Atrial conduction abnormalities in patients with systemic progressive sclerosis

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Background Atrial abnormalities in patients with progressive systemic sclerosis have not been evaluated in terms of intra-atrial conduction. We hypothesized that a delay in atrial conduction in these patients might produce diastolic abnormalities as well as atrial arrhythmias.

Objective To evaluate the atrial function of patients with progressive systemic sclerosis by using echocardiography to measure the intra-atrial electromechanical activation coupling interval.

Methods Twenty patients with progressive systemic sclerosis were assessed by Doppler echocardiography. Twenty age-matched healthy controls were also evaluated. Two-dimensional guided M-modes of ventricular long axes were recorded using simultaneous phono- and electrocardiograms of the apical four chamber view at the right lateral, septal and left lateral sites of the atrioventricular rings. Transmitral and tricuspid pulsed Doppler flow velocities were also recorded. Filtered P wave duration was measured on the signal averaged ECG to determine the duration of atrial electrical activation.

Results There was a delay in P on the electrocardiogram (P) at the onset of atrial contraction on long axis M-modes at all three atrioventricular ring sites in patients with progressive systemic sclerosis as compared with controls (P-right; 56 ± 13 vs 47 ± 10 ms, P-septal; 74 ± 14 vs 55 ± 10 ms, and P-lateral; 93 ± 16 vs 72 ± 11 ms, P<0.01). Inter-atrial conduction time [(P-lateral) − (P-right)] was delayed in patients with progressive systemic sclerosis, compared with healthy controls (37 ± 15 vs 25 ± 6 ms, P<0.01). Mitral A waves acceleration and deceleration times were also decreased in the patients. The interval was prolonged between P to the onset and the peak of the A wave in transmitral flow. Duration of the filtered P wave was significantly prolonged in progressive systemic sclerosis as compared with controls (124 ± 12 ms vs 106 ± 8 ms, P<0.01). PQ intervals, E waves and acceleration and deceleration times did not differ significantly in progressive systemic sclerosis vs, controls. The A wave acceleration rate on transmitral flow (peak A wave velocity/acceleration time) showed a significant correlation with inter-atrial conduction delay (r=0.55, P<0.01).

Conclusions Intra-atrial electromechanical coupling intervals were delayed in patients with progressive systemic sclerosis. Thus, the mechanical late diastolic filling time due to atrial contraction in the total diastolic phase was severely limited, and this resulted in a restricted mitral A wave. We should therefore evaluate patients with progressive systemic sclerosis for significant atrial abnormalities.

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Key Words: progressive systemic sclerosis, atrial function, echocardiography.

Introduction

Cardiac involvement in patients with progressive systemic sclerosis was established as a distinct clinicopathological entity in 1943 by Weiss et al.[1]. In such patients, in addition to the characteristic skin disease (scleroderma), involvement of the kidney, heart and lungs is common[2]. About 30% of patients with progressive systemic sclerosis exhibit cardiac involvement at autopsy[2,3]. Previous pathological studies of the heart in progressive systemic sclerosis revealed diffuse myocardial fibrosis, pericardial lesions, and fibrosis of the conduction system[3-5]. Involvement of the atrium in this disease has not been extensively evaluated, although atrial arrhythmias have been reported in approximately 10 to 20% of patients[6,7]. Previous echocardiographic studies[8-10] showed that patients with progressive systemic sclerosis exhibit left ventricular hypertrophy and an abnormal wall motion due to myocardial fibrosis that
Figure 1 Schema for recording points on the long axis M-mode and for measuring the intra-atrial electromechanical coupling interval with the long axis M-mode echocardiogram. Left panel: apical four-chamber view. M-mode echocardiograms were recorded on the left lateral (LT) and right lateral (RT) atrioventricular ring, and central fibrous body (SEP). Right panel: intervals between the onset of the P wave on the electrocardiogram to the onset of atrial contraction, recorded in the left lateral and right lateral atrioventricular rings, and in the central fibrous body.

