Prevalence of pulmonary hypertension in systemic sclerosis

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Abstract

Objective

To assess the prevalence of pulmonary arterial hypertension (PAH) in patients with the diagnosis of systemic sclerosis (SSc) followed at a tertiary university service.

Material and methods

Fifty-seven patients with SSc were studied by clinical assessment directed at the cardiopulmonary system, pulmonary function tests and Doppler echocardiography (ECHO). The following criteria were considered for the diagnosis of PAH: pulmonary artery systolic pressure (PASP) ≥ 40 mmHg and/or the presence of other direct and indirect signs of PAH detected upon ECHO.

Results

Sixteen patients (28%) were diagnosed with PAH upon ECHO, 13 based on PASP ≥ 40 mmHg and 3 based on direct and indirect signs of PAH; 8 patients had isolated PAH and 8 had PAH secondary to pulmonary fibrosis. Nine patients showed signs suggestive of cor pulmonale *upon ECHO; among these patients, 6 had pressure recordings ≥ 40 mmHg and 3 had a PSAP between 35 and 40 mmHg; one patient was asymptomatic and 8 showed signs suggestive of PAH upon clinical examination. Among the clinical and laboratory variables studied, a correlation was only observed between PAH and an elevated erythrocyte sedimentation rate (p = 0.004).*

Conclusions

The prevalence of PAH associated with SSc observed in this study was similar to those reported in the literature. However, the cut-off of PSAP measured by ECHO and used for the diagnosis of PAH associated with SSc needs to be revised.

Key words

Systemic sclerosis, pulmonary hypertension, echocardiography.

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Introduction

Systemic sclerosis (SSc) is an inflammatory connective tissue disorder associated with vascular dysfunction, which is clinically characterized by thickening of the skin, Raynaud's phenomenon and different forms of visceral manifestations that mainly affect the gastrointestinal tract, lungs, heart and kidneys (1). The complex physiopathology of SSc is reflected in the different clinical presentations and prognosis of the disease; the description of the follow up of SSc patients in ethnic and genetically different populations can contribute to a better understanding of the disease regarding its prevalence and prognostic factors (2-11). Pulmonary involvement is observed in more than 70% of patients with SSc and is the second most frequent visceral manifestation, exceeded only by esophageal involvement. The main forms of pulmonary involvement in SSc are interstitial lung disease, also known as fibrosing alveolitis or pulmonary fibrosis, and pulmonary vascular disease which leads to pulmonary arterial hypertension (PAH) (12, 13).

PAH is an important cause of morbidity and mortality in SSc. The frequency of PAH in SSc is uncertain, ranging from 5 to 50% depending on the method used for its investigation (12,13). Generally, the signs and symptoms related to PAH in SSc are insidious, especially during the initial phases of this complication, and up to one-third of patients might be asymptomatic (12, 13). Transthoracic two-dimensional Doppler echocardiography (ECHO) is a useful tool for the noninvasive measurement of pulmonary arterial pressure, showing 90% sensitivity and 75% specificity in the diagnosis of PAH in SSc (14). Pressure recordings are obtained indirectly based on the tricuspid regurgitation jet, with pulmonary artery systolic pressures (PASP) ≥ 30 mmHg being considered to be abnormal (14). ECHO is the non-invasive test recommended as part of a screening program for those at risk of developing PAH (15,16). A recent study comparing echocardiography, pulmonary function and cardiac catheterization in 137 SSc patients (52 with and 85 without pulmonary fibrosis) showed that a positive predictive accuracy of non-invasive tests are adequate for the diagnosis of advanced PAH (17); the value of ECHO in the prediction of early PAH in SSc still needs to be defined.

The objective of the present study was to determine the prevalence of PAH in patients with a diagnosis of SSc followed in a Brazilian tertiary university service using ECHO as the diagnostic method of screening.

Patients and methods

Patients

A cross-sectional study was conducted on patients with diagnosis of SSc followed at the Unit of Rheumatology of the University Hospital, Federal University of Minas Gerais (HC-UFMG), Brazil, during the period from November 2001 to March 2003. All patients fulfilled the preliminary criteria for the classification of SSc established by the American College of Rheumatology (18), and were subset in limited and diffuse SSc according to the criteria proposed by LeRoy *et al*. (19). Patients with SSc in overlap with other collagen tissue diseases or those with the diagnosis of mixed connective tissue disease (MCTD) according to Alarcon-Segovia criteria (20) were excluded from the study. The patients answered a questionnaire and were submitted to physical examination for the assessment of cardiorespiratory signs and symptoms. The patients were then referred for ECHO and pulmonary function tests after they had signed an informed consent form to participate in the study.

