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Pseudo-infarction pattern in diffuse systemic sclerosis. Evaluation using cardiovascular magnetic resonance☆

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ABSTRACT

Background: Diffuse systemic sclerosis (dSSc) is characterized by vascular lesions and fibrosis. Cardiac involvement, although silent, accounts for 36% of deaths. We hypothesized that cardiovascular magnetic resonance (CMR) can clarify the pathophysiology of Q waves in dSSc patients.

Patients–methods: 105 dSSc, aged 48 ± 2 years, with atypical symptoms and normal routine assessment, were evaluated by ECG and CMR using a 1.5 T system. Biventricular function was assessed by steady-state free-precession sequence (SSFP). To identify fibrosis, late gadolinium enhanced areas (LGE) were evaluated 15 min after injection of 0.2 mmol/kg gadolinium-DTPA and expressed as % of LV mass.

Results: Q waves in V1–V5 (Group A), II, III, AVF (Group B) and I, AVL, II, III, AVF, V1–V5 (Group C) were found in 25/105, 8/105 and 5/105 dSSc, respectively. In 25 dSSc with Q in V1–V6, patchy intramyocardial LGE was detected in 24/25 and involved 8 ± 2% of LV mass. LGE involved the intraventricular septum (IVS) in 11/24 and the lateral wall (LAT) in 5/24 dSSc. Only in 1/25 dSSc, an anterior, transmural LGE, due to LAD occlusion, was identified. In 8 dSSc with Q in II, III, AVF, patchy intramyocardial LGE was detected in the inferior wall and involved 5 ± 2% of LV mass. In 5 dSSc with Q in V1–V5, II, III, AVF, patchy intramyocardial LGE was detected in anterior and inferolateral wall and involved 9 ± 2% of LV mass.

Conclusion: CMR unveiled that the pattern of myocardial fibrosis in dSSc with Q waves is due to the systemic disease and not to CAD.

1. Introduction

Diffuse systemic sclerosis (dSSc) is a connective tissue disease, characterized by vascular lesions and fibrosis of all organs. Vascular lesions can provoke generalised impairment of the microcirculation and repeated focal hypoperfusion that finally contribute to irreversible fibrosis. Fibrosis has been already assessed in 12%–80% of autopsy studies [1,2]. Additionally, pathology studies documented the presence of diffuse patchy fibrosis unrelated to epicardial coronary artery stenosis [3], whereas other studies have shown concentric intimal hypertrophy associated with fibrinoid necrosis of intramural coronary arteries [4].

Cardiac involvement in dSSc may affect any structure of the heart and lead to pericarditis, myocarditis, arrhythmias, conduction defects, microvascular disease, fibrosis, pulmonary hypertension and heart failure. Myopericardial inflammation [5,6], perfusion's defects [7,8] and fibrosis [9–11] are included between the major causes of heart disease in dSSc, which is silent, at least in the early stages of the disease [11]. Although silent, cardiac involvement is a poor prognostic sign, accounting for 36% of deaths in dSSc [12,13].

The early detection of cardiac involvement plays a crucial role in risk stratification and treatment. ECG is a first line screening tool to detect arrhythmias, atrioventricular block (AV) and fibrosis [13]. However, there are no data about the pathophysiologic background of Q waves in dSSc patients and their correlation with the pattern of myocardial fibrosis, assessed by cardiovascular magnetic resonance (CMR). We hypothesized that CMR can clarify the pathophysiologic background of Q waves in dSSc patients. Our aim was to assess by CMR the pattern of myocardial fibrosis in dSSc with Q waves in their ECGs and use the

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CMR findings, as a potential gatekeeper to select those dSSc patients, who should undergo coronary angiography.

2. Patients–methods

2.1. Patients

One hundred-five dSSc patients, aged 48 ± 2 years with dSSc without any known past cardiac history, fulfilling the American College of Rheumatology criteria for the diagnosis of SSc [14] and/or LeRoy's classification criteria for SSc [15], with atypical cardiac symptoms including chest pain, supraventricular arrhythmias and recent onset of shortness of breath, but with normal routine clinical and echocardiographic evaluation, were evaluated by ECG and CMR. In those with Q waves in the ECG, a correlation between ECG and CMR was performed. The study was approved by the hospital ethics committee and all patients provided written inform consent. Patients' clinical characteristics are presented in Table 1.

2.2. Methods

2.2.1. ECG

ECGs from 105 dSSc patients with atypical cardiac symptoms but with normal routine clinical and echocardiographic evaluation, who underwent a CMR study, have been evaluated. Q waves were identified in 38/105 dSSc. According to the presence of Q waves, dSSc patients were classified as patients with Q in V1–V5 (Group A), II, III, AVF (Group B) and I, AVL, II, III, AVF, V1–V5 (Group C).