Echocardiography

We studied 20 Japanese patients, 16 women and four men; mean age 53, who were diagnosed with progressive systemic sclerosis according to the criteria of the American Rheumatism Association. The mean duration of the disease was 11 years (range 4–30 years). No patient was receiving drugs known to influence the electrophysiology of the heart. Patients with apparent respiratory failure, renal insufficiency, diabetes mellitus or hypertension were excluded from this study. The patients with progressive systemic sclerosis were clinically stable. As controls, we evaluated 20 age-matched normal subjects who lacked any clinical, electrocardiographic (ECG), or radiographic evidence of heart disease.

Methods

Patients

A standardized series of M-mode echocardiograms, guided from the cross-sectional display, was recorded in the left lateral decubitus position, by a 2.5 MHz phased array transducer with a Toshiba SSH-160A system. Echocardiograms were recorded at a paper speed of 100 mm s⁻¹, with a simultaneous lead II ECG showing a clear P wave, and with a phonocardiogram. The motion of the atrioventricular rings during the cardiac cycle was recorded with M-mode cursor directed from the apical four chamber view. The cursor was placed longitudinally through the right lateral and left lateral atrioventricular rings and through the central fibrous body (Fig. 1). At each site, the beam was oriented so
that it was parallel to the longitudinal component of the atrioventricular ring motion. We recorded a standard short axis left ventricular M-mode echocardiogram as well as pulsed Doppler records of transmitral and tricuspid blood flow to quantify the extent and velocity of movement; we digitized the M-mode echocardiograms of the atrioventricular rings. During ventricular systole, the atrioventricular ring moves towards the apex of the ventricle. During ventricular diastole, there is rapid movement in the reverse direction corresponding to ventricular diastole. There is, in addition, a clear second reverse movement that corresponds to atrial systole. During atrial systole, movement at the atrioventricular ring sites reflects the mechanical activity of the different regions of the two atria, while movement of the central fibrous body reflects the mechanical activity of the inter-atrial septum.

The following measurements were made from the data recorded:

(1) Echocardiogram of the atrioventricular ring (Fig. 1)

The time from the onset of the P wave on the ECG to the onset of atrial systole, as a point of inflection in the long axis M-mode on the left and right atria and the central fibrous body (P-LT, P-RT, and P-SEP) was measured. The inter-atrial conduction delay and interatrial electromechanical coupling interval delay [(P-LT) — (P-RT)] were calculated from data. Maximum, atrial contraction velocities were measured by digitizing the right and the left lateral atrioventricular ring by the long axis M-mode.

(2) Doppler echocardiogram (Fig. 2)

(a) The acceleration and deceleration time of the E and A waves, the time between the onset of the P wave on the electrocardiogram to the onset ( ), the peak (••••), and the end of the A waves ( ) were measured from mitral and tricuspid inflow Doppler velocity signals. ACT=double-headed arrow; DCT=double-headed broken arrow; A2=aortic component of the second heart sound; P2=pulmonary component of the second heart sound.

(b) The time between the onset of the aortic and pulmonary component of the second heart sound (A2, P2) to the onset of the E wave on transmitral and tricuspid blood flow (A2-MF, P2-TF) were measured. We also measured left ventricular end-diastolic and end-systolic dimensions and fractional shortening, and left atrial dimensions on the standard M-mode echocardiogram.

(3) Signal-averaged electrocardiogram

Signal-averaged P wave analysis was performed in 16 patients and 20 normal controls, using high resolution electrocardiography (VCM 3000, Fukuda Electronics, Tokyo, Japan), at 250 cycles/patient, using the P-triggered technique. Bipolar orthogonal leads X, Y, and Z were used according to the methods of Simson. The noise level was maintained at <0.5 μV. Data were recorded at a paper speed of 100 mm . s⁻¹ and with a 50 to 250 Hz bidirectional digital filter for frequency cut-off after 10-min of complete rest to minimize the variability in the PR interval. The P wave duration was manually calculated on the monitor (Fig. 3).

Reproducibility

To assess the reproducibility of atrial electromechanical coupling intervals, P-RT, P-SEP, and P-LT in all 20 patients and the 20 normal controls were measured independently by two observers (R.M. and S.F.).

