Pericardial Abnormalities Predict the Presence of Echocardiographically Defined Pulmonary Arterial Hypertension in Systemic Sclerosis-Related Interstitial Lung Disease*

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Objectives: **To determine the prevalence and significance of pericardial abnormalities in systemic sclerosis (SSc)-related interstitial lung disease (ILD).**

Methods: **Retrospective study of 41 subjects with SSc-related ILD who underwent evaluation including thoracic high-resolution CT (HRCT) imaging, transthoracic echocardiography (TTE), and pulmonary function testing. HRCT review evaluated the pericardium for the presence of pericardial effusion (PEf), thickness of the anterior pericardial recess (APR) [abnormal defined as > 10 mm], and pericardial thickening as calculated by total pericardial score (TPS) [abnormal defined as > 8 mm]. Pulmonary arterial hypertension (PAH) was defined as a pulmonary artery pressure > 35 mm Hg estimated by TTE.**

Results: **Fifty-nine percent had an abnormal pericardium, 49% had a PEf, 56% had an abnormal APR, and 49% had an abnormal TPS. An abnormal pericardium was more common in men than women. Subjects with and without pericardial abnormalities were otherwise similar with respect to age, SSc classification, autoantibodies, ILD radiographic pattern, and presence of esophageal dilation. Both groups had similar median percentage of predicted total lung capacity, percentage of predicted FVC, percentage of predicted FEV_1, and percentage of predicted diffusion capacity of the lung for carbon monoxide. Subjects with pericardial abnormalities were more likely to have coexistent PAH (35% vs 75%; p = 0.02) and a higher median right ventricular systolic pressure (31 mm Hg vs 44 mm Hg; p = 0.03). Multiple logistic regression revealed that TPS was the best individual predictor of the presence of TTE-defined PAH.**

Conclusions: **In patients with SSc-related ILD, pericardial abnormalities are commonly seen on HRCT, and their presence is strongly associated with echocardiographically defined PAH, with abnormal TPS as the best individual predictor.** ***(CHEST 2007; 131:988–992)***

Key words: interstitial lung disease; pericardial abnormalities; pulmonary arterial hypertension; systemic sclerosis

Abbreviations: APR = anterior pericardial recess; dcSSc = diffuse cutaneous systemic sclerosis; HRCT = high-resolution CT; ILD = interstitial lung disease; lcSSc = limited cutaneous systemic sclerosis; PAD = pulmonary artery diameter; PAH = pulmonary arterial hypertension; PEf = pericardial effusion; ppDLCO = percentage of predicted diffusion capacity of the lung for carbon monoxide; ppFVC = percentage of predicted FVC; RVSP = right ventricular systolic pressure; SSc = systemic sclerosis; TPS = total pericardial score; TTE = transthoracic echocardiography

Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by skin thickening, Raynaud phenomenon, and varying degrees of internal organ involvement. Based on the extent of cutaneous involvement, patients are typically classified as having either limited cutaneous SSc (lcSSc) or diffuse cutaneous SSc (dcSSc). Fifty to 80% of all SSc patients have pulmonary disease, with pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) the most common manifestations and the leading causes of morbidity and mortality.[1] In general, patients with lcSSc are at higher risk for

PAH, while patients with dcSSc are more likely to have progressive ILD[1]; many patients will have both.[2]

In SSc patients with PAH, a pericardial effusion (PEf) is common[3,4]; in fact, Steen[5] has suggested that a large PEf may be the presenting feature of PAH in SSc. In patients with hemodynamically severe idiopathic PAH, pericardial abnormalities, defined as pericardial thickening or PEf, are also common.

As the newer therapies for PAH improve symptoms, functional status, and may reduce mortality, early recognition of PAH in SSc patients is increasingly important. We hypothesized that in SSc patients with ILD, pericardial abnormalities identified on high-resolution CT (HRCT) would be associated with the presence of PAH. To test this hypothesis, we retrospectively evaluated a cohort of patients with SSc-related ILD to determine the prevalence and clinical significance of CT evidence of pericardial abnormalities.