Doppler echocardiography

Exams were performed by a single experienced professional using a Sonos 1500 HP echocardiograph equipped with a 2.5/2.0 transducer. The following parameters were analyzed during ECHO: heart chamber characteristics, alterations in contractility and diastolic relaxation, left ventricular systolic function, and valvar and pericardial alterations, in addition to the measurement of PASPin the presence of tricuspid regurgitation. When this measurement could not be obtained, other signs

of PAH were investigated including the determination of diastolic pulmonary artery pressure, pulmonary artery acceleration time (AcT), study of the shape of the pulmonary artery Doppler velocity curve, time to peak velocity (TPV)/ejection time (ET), isovolumic relaxation time of the right ventricle, ratio of pre-ejection period to ET (PEP/ET) in pulmonary flow, and pulmonary mean artery pressure.

The presence of PAH was defined as a PASP ≥ 40 mmHg estimated by ECHO based on the measurement of the tricuspid regurgitation jet using the equation of Bernoulli (PASP = $4VTR^2$ [maximum tricuspid regurgitant jet velocity] + RAP [right atrial pressure]), with the estimated RAPbeing 14 mmHg, and/or as the presence of direct or indirect signs of PAH. *Direct signs of PAH* other than a PASP ≥ 40 mmHg were diastolic pulmonary artery pressure ≥ 25 mmHg, AcT< 100 ms, presence of a mesodiastolic notch in the Doppler recording of the pulmonary valve, time to peak velocity (TPV)/ejection time (ET) < 0.36, prolonged isovolumic relaxation time of the right ventricle, PEP/ET in pulmonary flow ≥ 0.34, and pulmonary mean artery pressure ≥ 30 mmHg. *Indirect signs of PAH* were the presence of right ventricular dilatation associated with tricuspid and/or pulmonary regurgitation, right atrial dilatation, dilatation of the pulmonary arterial trunk, reduced "a" dip and midsystolic closure of the pulmonic valve, thickening of the right side of the interventricular septum, protrusion of the interventricular septum into the left ventricle during diastole, and hypertrophy of the free wall of the right ventricle (21).

Patients with other cardiovascular alterations able to trigger PAH (left-sided atrial or ventricular heart disease; left-sided valvular heart disease; history compatible with pulmonary thrombotic and/or embolic disease) were excluded from the study.

Pulmonary function tests

Simple spirometry was performed with a plethysmograph and the diffusion capacity of the lung for carbon monoxide (DLCO) was measured with a Collins DS2plus apparatus in the Laboratory of Pulmonary Function, HC-UFMG, according to the recommendations of the Brazilian Consensus on Spirometry (22).

High-resolution computed tomography of the chest (HRCT)

Patients with a diagnosis of PAH without known interstitial lung disease were referred for HRCT for the diagnosis or exclusion of pulmonary fibrosis associated with PAH. HRCT scans were obtained with a Siemens SOMATON ART tomograph (2 mm thick axial sections at 10 mm intervals using 1200 HU window width and -700 HU window level). In view of the presence of interstitial alterations, scans were also performed in ventral decubitus.

Statistical analysis

Data are reported as means and medians. The Student t-test, chi-square test, Pearson's correlation coefficient and ANOVA were applied to determine possible factors associated with the presence of PAH.

Results

Sixty consecutive patients with a diagnosis of SSc were initially evaluated. Two patients with rheumatic mitral valvulopathy (limited SSc) and one with mitral prolapse (diffuse SSc) were excluded, all of them with signs of mild PAH at ECHO. Of the 57 patients included in the study, 32 had diffuse SSc and 25 had limited SSc. The mean age of the patients was 42.6 years (SD ± 13.1), range 18 to 70 years, while the mean disease duration was 9.6 ± 6.9 years (range 1 to 30 years).

The prevalence of PAH was 28% (16/57 patients), including 8 patients with isolated PAH (4 with diffuse SSc and 4 with limited SSc) and 8 cases secondary to pulmonary fibrosis (5 with diffuse SSc, 3 with limited SSc). PASP could not be measured in 4 patients due to the absence of tricuspid regurgitation; one of these patients (diffuse SSc) showed an altered AcT compatible with PAH, with the PASP estimated by this method being 48.5 mmHg. The other 3 patients without a tricuspid regurgitation jet showed no direct or indirect signs of PAH.