Data analysis

Values taken from three successive beats were averaged, and expressed as the mean ± standard deviation (SD) for groups of measurements. An unpaired Student t-test was used as appropriate. A level of P<0.05 was considered statistically significant.

Results

Clinical backgrounds

The patients with progressive systemic sclerosis and the control group did not differ significantly as regards age,
resting heart rate, and systolic or the diastolic blood pressure. Left ventricular end-diastolic and end-systolic dimensions and fractional shortening were also similar between the two groups. Left atrial dimensions did not differ significantly between the groups (3.3 ± 0.4 cm in the normal subjects vs 3.5 ± 0.6 cm in patients with progressive systemic sclerosis.

**M-mode and Doppler echocardiographic parameters**

Tables 1–3 show the results of M-mode and Doppler echocardiographic measurements. In the patients with progressive systemic sclerosis the interval between P on the electrocardiogram (P) and the onset of atrial contraction on long axis M-modes was significantly prolonged in all three atrioventricular ring sites (P-right; 56 ± 13 vs 47 ± 10 ms, P-septal; 74 ± 14 vs 55 ± 10 ms, and P-lateral; 93 ± 16 vs 72 ± 11 ms, P<0.01). The inter-atral electromechanical coupling interval delay, calculated as \([P-LT] - (P-RT)\), was also significantly prolonged (37 ± 15 vs 25 ± 6 ms, P<0.01). Maximal atrial contraction velocity was higher on the left lateral site in patients with progressive systemic sclerosis than in the normal subjects (65 ± 18 vs 47 ± 10 ms, P<0.01). The interval from P to the onset and peak of the A wave in transmitral flow was significantly prolonged in progressive systemic sclerosis (P-onset A; 81 ± 27 vs 68 ± 15 ms, P<0.01), PQ intervals, P-end of tricuspid A wave did not differ significantly between the two groups. The duration of the filtered P wave was significantly prolonged in progressive systemic sclerosis (124 ± 12 ms vs 106 ± 8 ms, P<0.01).

The acceleration rate of the A wave on transmitral flow showed a significant correlations with
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Discussion

The present study showed the significant atrial abnormalities in patients with progressive systemic sclerosis. Evaluation of the severity of the cardiac abnormalities in patients with progressive systemic sclerosis is the key to the prognosis. Bennet et al. pointed out that electrocardiographic abnormalities have the greatest influence on the survival in such patients. Left ventricular function has been evaluated non-invasively. The presence of left ventricular disease is, of course, considered to be important for the prognosis. The atrial contribution to diastolic filling is no less important than early diastolic filling. This important atrial contribution to diastolic filling is well known in patients with dual chamber pacemakers. Atrial lesions in progressive systemic sclerosis have not been extensively evaluated at histological autopsy. Atrial arrhythmias in these patients, on the other hand, have been analysed by the standard 12-lead electrocardiogram, and the Holter ambulatory electrocardiogram. These studies show that the incidence of atrial arrhythmia occurs in 10–20% of patients with progressive systemic sclerosis. Atrial fibrillation influences ventricular function as well as causes thromboembolic disorders. Atrial function is, therefore, important in patients with progressive systemic sclerosis. Atrial function was evaluated in the present study by using the M-mode echocardiogram. During atrial contraction, we found a delay in the electromechanical conduction time in the atrium and a restriction in late diastolic left ventricular filling in patients with progressive systemic sclerosis. A prolongation of atrial electrical activation was also confirmed by use of the signal averaged ECG.

