electrocardiogram was recorded simultaneously. Data was recorded from the average of three cardiac cycles. M-mode and Doppler measurements were performed adhering to American Society of Echocardiography guidelines [12]. Peak systolic (Sm) and early (Em) and late (Am) diastolic velocities were obtained from the mitral lateral, septal and tricuspid lateral annuluses. The myocardial performance index (MPI) was calculated using TDI methods for right and left ventricles [13].

Left atrial mechanical function

Left atrial volumes were measured echocardiographically by the biplane area length method from the apical four-chamber views. LA maximal volume (Vmax) was recorded at the onset of the mitral opening, LA minimal volume (Vmin) at the onset of mitral closure, and LA presystolic volume (Vp) at the beginning of the atrial systole (P wave on ECG). LA emptying function parameters were calculated according to the LA maximal, minimal and presystolic volumes (LA passive emptying volume = Vmax–Vp, LA passive emptying fraction = [Vmax–Vp]/Vmax, LA active emptying volume = Vp–Vmin, LA active emptying fraction = [Vp–Vmin]/Vp and total emptying volume = Vmax–Vmin) [14, 15]. All volume measurements were corrected with respect to the body surface area (BSA).

Atrial electromechanical coupling

Tissue Doppler echocardiography was performed with transducer frequencies of 3.5–4.0 MHz by adjusting the spectral pulsed Doppler signal filters until a Nyquist limit of 15 to 20 cm/s was reached, and by using the minimal optimal gain. The monitor sweep speed was set at 100 mm/s. In the apical four-chamber view, the pulsed Doppler sample volume was placed at the level of LV lateral mitral annulus, septal mitral annulus, and RV tricuspid annulus. Atrial electromechanical coupling (PA), the time interval from the onset of the P wave on the surface electrocardiogram to the beginning of the late diastolic wave (Am); was obtained from the lateral mitral annulus (PAlat), septal mitral

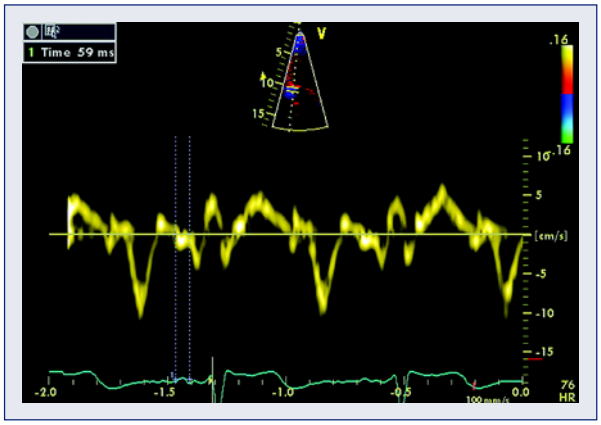

Figure 1. Measurement of time interval from the onset of P wave on surface electrocardiogram to the beginning of Am wave (PA) interval with tissue Doppler imaging.

annulus (PAsep), and tricuspid annulus (PAtricus) (Fig. 1). The difference between PAlat and PAtricus was defined as the interatrial electromechanical delay, while the difference between PAsep and PAtricus was defined as the intraatrial electromechanical delay [16]. These PA measures were corrected with respect to the heart rate.

Electrocardiography

A 12-lead electrocardiogram was used to measure the maximum (Pmax) and minimum (Pmin) P wave durations. The difference between the Pmax and the Pmin was defined as Pd (Pd = Pmax – – Pmin). The paper speed was 50 mm/s. The Pd were measured manually. Mean values for three complexes were calculated in each lead.

Statistical analysis

All continuous variables were expressed as mean ± standard deviation and median (min–max). Categorical data is given as counts (percentages) and analyzed with the χ^2 test. Mean values of continuous variables were compared within groups using the Student *t* test or Mann-Whitney U test, and their distributions were evaluated by the Kolmogorov-Smirnov and Shapiro-Wilk test. Pearson's correlation and Spearman rho were used to assess the relationship between continuous variables. Stepwise, multiple regression analysis was used to identify the significant determinants of interatrial electromechanical delay. All predeterminant independent variables which correlated with a p value of less than 0.1 in Pearson's correlation were inserted into a stepwise, multiple regression analysis. P values < 0.05 were accepted as statistically significant.