Nine patients with PAH presented signs suggestive of *cor pulmonale* upon ECHO (hypertrophy of the right ventricle, thickening of the right side of the interventricular septum, right ventricular dilatation associated with tricuspid and/or pulmonary regurgitation, right atrial dilatation and protrusion of the interventricular septum into the left ventricle during diastole); of these, three had pressure recordings between 35 and 40 mmHg and six had a PASP ≥ 40 mmHg. One of the 16 patients with PAH was asymptomatic despite a PASP of 40 mmHg associated with right atrial and ventricular dilatation and reduced DLCO (64%). Eight patients with PAH showed hyperphonesis of the second bulla, all with PASP ≥ 40 mmHg; one of them also presented a murmur of tricuspid insufficiency and impulsion of the right ventricle upon precordial palpation and another patient had lower limb edema. Determination of the DLCO was not possible in two of the 16 patients with PAH due to difficulties in performing the maneuvers necessary for the exam (one patient did not adequately understand the instructions and the other presented severe restrictive disturbances).

Analysis of the pressure recordings showed that 17 patients had PASP ≥ 35 and <40 mmHg (Table I). Three of them (2 patients with limited SSc and one with diffuse SSc) had clinical complaints of dyspnea and showed alterations in the right chambers upon ECHO suggestive of *cor pulmonale*, and these patients were thus classified as having PAH. Two of these patients presented tomographic and/or spirometric changes compatible with interstitial lung disease in the absence of a disproportional reduction in DLCO, while the other patient (limited SSc) showed no signs of interstitial lung disease and had a normal DLCO (78%). In this group (PASP ≥ 35 and < 40 mmHg), four patients were unable to perform the maneuvers required for the measurement of DLCO, while only one of the patients who did (asymptomatic, with diffuse SSc) presented an isolated reduction in DLCO (60%) without alterations upon chest HRCT. Twenty-

Table I. Pulmonary arterial systolic pressure (PASP) and alterations in the right chambers.

PASP	Number of patients (n = 57)	Right chamber alterations detected by echo (n = 9/57, 15.8%)
Not measured based on the tricuspid regurgitation jet	4* (7%)	0 (0%)
< 30 mmHg	2 (3%)	0 (0%)
≥ 30 and < 35 mmHg	21 (37%)	0 (0%)
≥ 35 and < 40 mmHg	17 (30%)	3 (5,3%)
≥ 40 mmHg	13 (23%)	6 (10,5%)
Total	57 (100%)	9 (15,8%)

*: 3 of these patients did not present direct or indirect alterations suggestive of pulmonary hypertension and one patient showed an AcT< 100 ms suggestive of pulmonary hypertension.

Table II. Clinical and laboratory characteristics of patients with and without pulmonary hypertension (PAH).

	With PAH	Without PAH
Age (years)*	44.1 ± 13.2	42.1 ± 13.2
Women (%)	13 (81%)	36 (88%)
Disease duration (years)*	7.7 ± 4.9	10.4 ± 7.4
Clinical form		
Diffuse	9 (56%)	23 (56%)
Limited	7 (44%)	18 (44%)
Arterial hypertension	6 (37%)	12 (29%)
Smokers	1 (6%)	4 (10%)
Raynaud's phenomenon	16 (100%)	40 (98%)
Ulcers of the digital pulps	13 (81%)	33 (81%)
Telangiectasia	14 (87%)	34 (83%)
Pulmonary fibrosis	8 (50%)	22 (54%)
ANA	14 (87%)	35 (85%)
Anticentromere	2 (15%)	6 (15%)
Anti-Scl 70	1 (8%)	2 (6%)
Anti-RNP	7 (54%)	14 (41%)
ESR †*	46 ± 28	29 ± 23
DLCO (%)*	76.2 ± 26.2	75.2 ± 20.7

* Data are reported as means ± SD; † P= 0.004.

one patients had PASP ≥ 30 and <35 mmHg, while only two patients (one with diffuse SSc and one with limited SSc) had a PASP< 30 mmHg.

Analysis of the epidemiological, clinical and laboratory factors revealed a correlation only between PAH and an elevated erythrocyte sedimentation rate (ESR) (p = 0.004) (Table II). No correlation was observed between PAH and DLCO (p = 0.811).