Methods for evaluating the intra-atrial electromechanical coupling interval

Invasive electrophysiological techniques can be used to measure the electrical conduction time from the right atrium to the coronary sinus behind the left atrium. Josephson et al. and Leier reported that the normal values for electrical conduction were 77 ± 8 ms, range 62 to 88 ms. These values greatly exceed those of the delay in the electromechanical coupling interval, as measured in the present control study. However, these values may be related to a prolongation in left-sided conduction from the atrial muscle to the coronary sinus. Wang et al. were the first to demonstrate M-mode echocardiographic assessment of intratrial conduction time. The inter-observer reproducibility of this method was also assessed, with mean differences less than 5 ms, which is consistent with our reproducibility study, with a root mean square of 5–7 ms. One problem was that the measurements were obtained with reference to the P wave on the electrocardiogram, so that the calculation of conduction time from the sinus node to the atrium was not included. The (P-LT) – (P-RT) that we measured in this study can detect considerable delays in inter-atrial conduction when the time from the electrical activation of the atrium to mechanical contraction is the same in each atrium. These parameters, obtained by M-mode, are easily measured in the clinical setting, and are useful in estimating atrial function, in addition to standard echocardiography. Bachman's bundle, which arises from the sinus node in the left atrium through the right atrium, is supposed to have an important effect on inter-atrial conduction time in this study. We have no detailed information about this, but these inter-nodal pathways may play an important role in inter-atrial electromechanical coupling intervals which we measured in progressive systemic sclerosis.

The geometrical distance between the two atria is an important determinant factor for atrial conduction. The left atrial dimension was similar between patients and normal controls in our study. Furthermore, intraatrial block in patients older than 60 years is considered to be common. Measurements of atrial conduction in our patients and normal controls may be influenced to some extent by intra-atrial block.

Clinical significance of interatrial conduction delay in progressive systemic sclerosis

Atrial lesions in patients with progressive systemic sclerosis have not previously been evaluated in detail. The atrial disorder in such patients may be caused by direct damage to the tissue as a result of progressive systemic sclerosis, and as well as by indirect damage from atrial...
overload due to left ventricular disease. These lesions may influence the mechanical function of the atrium. Pathological study of cardiac lesions in patients with progressive systemic sclerosis has mainly involved the myocardium, and has shown various degrees of fibrosis. The atrial muscle is likely to be similarly involved. A mild degree of direct atrial damage related to progressive systemic sclerosis may not cause direct mechanical dysfunction of the atrium, but inter-atrial conduction delay may be a cause of atrial fibrillation. The present study demonstrated delayed contraction of the atrium in patients with progressive systemic sclerosis. The mean difference in inter-atrial conduction between the normal subjects and the patients with progressive systemic sclerosis was 12 ms. While this delay, as a possible cause of atrial dysfunction is not very long, a delay of nearly 10% in the total PQ interval can produce an anisoelectrical field in the left atrium. Our data clearly demonstrated that the delay in inter-atrial conduction caused the increased A wave acceleration, which means that there was a high inflow pressure drop during atrial contraction. The mechanical problem in the contraction of the left atrium caused by this delay is obvious. The short interval of atrial contraction is an important limitation to the atrial contribution to total diastolic filling. Disease of the left ventricle may also affect atrial contraction, as may elevation of left ventricular diastolic pressures. We were careful to exclude secondary left ventricular hypertrophy, although a minor prolongation of the isovolumic interval was observed in patients with progressive systemic sclerosis. Our patients had minor abnormalities in the E wave. Therefore, our finding of a delay in atrial contraction is thought to be mainly due to an atrial lesion, not to an elevation of the left ventricular diastolic pressure. This study is the first detailed description of delayed atrial conduction in progressive systemic sclerosis.

**Limitations of this study**

Electrical delays in recording the electrocardiogram and echocardiogram are possible sources of error, but are likely to be small and may occur to a similar extent with both methods. The delay between electrical activation and mechanical contraction was not calculated separately in this study. Nevertheless, measurement of the total time interval is useful in estimating atrial function. We confirmed the presence of an atrial delay in the atrium by the signal averaged ECG. Disease activity was not evaluated in this study. To assess the primary cardiac abnormality in progressive systemic sclerosis, we chose patients in a stable condition; those we excluded suffered changes due to severe renal or pulmonary dysfunction.

In conclusion, patients with progressive systemic sclerosis exhibited a delay in the intra-atrial electromechanical coupling interval, a phenomenon not previously reported. These abnormalities were not unusual in the patients studied. Intra-atrial conduction time is an important determinant of atrial and diastolic function. Thus, we should evaluate patients with progressive systemic sclerosis for significant atrial abnormalities.

**References**


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