Pulmonary hypertension in scleroderma and its relation to disease activity
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Aim
The aim of this study was to screen for pulmonary hypertension (PH) in scleroderma patients using Doppler echocardiography, and correlate it with inflammatory parameters of the disease.

Patients and methods
Doppler echocardiography was performed in 39 patients with scleroderma (three men and 36 women) and was compared with 20 age-matched and sex-matched healthy controls. Fifteen (38.5\%) patients had limited scleroderma and 24 (61.5\%) patients had diffuse scleroderma. PH was diagnosed if the peak systolic pressure gradient at the tricuspid valve was more than 25 mmHg. All patients were subjected to full assessment of history, rheumatological examination, laboratory studies, chest radiography, and pulmonary function tests.

Results
In 39 scleroderma patients, PH was detected in five patients (12.8\%); four of them had limited scleroderma and one had diffuse scleroderma. The range of pulmonary artery systolic pressure was 37–63 mmHg (mean ± SD = 49.2 ± 10.1). There was a highly statistically significant difference between patients and controls ($P < 0.0001$). There were no significant differences between patients with and without PH in clinical features, except for arthritis and Raynaud’s phenomena ($P < 0.04$, $0.01$). Significant differences in the level of erythrocyte sedimentation rate, complement, and anticentromere antibodies were found in patients with PH versus those without PH ($P < 0.04$, $<0.03$, $<0.002$, respectively). There was a statistically significant correlation between pulmonary artery pressure with disease duration ($P < 0.001$) and Valentini Disease Activity Index ($P < 0.001$).

Conclusion
Patients with scleroderma have an increased risk of pulmonary arterial hypertension. Echocardiography should be used as a screening tool in patients who are at a higher risk of developing PH.

Keywords: echocardiography, pulmonary hypertension, scleroderma, screening

Introduction
Systemic sclerosis (SSc) is a heterogeneous disorder characterized by dysfunction of the endothelium, dysregulation of fibroblasts resulting in excessive production of collagen, and abnormalities of the immune system [1]. These processes lead to progressive fibrosis of the skin and internal organs, resulting in premature organ failure and death. Although the cause of SSc is unknown, genetic and environmental factors are believed to contribute toward host susceptibility [2]. SSc is divided into diffuse cutaneous (dcSSc) and limited cutaneous (lcSSc) syndromes depending on the extent of skin thickening. Skin thickening confined to the elbows, knees, or face characterizes lcSSc, whereas dcSSc indicates more extensive disease. Most dcSSc patients (about 60\%) are Scl–70 positive (antitopoisomerase I), whereas 88.7\% of lcSSc patients are anticentromere antibody positive [3]. Whether presenting in the limited or diffuse form, SSc is a systemic disease with the potential for multiple organ involvement, including the gastrointestinal, cardiac, renal, and pulmonary systems [1]. However, SSc-related pulmonary arterial hypertension (SSc-PAH) has emerged as a leading cause of mortality [4]. It affects mainly women in the prime of their life [5] and is associated with significant morbidity, including pain, disability, depression [6], and reduced quality of life [7].

PAH is a devastating vascular complication of a number of connective tissue diseases, including SSc, where it has a major impact on the clinical course and overall survival and is the single most common cause of death in patients affected by this syndrome [8]. PAH most commonly occurs as a late complication in patients with limited cutaneous disease and anticientromere antibodies. Although echocardiography is a useful screening tool, heart catheterization is required to diagnose PAH before initiating therapy. Prognosis
and therapeutic response are worse in SSc-PAH than in other PAH categories (median survival 1–3 years) [9]. Pulmonary hypertension (PH) is defined as a resting mean pulmonary artery pressure of at least 25 mmHg. The WHO classification recognizes five categories of PH: (1) PAH; (2) PH associated with left heart disease; (3) PH associated with lung disease/hypoxia; (4) thromboembolic PH; and (5) PH associated with multisystem disease. SSc patients may have category (1), (2), or (3) PH [10]. Although remarkable advances have been achieved in elucidating the pathogenesis of PAH over the past two decades, leading to the development of disease-targeted therapies for the idiopathic form of this condition, the response to therapy is suboptimal in SSc-PAH and survival remains very poor [11,12]. Approved therapies include prostacyclins, endothelin antagonists, and phosphodiesterase type-5 inhibitors [9].

**Patients and methods**

**Study population**

This is a cross-sectional study carried out on scleroderma patients attending the outpatient clinic of the Department of Rheumatology and Rehabilitation and from all private clinics of all rheumatologists and internal medicine doctors at Minia University Hospital, Egypt, over 5 years (from February 2008 to March 2013). None of the patients had been treated previously with medication for PAH. Informed consent was obtained from all patients before their entry into the study. Thirty-nine scleroderma patients were recruited, between 18 and 60 years of age, and no children were included. Eight patients were symptomatic for PH. Only three of these patients had PH. Exclusion criteria included thromboembolism, diabetes mellitus, systemic arterial hypertension, pregnancy, hypercholesterolemia, rheumatic heart, etc.