Discussion

Since the advent of angiotensin-converting enzyme inhibitors for the treatment of scleroderma renal crisis, pulmonary involvement is the leading cause of death in patients with SSc (1-2). Analysis of the causes of death of 2000 patients with SSc followed at the University of Pittsburgh over the last 20 years revealed that 211 patients had died of pulmonary causes, 113 due to isolated pulmonary hypertension and 98 due to pulmonary fibrosis, corresponding to 21.5% of the 981 deaths and 44% of the scleroderma related deaths observed at that service (23). Since the onset of clinical manifestations of pulmonary involvement in SSc is usually late, efforts have been directed at identifying clinical and laboratory variables that permit the identification of patients at high risk to develop interstitial and vascular lung disease, as well as at the early diagnosis of these complications. The assessment of PAH in SSc include ECG, chest radiography, echodopplercardiography, pulmonary function tests and right heart catheterization. The primary limitation of ECG and chest radiography is the low sensitivity for PAH. The finding of isolated reduction in DLCO is suggestive of PAH in SSc. Despite ECHO being considered the most accurate non-invasive method for assessment of PAH, right heart catheterization is the gold standard method in the measurement of pulmonary pressure (24).

The etiopathogenesis of PAH in SSc is highly complex and seems to comprise a sequence of events starting with some damage associated with pulmonary endothelial dysfunction, followed by vasospasm, vascular remodeling and predisposition to thrombosis in small pulmonary vessels. It is currently believed that endothelial damage to small pulmonary arteries and arterioles is the initial alteration in the process which eventually leads to vasospasm and vascular remodeling (13, 25). An increase in the circulating levels of endothelin-1, a vasoconstrictor peptide, has been correlated with vascular and fibrotic manifestations in SSc, especially in patients with limited SSc and PAH or with scleroderma renal crisis, supporting the lesion/endothelial dysfunction theory (26).

In limited SSc, PAH generally occurs as an isolated manifestation which continues to be subclinical until arterial damage results in dyspnea during the intermediate and late phases of the disease (12, 13). In diffuse SSc, isolated PAH is rare and is normally associated with advanced pulmonary fibrosis, leading to the onset of additional cardiopulmonary symptoms. Some autoantibodies have been correlated with the presence of PAH in the different clinical forms of SSc, such as anti-Th/To (27) with limited SSc and anti-U3RNP with the diffuse form (28). However, detection of these autoantibodies is still not a routine procedure at university services in Brazil. The low prevalence of SSc patients with limited cutaneous involvement in our study is probably associated to referral bias to a tertiary university service.

A reduction in carbon monoxide diffusing capacity disproportional to the decline in forced vital capacity (FVC) has been considered as an important

Table III. Main data regarding the prevalence of pulmonary arterial hypertension (PAH) in systemic sclerosis.

Reference	Type of study	Characteristics of the study population	Diagnostic criteria for PAH	Prevalence (%)
Stupi *et al*. (1986)	Retrospective	673 (CRESTsyndrome)	Mean PAP> 20 mmHg. PASP/PADP> 30/15mmHg and PCP< 12 mmHg upon catheterization (CAT) and/or clinical signs of cor pulmonale	9% (isolated PAH and secondary to pulmonary fibrosis)
Sampaio-Barros *et al*. (1995)	Prospective	95 (diffuse and limited forms)	PASP≥ 30 mmHg determined by echo	30% (10 isolated PAH and 19 secondary to pulmonary fibrosis)
Sacks *et al.* (1996)	Retrospective	1257 (580 limited form and 677 diffuse form)	Mean PAP> 30 mmHg upon CATor tricuspid regurgitation with dilatation of the right ventricle determined by echo	5.8% (isolated PAH) 10% in the limited form 2% in the diffuse form
Koh *et al*. (1996)	Retrospective	344 (140 diffuse form and 204 limited form)	Mean PAP≥ 25mmHg with PCP ≤ 12mmHg upon CAT or PASP≥ 35 mmHg determined by echo or evidence of right ventricle and pulmonary artery dilatation and/or tricuspid regurgitation or paradox movement of the interventricular septum on echo scans	4.9% (isolated PAH and PAH due to pulmonary fibrosis)
Battle *et al*. (1996)	Cross-sectional	34 (29 diffuse form and 5 limited form)	PASP≥ 30 mmHg determined by echo	35% (isolated PAH and PAH due to pulmonary fibrosis)
Murata *et al*. (1997)	Prospective	135 (limited and diffuse forms) with or without another underlying connective tissue disease	PASP≥ 40 mmHg and/or signs of right ventricular overload upon echo or mean PAP≥ 20 mmHg upon CAT	22% (isolated PAH and PAH due to pulmonary fibrosis)
Yamane *et al*. (2000)	Cross-sectional	125 (55 diffuse form and 70 limited form)	PASP≥ 40 mmHg upon echo	16% (isolated PAH and PAH due to pulmonary fibrosis)
MacGregor *et al*. (2001)	Retrospective	930 (295 diffuse form and 635 limited form)	PASP≥ 30 mmHg determined by echo	13% (isolated PAH and PAH due to pulmonary fibrosis)
Mukerjee *et al*. (2003)	Prospective	722 (diffuse and limited forms)	Mean resting PAP≥ 25 mmHg or ≥ 30 mmHg during exercise upon CAT	12% (isolated PAH and PAH due to pulmonary fibrosis)
Present study (2004)	Cross-sectional	57 (32 diffuse form, 25 limited form)	PASP≥ 40 mmHg or direct and/or indirect evidence of PAH upon echo	28% (isolated PAH and due to pulmonary fibrosis)