Results

Baseline demographic and clinical characteristics

Clinical and laboratory findings of the subjects are shown in Table 1. The median disease duration was 60 (range 12–276) months. Age, sex, body mass index (BMI), heart rate, systolic and diastolic blood pressures and exercise capacity were similar in both groups ($p > 0.05$). Pmax and Pd were significantly higher in patients with scleroderma (106.82 ± 11.29 *vs* 100.00 ± 8.85, $p = 0.004$ and 25 [10–60] *vs* 20 [0–30], $p = 0.000$, respectively) whereas Pmin was significantly lower in the scleroderma group (75.45 ± ± 11.84 *vs* 83.33 ± 9.17, $p = 0.004$).

Table 1. Clinical and laboratory characteristics of the study population.

	Scleroderma (n = 26)	Controls (n = 24)	P
Age (years)	48.50 (21–71)	46.00 (22–56)	0.122**
Female/male (%)	24/2 (92.3/7.7)	22/2 (91.7/8.3)	1.000***
BMI [kg/m^2]	25.96 ± 4.65	27.00 ± 4.88	0.985*
Heart rate [bpm]	79.27 ± 8.99	80.16 ± 11.05	0.886*
SBP [mm Hg]	125.41 ± 7.96	123.08 ± 9.39	0.250*
DBP [mm Hg]	71.13 ± 6.62	68.20 ± 6.43	0.198*
Six-minute walking test [m]	531.82 ± 57.94	515.42 ± 37.66	0.844*
Pmax [ms]	106.82 ± 11.29	100.00 ± 8.85	0.024
Pmin [ms]	75.45 ± 11.84	83.33 ± 9.17	0.004
Pd [ms]	25 (10–60)	20 (0–30)	0.000**
Disease duration (months)	60.00 (12.00–276.00)	–	–

BMI — body mass index; SBP — systolic blood pressure; DBP — diastolic blood pressure; Pmax — maximum P wave duration; Pmin — minimum P wave duration; Pd — P wave dispersion; *independent t test; **Mann-Whitney U test; ***Fisher's Exact χ^2

Table 2. Echocardiographic characteristics of the study population.

	Scleroderma (n = 26)	Controls (n = 24)	P
LV end-diastolic dimension [mm]	44.91 ± 3.80	46.58 ± 3.02	0.149*
Septum thickness [mm]	9.45 ± 0.74	9.08 ± 0.88	0.038*
LVEF (%)	65.22 ± 3.91	66.33 ± 4.87	0.197*
LV mass index (g/m^2]	78.60 ± 15.43	76.08 ± 14.20	0.217*
LA diameter [mm]	36.23 ± 4.14	35.79 ± 3.68	0.318*
Mitral E wave [m/s]	0.67 ± 0.14	0.73 ± 0.15	0.162**
Mitral A wave [m/s]	0.76 ± 0.15	0.65 ± 0.16	0.088*
Deceleration time [ms]	215.41 ± 37.31	191.25 ± 27.74	0.023*
LV E/A	0.94 ± 0.37	1.18 ± 0.34	0.016**
LV E/Em	5.8 (3.98–11)	5.4 (3.40–9.20)	0.037**
LV Sm [cm/s]	8.45 ± 1.36	8.13 ± 1.35	0.507*
LV Em [cm/s]	11.05 ± 3.05	11.19 ± 3.71	0.833*
LV Am [cm/s]	11.61 ± 2.60	10.79 ± 2.68	0.380*
LV MPI	0.41 ± 0.03	0.34 ± 0.04	0.000*
RVFAC (%)	46.95 ± 5.41	49.63 ± 4.81	0.045*
TAPSE [mm]	23.32 ± 1.62	25.75 ± 2.77	0.000*
RV Sm [cm/s]	13.77 ± 1.72	15.04 ± 1.76	0.001**
RV Em [cm/s]	15.22 ± 2.79	14.58 ± 2.86	0.734*
RV Am [cm/s]	16.82 ± 4.18	17.54 ± 5.20	0.715*
RV IVCTc [ms]	67.36 ± 10.23	54.33 ± 7.03	0.000*
RV IVRTc [ms]	65.68 ± 7.02	47.42 ± 3.68	0.000*
RV MPI	0.41 ± 0.03	0.31 ± 0.04	0.000*
P_{Acct} [ms]	119.82 ± 11.11	142.04 ± 13.51	0.000*
RA diameter [mm]	29.18 ± 2.44	29.91 ± 2.60	0.254*