Informed consent obtained from subject or their legally authorized representatives and documented prior to research involvement, this approval is valid for one year from date of IRB.

**Clinical evaluation**

All the patients were subjected to a thorough assessment of history by the same rheumatologist including symptoms related to PH (chest pain, fainting or near fainting during physical activity, and dyspnea), general examination, and rheumatological evaluation, which included the assessment of the scleroderma disease activity index. The Valentini Disease Activity Index for all patients with SSc was adopted by the ESSG and the Scleroderma Clinical Trials Consortium at a symposium held in 2002 [13,14]. It includes 10 variables with weights ranging from 0.5 to 2.0 and resulting in a total score ranging from 0 to 10. This index includes the following parameters: modified Rodnan skin score of greater than 14 (1.0), scleredema (0.5), change in skin symptoms in the last month (2.0), digital necrosis (0.5), change in vascular symptoms in the last month (0.5), arthritis (0.5), lung diffusion capacity of less than 80% predicted (0.5), change in cardiopulmonary symptoms (2.0), erythrocyte sedimentation rate (ESR) of greater than 30 mm per first hour (1.5), and hypocomplementemia (1). The total disease activity index score was 10.0. All clinical assessments were carried out by the same rheumatologist for all patients.

**Laboratory studies**

Antinuclear antibody can be detected by an indirect immunofluorescence assay and ESR can be detected by the Westergren test. Measurement of anticardiolipin antibodies was performed using a commercially available anticardiolipin enzyme-linked immunosorbent assay. If the titer of anticardiolipin was above 3.2 U/ml, the result was defined as positive, complements 3 and 4 (Diffuplate, USA). Special tests, such as anticentromere and antitopoisomerase, were also used. Other routine laboratory tests, such as complete blood picture, renal function test, serum cholesterol, fasting and random blood sugar, and pregnancy test (for suspected women), were carried out for all patients.

**Radiography and pulmonary function tests**

Chest radiography, anteroposterior and lateral views, and pulmonary function tests were carried out for all patients to exclude evidence of parenchymal lung disease. Also, radiography of both hands was carried out.

**Echocardiographic evaluation**

Two-dimensional, M-mode, color flow mapping, and spectral Doppler echocardiography were carried out using a Vivid 3 Expert GE echocardiography machine (model vivid 3 Expert; GE Vingmed Ultrasound, Horten, Norway) with a 5 MHz transducer for pediatric patients. Patients were examined in the parasternal long and short axis, and four-chamber projections. Special attention was paid to the detection of tricuspid regurgitation. To estimate pulmonary artery systolic pressure (PASP), the maximum transtricuspid pressure gradient was calculated using the simplified Bernoulli equation [15,16]. The estimate of right atrial pressure, 10 mmHg, was added to the pressure gradient to calculate the right ventricular systolic pressure, which...
was considered equal to the PASP in the absence of right ventricular outflow obstruction. The Doppler recordings were reviewed by one echocardiographer who had no previous knowledge of the patient’s condition or his/her data. Right ventricular dilatation was defined as ventricular area greater than the left ventricular area obtained using planimetry from the apical four-chamber view. Right ventricular dilatation with flattening of the ventricular septum was considered indicative of right ventricular overload. PH was diagnosed if the peak systolic pressure gradient at the tricuspid valve was more than 25 mmHg. The severity of PH is classified as mild (PASP <45 mmHg), moderate (PASP from 45 to 59 mmHg), or severe (PASP≥60 mmHg) [15]. Accordingly, patients enrolled in our study were subdivided into two groups: group IIA, patients with PAH; group IIB, patients without PAH.

Statistical analysis was carried out using an SPSS 11 [17] database (Foster City, UK). Quantitative variables, such as pulmonary function tests, were described as mean ± SD. Qualitative variables, such as symptoms, age, and sex, were described as numbers and percentages. Student’s t-test was used for comparison of the means of quantitative variables. The χ²-test was used to compare the frequencies (numbers and percentages) for qualitative variables. Correlations between variables were assessed using Pearson’s test. Odds ratios (ORs) and 95% confidence intervals were also calculated. Linear regression analysis was carried out to examine the predictors contributing toward PAH in scleroderma. Differences were considered significant at a P value of less than 0.05.

Results
Comparisons of demographic data of all scleroderma patients and controls are shown in Table 1.

Comparison of patients with and without pulmonary arterial hypertension according to the Doppler echocardiographic findings
PAH was detected in five (12.8%) of 39 scleroderma patients. PASP ranged from 37 to 63 mmHg (49.2 ± 10.1). Scleroderma patients (group II) were subdivided into two groups:

Group IIA included five (12.8%) patients who had PAH, their age ranged from 30 to 50 years, mean ± SD 41.8 ± 9.2.