2.3. CMR evaluation

2.3.1. CMR functional study

Cardiovascular magnetic resonance examination was performed by 1.5 T Philips Intera system. For each patient, localizing scans were obtained to define the long (2-chamber) axis of the left ventricle. A mid ventricular short axis view was prescribed, and used to plan a 4-chamber view. The short axis orientation was then defined accurately, perpendicular to both the 2- and 4-chamber views. To cover the entire left ventricle, 10 contiguous (gap = 0 mm) short axis slices were acquired in each study. The imaging sequence was a 2D, multiphase (16 cardiac phases were acquired per cardiac cycle resulting to a temporal resolution of 47 ms for a heart rate of 80 beats/min), steady-state free-precession (SSFP) sequence (TE = 1.5 ms, TR = 3.1 ms, flip angle = 70°, slice thickness = 8 mm, acquired in-plane spatial resolution = 1.8 mm × 2.0 mm) characterized by the application of balanced gradients in all directions. Left ventricular ejection fraction (LVEF) <55% was considered abnormal.

2.3.2. CMR evaluation of fibrosis

For fibrosis assessment (late gadolinium enhanced images = LGE), ECG-triggered T1-W multislice spin-echo images were obtained 15 min after the IV injection of 0.2 mmol/kg gadolinium-DTPA in short, horizontal and vertical long axis, using an a 3D–T1-TFE sequence, preconditioned with a 180 degrees inversion pulse (flip angle = 15°, TE = 1.4 ms, TR = 5.5 ms, TI 225 to 275 ms as individually optimized to null myocardial signal, matrix 256 × 192 and slice thickness = 5 mm). LGE areas were expressed as a proportion of LV mass (% LV mass) [16].

2.3.3. Image analysis

Cine images were used for the evaluation of left (LV), right (RV) ventricular volumes and ejection fractions. LV endocardial borders were outlined on the end-systolic and end-diastolic short axis view images covering the entire LV. Papillary muscles were considered as part of LV cavity. LVEF/RVEF was calculated as follows: LVEF/RVEF = [(volume at end-diastole − volume at end-systole) / volume at end-diastole].

To assess the contrast-enhanced images (LGE), all short-axis slices from base to apex were inspected visually to identify areas of normal (completely nulled) myocardium. Mean signal intensity and standard deviation (SD) was derived and a threshold of >2 SD exceeding the mean was used to define areas of LGE. Summing the planimetered areas of LGE in all short-axis slices yielded the total volume, which was also expressed as a proportion of total LV myocardium (% LGE). The LGE analysis was evaluated by two experienced readers blinded to patient's identity and clinical profile. An inter-reader evaluation of concordance, using kappa coefficient (the closer to 1, the better concordance) showed that the level of concordance was very good (kapa value = 0.86).

2.4. Statistical analysis

Data, presented as mean ± SD, were compared by two-sided Student's t-test and Fisher's exact test. P values < 0.05 were considered significant.

3. Results

Q waves in V1–V5 (Group A), II, III, AVF (Group B) and I, AVL, II, III, AVF, V1–V5 (Group C) were identified in 25/105, 8/105 and 5/105 dSSc patients, respectively.

Among the 25 dSSc patients with Q in V1–V6, patchy intramyocardial LGE was detected in 24/25 and involved 8 ± 2% of LV mass. LGE involved the intraventricular septum (IVS) in 11/24 and the lateral wall (LAT) in 5/24 dSSc patients. The anterior wall and the apex were affected in 5/24 dSSc patients. Combined lesions involving more than one area were identified in 8/24 dSSc patients. Only in 1/25 dSSc patients, an anterior, transmural LGE, as a result of myocardial infarction, due to LAD occlusion, was identified.

Table 1
SSc patient clinical characteristics.

Patients characteristics	SSc patients (N = 105)
Age (years)	48 ± 2
Sex (F/M)	101/4
Diabetes	24/105
Dyslip/a	12/105
Smoking	7/105
Hypertension	22/105
CRP mg/L; mean, SD (normal range 0–5)	6 ± 1
ESR, mm/hr; mean, SD (normal range 0–10)	10 ± 0.5
Family history IHD, n	9/105
Disease duration; (years)	6 ± 5
Maximum MRSS	28 ± 2
Digital ulcers, n (past or current)	93/105
Vascular lesions, n	45/105
Tendons/joints lesions, n	52/105
Muscular lesions, n (%)	35/105
Gastrointestinal lesions, n (%)	61/105
Interstitial lung disease, n (%)	87/105
Positive for antitopoisomerase I antibodies, n	105/105
Positive for anticentromere antibodies, n	0
Positive for anti-RNA polymerase III antibody (anti-Pol III)	72/105
ACE/AT-II, n	32/105
Ca channels blockers, n	92/105
Statins, n	46/105
Current prednisone, n	15/105
Current Bosentan, n	25/105
Current Sildenafil, n	45/105
Current NSAID, n	38/105
Current non-biologic DMARDs, n	72/105
Current methotrexate, n	38/105
Any current biologic DMARD, n	0

MRSS: modified Rodnan skin score.