LV — left ventricle; EF — ejection fraction; LA — left atrium; Sm — systolic myocardial velocity; Em — early myocardial diastolic velocity; Am — late myocardial diastolic velocity; MPI — myocardial performance index; RVFAC — right ventricle fractional area change; TAPSE — tricuspid annular plane systolic excursion; RV — right ventricle; IVCTc — corrected isovolumetric contraction time; IVRTc — corrected isovolumetric relaxation time; P_{Acct} — pulmonary artery acceleration time; RA — right atrium; *independent t test; **Mann-Whitney U test

Echocardiographic characteristics

Echocardiographic characteristics of the study groups are shown in Table 2. LV end-diastolic dimension, LVEF, LV mass, LA and RA dimensions and LV Sm were similar in both groups. Right ventricle fractional area change (RVFAC) and tricuspid annular plane systolic excursion (TAPSE) were significantly lower in patients with scleroderma (46.95 ± 5.41 *vs* 49.63 ± 4.81 and 23.32 ± 1.62 *vs* 25.75 ± 2.77, $p < 0.05$, respectively). In Doppler and tissue Doppler echocardiographic examination, LV E/A ratio was significantly lower (0.94 ± 0.37 *vs* 1.18 ± 0.34, $p = 0.016$) while LV deceleration time was higher in patients with scleroderma (215.41 ± ± 37.31 *vs* 191.25 ± 27.74, $p = 0.023$). RV corrected isovolumetric relaxation time and P_{Acct} were also lower in the scleroderma group (65.68 ± 7.02 *vs* 47.42 ± 3.68 and 119.82 ± 11.11 *vs* 142.04 ± 13.51, $p < 0.05$, respectively). LV and RV MPI values were significantly higher in scleroderma patients (0.41 ± ± 0.03 *vs* 0.34 ± 0.04, $p = 0.000$ and 0.41 ± 0.03 *vs* 0.31 ± 0.04, $p = 0.000$, respectively).

Left atrial mechanical function

LA volume indices are shown in Table 3. Vmax, Vp, Vmin and LA passive emptying volumes were similar in both groups ($p > 0.05$). LA active emptying volumes and LA total emptying volumes were significantly increased in the scleroderma group compared to healthy controls (9.16 [5.88–19.65] *vs* 5.83 [2.38–12.50], $p = 0.000$ and 16.39 [9.04– –28.25] *vs* 14.96 [5.35–20.19], $p = 0.037$). LA passive emptying fraction was decreased in patients with scleroderma (29.63 [12.10–48.95] *vs* 35.05 [16.30–65.20], $p = 0.051$). In addition, LA active emptying fraction was significantly increased in scleroderma patients (56.97 ± 8.95 *vs* 42.35 ± 7.80, $p = 0.000$).

Table 3. Left atrial volume measurements of the study population.

	Scleroderma (n = 26)	Controls (n = 24)	P
Vmax [mL/m^2]	25.65 ± 7.72	22.45 ± 6.48	0.236**
	23.13 (11.81–38.98)	23.17 (10.16–34.52)	
Vp [mL/m^2]	18.37 ± 6.31	14.32 ± 5.30	0.060**
	17.41 (9.03–30.73)	14.35 (4.91–23.08)	
Vmin [mL/m^2]	7.91 ± 2.90	8.24 ± 3.25	0.568*
	7.76 (2.77–13.96)	8.43 (2.48–14.33)	
LA PEV [mL/m^2]	7.28 ± 3.52	8.12 ± 3.37	0.534**
	6.85 (2.35–15.23)	7.85 (2.67–14.55)	
LA PEF (%)	28.28 ± 10.76	36.80 ± 12.82	0.051**
	29.63 (12.10–48.95)	35.05 (16.30–65.20)	
LA AEV [mL/m^2]	10.49 ± 4.25	6.08 ± 2.64	0.000**
	9.16 (5.88–19.65)	5.83 (2.38–12.50)	
LA AEF (%)	56.97 ± 8.95	42.35 ± 7.80	0.000*
	57.35 (39.50–69.79)	42.36 (29.92–55.30)	
LA TEV [mL/m^2]	17.76 ± 5.84	14.18 ± 3.93	0.037**
	16.39 (9.04–28.25)	14.96 (5.35–20.19)	

Vmax — left atrial maximum volume; Vp — left atrial volume at the beginning of atrial systole; Vmin — left atrial minimal volume; LA — left atrium; PEV — passive emptying volume; PEF — passive emptying fraction; AEV — active emptying volume; AEF — active emptying fraction; TEV — total emptying volume; *independent t test; **Mann-Whitney U test

Table 4. Atrial electromechanical coupling findings measured by tissue Doppler imaging.