Mean PAP: mean pulmonary artery pressure; PSAP: pulmonary systolic artery pressure; PADP: pulmonary artery diastolic pressure; PCP: pulmonary capilar pressure.

predictive factor of vascular pulmonary disease in SSc. In a retrospective case-control study, Steen and Medsger (29) observed that patients with SSc and PAH showed a markedly reduced DLCO at an average of 4.5 years prior to the diagnosis of PAH when compared to controls ($p < 0.0001$). A FVC/DLCO ratio between 1.6 and 1.8 may help identify patients with a higher probability of vascular pulmonary disease (23). Our study population included cases of severe pulmonary fibrosis without secondary PAH, associated with significantly reduced DLCO but proportional to the decline of FVC, as well as patients with an isolated reduction in DLCO showing no criteria for the diagnosis of PAH or interstitial lung disease. A prospective follow-up of these patients would be more adequate for a better assessment of this association.

The association between PAH and an elevated ESR observed in the present study has also been reported by Yamane and co-workers (30), who found a 16% prevalence of PAH (6 patients with PAH secondary to pulmonary fibrosis and 14 with isolated PAH) in a

population of 125 patients, establishing a PASP ≥ 40 mmHg determined by ECHO for the diagnosis of PAH as done here. An increase in ESR has also been associated with a higher severity and mortality related to interstitial lung disease in SSc (31). Although not confirmed in other studies, the association between PAH and increased ESR has been proposed by some investigators to be suggestive of the presence of pulmonary inflammatory activity and as a possible indicator of poor prognosis for both interstitial and pulmonary vascular involvement (32). However, until today the early diagnosis of PAH related to SSc still depends on routine investigations including a combination of pulmonary function tests and ECHO.

The first series of patients with SSc and PAH was described by Sackner in 1964 (33), followed later by other series (28, 30, 34-40) (Table III).

Comparison of the present findings with those reported in the literature is difficult due to differences between the study populations, the methods applied to investigate PAH and the criteria used to define its presence. Studies employing right ventricle catheterization for the diagnosis of PAH have demonstrated a prevalence ranging from 5 to 12%, while those using ECHO have revealed higher prevalences, ranging from 13 to 35% (28, 29, 34-40).

Right heart catheterization is considered to be the more reliable diagnostic method to determine the prevalence of PAH related to SSc. However, data obtained from these studies might underestimate the prevalence of this complication, since patients referred for this exam are usually symptomatic (25). With respect to studies using ECHO, the greatest difficulty encountered in the comparison of the results is the cut-off of PASPsuggestive of PAH. Concerned with the early diagnosis of pulmonary vascular damage in SSc in view of its severity, some investigators have used a PASP ≥ 30 mmHg determined by ECHO, with emphasis on the study of Denton and co-workers (14). However, the criticism that can be raised regarding this cut-off is that it might lead to an overestimation of cases of PAH related to SSc.

MacGregor and co-workers (38) reported a cumulative prevalence of PAH of 13%, considering PASPrecordings ≥ 30 mmHg, measured by ECHO based on the tricuspid regurgitation jet, for the presence of PAH. However, in that study retrospective analysis of PAH progression over five years revealed that PASPremained unchanged in most patients, while almost one-third of patients showed a decline in PASP levels. Nevertheless, pressure readings ≥ 30 mmHg at any time during follow-up were associated with a 20% higher mortality risk at 20 months, being higher in patients with elevated PASP upon PAH manifestation, in individuals presenting pressure rises throughout follow-up, in men, older subjects, and patients with limited SSc.