Materials and Methods

Subjects

We identified 41 subjects who consented to enroll in our institutional review board-approved and Health Insurance Portability and Accountability Act-compliant ILD database with SSc-related ILD who had undergone a comprehensive evaluation that included the following: history and physical examination, rheumatologic serologic testing, pulmonary function testing, thoracic HRCT imaging, and transthoracic echocardiography (TTE). All were seen at National Jewish Medical and Research Center between 1998 and 2004. All subjects met current American College of Rheumatology criteria for the diagnosis of SSc.[6] The diagnosis of ILD was made based on the presence of respiratory symptoms, abnormal pulmonary physiology, and diffuse parenchymal lung disease on thoracic HRCT. No subject had symptomatic or previously identified pericardial abnormalities prior to the evaluation.

Analysis of Pericardial Abnormalities

Two expert thoracic radiologists (S.M., D.A.L.), blinded to clinical information, performed measurements of the pericardium as described by Bacque-Juston et al.[7] Briefly, using conventional mediastinal window settings (level, 50 Hounsfield units; width, 350 Hounsfield units; 5 mm slice thickness), the presence or absence of a PEf was recorded (Fig 1, *top left*, *A*, and *top right*, *B*). Measurement of pericardial thickening was performed at the one level between the aortic root and the diaphragm that displayed the maximal circumferential extent of the pericardium. Thickness was measured at four points around the circumference: the anterior, posterior, left lateral, and right lateral pericardium. The total pericardial score (TPS) was calculated and defined as the sum of these four measurements, with > 8 mm defined as abnormal (Fig 1, *center left*, *C*, and *center right*, *D*). The sagittal dimension of the anterior pericardial recess (APR) was measured anteriorly between the ascending aorta and the pulmonary trunk (Fig 1, *bottom left*, *E*, and *bottom right*, *F*). An abnormal APR was defined as > 10 mm. The central pulmonary artery diameter (PAD) was assessed at its point of maximal dilation.

The presence of PAH was estimated by two-dimensional TTE (M-mode, Doppler, and color flow Doppler). Subjects were considered to have PAH if the estimated pulmonary artery pressure was > 35 mm Hg. Pulmonary function testing, thoracic HRCT imaging, and TTE data were collected within the closest intervals in time (median interval, 1 day; range, 1 to 1,080 days).

Statistical Analysis

We assessed differences between groups using Fisher exact test for categorical variables and Wilcoxon rank-sum test for continuous variables. Multiple logistic regression analysis included the following variables: PEf, APR, TPS, rank TPS, PAD, esophageal dilation, ILD pattern, percentage of predicted total lung capacity, percentage of predicted FVC (ppFVC), percentage of predicted FEV_1, percentage of predicted diffusion capacity of the lung for carbon monoxide (ppDLCO), ppDLCO/alveolar volume, gender, age, and SSc type (lcSSc, dcSSc).

Results

Twenty four of 41 subjects (59%) had an abnormal pericardium by HRCT. Twenty of 41 subjects (49%) had a PEf, 23 of 41 subjects (56%) had an abnormal APR, and 20 of 41 subjects (49%) had an abnormal TPS.

An abnormal pericardium was more common in men than women. Subjects with and without pericardial abnormalities were otherwise similar with respect to age, SSc classification, autoantibodies, ILD pattern, presence of esophageal dilation, and pulmonary physiology (Table 1). Subjects with pericardial abnormalities were more likely to have a higher median right ventricular systolic pressure (RVSP) and coexistent TTE-defined PAH (Table 2). Patients with TTE-defined PAH demonstrated similar pulmonary physiology but were more likely to have a PEf, an abnormal APR, and an abnormal TPS (Table 3).

Multiple logistic regression revealed that TPS was the best individual predictor of PAH. For every approximate 3-mm increase in TPS, the odds of PAH increased by 13% (95% confidence interval, 1.04 to 1.23; $p = 0.005$). Increases in TPS were associated with increased RVSP ($r = 0.51$, $p = 0.0008$, Spearman ρ).

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