	Scleroderma (n = 26)	Controls (n = 24)	P
PA lateral$_c$ [ms]	63.78 ± 7.91	58.31 ± 5.52	0.003*
	63.15 (52.40–79.48)	58.50 (5.52–71.06)	
PA septum$_c$ [ms]	58.22 ± 5.95	53.00 ± 6.08	0.001**
	57.25 (50.62–72.00)	51.81 (42.58–70.87)	
PA tricuspid$_c$ [ms]	47.34 ± 6.00	48.92 ± 5.52	0.290*
	45.83 (34.56–58.89)	48.16 (39.95–61.15)	
PA lateral–PA tricuspid [ms]	16.44 ± 5.30	9.39 ± 2.84	0.000**
	16.50 (7.28–26.38)	9.44 (3.79–15.78)	
PA septum–PA tricuspid [ms]	10.89 ± 3.25	4.08 ± 3.57	0.000**
	11.33 (4.88–16.06)	4.00 (0–12.90)	

PA — time interval from the onset of P wave on surface electrocardiogram to the beginning of Am wave interval with tissue Doppler imaging; PA lateral–PA tricuspid — interatrial electromechanical delay; PA septum–PA tricuspid — intraatrial electromechanical delay; *independent t test; **Mann-Whitney U test

Atrial electromechanical coupling

Table 4 shows atrial electromechanical coupling findings measured by TDI. PAlat and PAsep were significantly higher in patients with scleroderma compared to controls (63.15 [52.40–79.48] *vs* 58.50 [5.52–71.06], 57.25 [50.62–72.00] *vs* 51.81 [42.58–70.87], $p \leq 0.05$). However, PA tricuspid was similar in both groups (45.83 [34.56–58.89] *vs* 48.16 [39.95–61.15], $p = 0.290$). Increased interatrial (PAlat–PAtricus) and intraatrial (PAsep––PAtricus) electromechanical delays were observed in patients with scleroderma (16.50 [7.28–26.38] *vs* 9.44 [3.79–15.78] and 11.33 [4.88–16.06] *vs* 4.00 [0––12.90], $p < 0.05$, respectively).

Relationship between interatrial electromechanical delay and other clinical and laboratory characteristics

Interatrial electromechanical delay was positively correlated with disease duration and LA diameter ($r = 0.524$, $p = 0.006$ and $r = 0.419$, $p = 0.033$, respectively) and negatively correlated with LV E wave, TAPSE, RV E wave and exercise capacity ($r = –0.461$, $p = 0.018$, $r = –0.513$, $p = 0.007$,

Table 5. Correlation between interatrial electromechanical delay and clinical echocardiographic characteristics.

	r	p
Age (years)	0.250	0.218
Body mass index [kg/m^2]	0.237	0.244
Disease duration (months)	0.524	0.006
Exercise capacity (%)	–0.436	0.043
Six-minute walking distance [m]	–0.645	0.001
New York Heart Association	0.335	0.038
LV MPI	0.316	0.116
LV E wave [m/s]	–0.461	0.018
LV E/A	0.020	0.923
LV E/Em	0.049	0.813
LA [mm]	0.419	0.033
RV MPI	0.197	0.335
TAPSE [mm]	–0.513	0.007
RV Em [cm/s]	–0.563	0.003
LA passive emptying fraction	0.068	0.740
LA active emptying fraction	–0.086	0.677

LV — left ventricle; LA — left atrium; RV — right ventricle; MPI — myocardial performance index; TAPSE — tricuspid annular plane systolic excursion

Table 6. Relation between interatrial electromechanical delay and clinical and echocardiographic characteristics.

	β	t	p
Disease duration (months)	0.29	1.54	0.141
Sex	0.13	0.58	0.569
LVEF (%)	0.02	0.11	0.910
LV MPI	0.12	0.61	0.547
LV E/E'	0.18	0.90	0.382
LV E/A	0.03	0.17	0.866
LV E wave [m/s]	–0.52	–2.72	0.013*
LV A wave [m/s]	–0.07	–0.33	0.742
LV S wave [m/s]	0.31	1.55	0.138
RV MPI	0.06	0.31	0.757
TAPSE [mm]	–0.27	–1.37	0.186
LA passive emptying fraction	0.10	0.44	0.665
LA active emptying fraction	–0.08	–0.39	0.702

LVEF — left ventricular ejection fraction; rest abbreviations as in Table 5; *$p < 0.05$ is significant

r = –0.563, p = 0.003 and r = 0.436, p = 0.043, respectively). No significant correlation was found between interatrial electromechanical delay and age, BMI, LV MPI, LV E/A, LV E/E' or RV MPI (Table 5). In stepwise linear regression analysis, LV E wave was demonstrated to be an independent factor of interatrial electromechanical delay (R^2 = = 0.270, β = –0.52, p = 0.013; Table 6).