Mukerjee *et al*. (40) identified PAH in 89 (12%) of 722 patients followed up over a period of 4 years, with mean survival rates of 81, 63 and 56% at 1, 2 and 3 years after diagnosis, respectively. Elevated right atrial pressure was the best predictive factor of mortality, with no significant difference in survival being observed between patients with isolated PAH and those with PAH associated with pulmonary fibrosis. In that study, patients were initially submitted to ECHO screening. Patients with PASP readings > 35 mmHg upon ECHO, associated with a DLCO < 50% or with a 20% fall in DLCO over a one-year period without pulmonary fibrosis or with dyspnea of no apparent cause, were referred for catheterization. Patients with a mean resting pulmonary arterial pressure >25 mmHg or >30 mmHg during exercise determined by catheterization were diagnosed as having PAH. A total of 164 patients showed alterations suggestive of PAH upon ECHO screening; of these, 12 did not undergo catheterization due to advanced age or to the presence of multiple comorbidities and 5 refused the exam. Of the 147 patients who were submitted to catheterization, 36 did not fulfill the criteria for a diagnosis of PAH by catheterization, while 22 had PAH due to other causes (pulmonary thromboembolism and postcapillary PAH).

The natural history of PAH in SSc is still not well understood; it is believed that some patients have a poor prognosis, while the evolution of pulmonary vascular disease is slower in others, accompanied by a slower rise in pulmonary pressure. Although some similarities seem to exist between primary PAH and PAH associated with SSc, this does not apply to all cases. A better understanding of the natural history of PAH related to SSc depends not only on the standardization of a routine procedure for the diagnosis of this complication, but also on the monitoring of its evolution and therapeutic response on the basis of serial pulmonary arterial pressure measurements together with the evaluation of the degree of functional impairment (14, 17). Therefore, reassessment of the echocardiographic criteria applied to the diagnosis of PAH in SSc is necessary in order to prevent the overestimation of cases and to permit the comparison of its characteristics between different populations and with PAH related to other connective tissue diseases. It should be emphasized that ECHO is an observer-dependent exam, i.e., its accuracy is intimately related to the experience of the examiner, while heart catheterization continues to be the gold standard for the diagnosis of PAH in SSc and should always be performed to confirm the diagnosis of PAH in therapeutic assessment. The combination of clinical variables, pulmonary function tests and ECHO, as proposed in some studies (17, 39, 40), might result in a better criterion for the initial diagnosis of PAH in SSc, overcoming the deficiencies of ECHO as a single parameter. This would be of great help in services where easy access to catheterization for the confirmation of the diagnosis of PAH is not available.

The sixth meeting of OMERACT, analyzing instruments currently used in clinical trials of SSc, defined important aspects that complement these observations. With respect to DLCO, it was established that this factor can be influenced by both interstitial and pulmonary vascular involvement in such a way that its usefulness for the differentiation between these two forms of pulmonary involvement in SSc has yet to be determined. The benefits of right

heart catheterization, considered to be the gold standard for pulmonary arterial pressure measurements, has been well documented in terms of both the diagnosis and assessment of the therapeutic response of primary PAH or PAH associated with SSc. However, this technique requires standardization among different services, which use it for the assessment of PAH related to SSc to permit future comparisons between cohorts. ECHO offers some advantages over right heart catheterization, being noninvasive, more accessible and less expensive, but shows limitations in the interpretation of the results and PASP measurement is not possible in 20 to 30% of the patients (41). The accuracy of ECHO compared to right heart catheterization has been verified, but further tests to validate its sensitivity in SSc are still required.

In conclusion, the prevalence of PAH associated with SSc observed in the present study was similar to those reported in other investigations despite the limitations in this comparison. The study of PAH by ECHO is an accessible practice that is useful for the early diagnosis of pulmonary vascular involvement in SSc. However, the cut-off of PASP measured by ECHO and used for the diagnosis of screening of PAH related to SSc, as well as the possibility of an association between this parameter and other echocardiographic, clinical and pulmonary function variables, needs to be revised in order to standardize criteria for to request right heart catheterization for the confirmation of the diagnosis and follow-up of PAH in SSc.

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