Discussion

This study showed that in patients with scleroderma, firstly, diastolic and systolic functions of left and right ventricles and LA mechanical functions were impaired; secondly, intra-interatrial electromechanical delay was increased and Pd was higher; and lastly, LV E wave was demonstrated to be an independent factor of interatrial electromechanical delay.

Ithas already been demonstrated that fibrosis due to collagen deposition leads to RV and LV systolic and diastolic dysfunction [4]. Poanta et al. [17] also showed that diastolic function parameters were impaired in asymptomatic scleroderma patients compared to controls. D'Andrea et al. [18] reported LV myocardial involvement in asymptomatic patients with scleroderma. Recently, subclinical biventricular impairment was demonstrated in scleroderma patients by the use of pulsed-wave TDI [19]. Likewise, our study found that both ventricle diastolic and systolic functions were impaired before any clinical sign or symptom in patients with scleroderma. Otherwise, in our study, isolated systolic dysfunction was not shown to be present. The finding of LV global dysfunction was demonstrated by the abnormal MPI. So, we deduced that addition of MPI to standard measurements may provide early detection of heart involvement.

RV dysfunction in scleroderma patients is related to the specific collagen deposition. It is also known that due to the specific changes in scleroderma, pulmonary hypertension may develop. The presence of pulmonary hypertension will also lead to the development of RV dysfunction. It has been shown that structural abnormalities of small coronary arteries and arterioles are present in scleroderma-related pulmonary hypertension and cause impaired RV function due to ischemia of the RV [20]. Given late presentation of the signs of pulmonary hypertension, physicians cannot be expected to make a diagnosis of pulmonary hypertension based on clinical features alone. Earlier detection of pulmonary hypertension in scleroderma is crucial so as to allow earlier treatment and prevent disease progression. The estimation of systolic pulmonary artery pressure by Doppler echocardiography depends on an adequate Doppler signal from

tricuspid regurgitation. It may be absent in 26% of patients [21]. Thus, latent pulmonary hypertension may not be determined in asymptomatic scleroderma patients. Huez et al. [22] suggested that RV dysfunction is related to latent pulmonary hypertension. Patients in our study also showed no clinical evidence of pulmonary hypertension, and systolic pulmonary artery pressure estimated by Doppler echocardiography was < 35 mm Hg. Nevertheless, P_{Acct} as an indicator of pulmonary hypertension and RV diastolic dysfunction is shorter in scleroderma patients than in the control group. So, in our study, RV dysfunction may be a preclinical warning of asymptomatic pulmonary hypertension.

Atrial enlargement is known to be associated with increased mortality in the general population [23]. LA diameter is correlated with cardiovascular disease and is accepted as a risk factor of AF [23, 24]. A recently published study showed that cardiac arrhythmias, especially those of supraventricular origin, are most frequent in sclerodema patients [25]. Assessment of atrial functions may be based on the atrial volumes. Direct damage to the atrial tissue, and indirect damage arising from atrial overload, may influence the mechanical functions of the atrium. LA function is an important determinant of ventricular filling [26]. It has been demonstated that in diabetic patients, decreased LA passive emptying volume is related to increased end-diastolic LV pressure, whereas, increased LA active emptying volume is associated with compensatory mechanisms in LA contraction [14]. We also showed that LA mechanical functions and diastolic function parameters were impaired in patients with scleroderma. So, we speculate that atrial arrhythmias may develop in these patients due to impaired LA functions.

Interatrial electromechanical coupling times may be prolonged due to atrial tissue damage in scleroderma patients [27]. Deniz et al. [28] found an increase in intraatrial mechanical delay in paroxysmal AF patients. Earlier invasive studies have stated the normal values for electrical conduction as 77 ± 8 ms [29]. In previous studies, electromechanical coupling intervals were also used in different clinical manifestations [30]. This method can be used as an early marker to detect paroxysmal AF. The geometrical distance between two atria is an important determining factor for atrial conduction, and inter-nodal pathways may play an important role in interatrial electromechanical delay [31]. Conventionally, atrial electrical function has been evaluated from electrocardiography (ECG) and invasive electrophysiological techniques [32]. Mostly because of the high cost and because they are invasive, the current use of electrophysiological techniques is limited. Fujimoto et al. [33] demonstrated the presence of abnormal atrial contractions in scleroderma. Abnormal atrial contractions may be supposed to affect atrial electrical conduction. Consistent with the earlier studies, we demonstrated the delayed interatrial electromechanical coupling intervals in scleroderma patients [31, 34].

Atrial arrhythmias have been evaluated by both short period ECG and ambulatory ECG [5, 6]. Pd is a simple electrocardiographic predictor of paroxysmal lone AF [8]. In addition, changes in LA microarchitecture may predispose to paroxysmal AF by decreasing atrial myocardial contraction and increasing Pd [35]. Can et al. [34] reported that patients with scleroderma showed increased Pd and Pmax values. In another study, longer signal averaged P wave durations were demonstrated in patients with scleroderma [31]. In this study, we also demonstrated an increased Pd in scleroderma patients. It may be concluded that these patients had an increased risk of AF. Due to the limitations of Pd evaluation methods, Dilaveris et al. [36] demonstrated different methods of P wave analysis using a 12-lead ECG. Nevertheless, P wave measurements from the standard surface ECG were readily available, simple to operate and cheaper than other methods. In addition, other methods are not widely commercially available. In our study, we used surface ECG to evaluate Pd.

Studies have investigated whether the echocardiographic parameters of the LA predicts the development of AF [37]. Choi et al. [38] demonstrated that reduced A', which is a parameter of LA contractile function, might be an important predictor for the development of nonvalvular AF. LA dilatation is frequently observed in LV diastolic dysfunction. Impaired ventricular relaxation is related to a lower atrio-ventricular gradient. So, this may cause a reduction of early transmitral flow (low E wave velocity) in the relaxation type of diastolic dysfunction [39]. A relation between LA dilatation and interatrial electromechanical delay has been demonstrated in previous studies [16, 40]. In the present study, LV E wave was negatively correlated with interatrial electromechanical delay and may be accepted as an independent factor of the interatrial electromechanical delay.

Clinical implications

There are three main implications of our study. The identification of a risk of AF process could be

of interest in asymptomatic scleroderma patients. The assessment of LA mechanical and electromechanical functions is accepted as a risk factor of AF. We showed that LA mechanical functions were impaired and interatrial electromechanical delays were prolonged in asymptomatic scleroderma patients. However, current use of these echocardiographic methods is limited. We also showed that LV E wave derived by pulse wave Doppler was demonstrated to be an independent factor of the interatrial electromechanical delay. So, we concluded that addition of reduced LV E wave to these methods may give additional information on the process of risk stratification of AF. Moreover, LV E wave can be readily measured and is simpler to operate than other echocardiographic methods at the bedside during routine echocardiographic examination.

Pulmonary hypertension may lead to significant RV dysfunction. Earlier detection of pulmonary hypertension in scleroderma is crucial to initiating earlier treatment and preventing disease progression. We found that P_{Acct} as an indicator of pulmonary hypertension and RV diastolic dysfunction is shorter in scleroderma patients. So, we deduced that RV dysfunction may be a preclinical warning of asymptomatic pulmonary hypertension.

Our study did not find isolated systolic dysfunction. LV global dysfunction was demonstrated by the abnormal MPI. Addition of MPI to standard measurements may provide early detection of heart involvement. It is possible that it may be used to determine LV global function instead of isolated systolic dysfunction. But further studies are needed before this can be used in clinical practice. Thus, ventricular function, especially MPI, is important in evaluating these patients before the onset of symptoms.

Limitations of the study

We did not follow up in terms of the development of AF. This may be the most important limitation of our study. Such patients must be followed-up for a longer period to determine atrial arrhythmia. Further studies with follow-up are necessary to investigate whether AF occurs in scleroderma patients. In addition, our study is limited by the lack of other investigations of cardiac involvement, such as invasive correlation for diastolic dysfunction and myocardial scintigraphy or magnetic resonance. A final limitation of our study is the relatively small group of patients.

Conclusions

This study showed that in patients with asymptomatic scleroderma: firstly, diastolic and systolic functions of left and right ventricles and LA mechanical functions were impaired; secondly, that intra-interatrial electromechanical delays were prolonged and Pd was higher; and thirdly, that LV E wave was demonstrated to be an independent factor of the interatrial electromechanical delay. Reduced LV E wave may also give additional information on the process of risk stratification of AF.

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