Group IIB included 34 (87.2%) patients who had no PAH; their age ranged from 18 to 60 years, mean ± SD 37.1 ± 10.9.

The comparison between group IIA and group IIB to determine whether there is any association of PAH with inflammatory parameters of scleroderma or other risk factors for PAH showed no significant differences between the two groups in demographic and clinical features, except for arthritis, Raynaud’s phenomenon, and duration of the disease (P < 0.04, <0.01, and <0.001); there was a highly statistically significant difference between the two groups as regarding the duration of Raynaud’s phenomenon.

| Table 1 Comparison of demographic data of all scleroderma patients and controls |
|-----------------------------------------------|-----------------------------------------------|
| Demographic data                              | Range (mean ± SD)                             |
| Group II (n=39) (scleroderma)                  | Group I (n=20) (control)                      |
| Age (years)                                    | 18–60 (37.7 ± 10.7)                           | 20–62 (38.9 ± 11.9) |
| Age at onset (years)                           | 13–45 (28.4 ± 9.3)                            | –                     |
| Duration of disease (years)                    | 1–36 (9.3 ± 7.02)                             | –                     |
| Sex [N (%)]                                    | Male 3 (7.7)                                  | Female 36 (92.3)      |
|                                              | 1 (5)                                         | 19 (95)               |

| Table 2 Comparison of demographic and clinical features in scleroderma patients with and without pulmonary arterial hypertension |
|---------------------------------------------------------------|
| Scleroderma patients with PAH (N=5, 12.8%)                    | Scleroderma patients without PAH (N=34, 87.2%)  |
| Age (years)                                                   | Age at onset of the disease (years)            |
| Range                                                        | Mean ± SD                                     | Mean ± SD                                     | P value |
| Range                                                        | 30–50                                         | 18–60                                         | 0.37    |
| Mean ± SD                                                    | 41.8 ± 9.2                                    | 37.1 ± 10.9                                   |         |
| Arthritis                                                    | 4 (80)                                        | 10 (29.4)                                     | 0.04*   |
| Skin thickening                                               | 5 (100)                                       | 23 (67.6)                                     | 0.07    |
| Telangiectasias                                              | 3 (60)                                        | 6 (126)                                       | 0.07    |
| Calcification                                                | 0                                             | 5 (14.7)                                      | 0.4     |
| Tendon friction rub                                          | 3 (60)                                        | 8 (23.5)                                      | 0.2     |
| Echophaegal                                                  | 1 (20)                                        | 11 (32.3)                                     | 0.5     |
| Raynaud’s phenomenon                                         | 4 (80)                                        | 7 (20.5)                                      | 0.01*   |
| Duration                                                     | 16.8 ± 13.9                                   | 0.37 ± 0.87                                   | 0.0001  |
| Time proceeding scleroderma onset                            | 1.1 ± 0.74                                    | 0–0                                           | 0.0001  |

PAH, pulmonary arterial hypertension.  
*Significant; **Highly significant.
and the time of Raynaud’s proceeding the onset of scleroderma (Table 2).

However, laboratory parameters had significantly higher values of ESR, complement, anticentromere antibody, and diffusing lung capacity of carbon monoxide (DLCO) in group IIA ($P < 0.04$, $<0.03$, $<0.002$, and $<0.0001$, respectively) as shown in Table 3.

No signs of vasculitis and antiphospholipid syndrome were found in patients with PAH. Pulmonary artery pressure differed significantly between the two subgroups subset ($P < 0.0001$). The degree of PAH was mild in two, moderate in two, and severe in one patient as shown in Table 4 (Fig. 1).

The mean and SD of disease duration in patients with and without PAH was $18.5 \pm 11.1$ and $7.89 \pm 5.2$, respectively. The mean Valentini Disease Activity Index in patients with and without PAH was $8.6 \pm 0.6$ and $3.4 \pm 1.3$, respectively. There was a highly statistically significant difference between these groups of patients in the disease activity index and disease duration ($P < 0.0001$) (Figs 2 and 3).

OR of possible risk factors for the development of PAH in scleroderma patients are shown in Table 5.

### Table 3 Comparison of laboratory features in scleroderma patients with and without pulmonary arterial hypertension

|                      | Scleroderma patients with PAH ($N=5$, 12.8%) [N (%)] | Scleroderma patients without PAH ($N=34$, 87.2%) [N (%)] | $P$ value<br><sup>a</sup> |
|----------------------|------------------------------------------------------|--------------------------------------------------------|------------------------|
| Hb (g) (%)           |                                                      |                                                        | 0.1                   |
| Range                | 8–11                                                 | 79–14                                                 |                       |
| Mean ± SD            | 10.2 ± 0.8                                           | 11.1 ± 1.4                                            |                       |
| WBC (mm<sup>3</sup>) |                                                      |                                                        |                       |
| Range                | 4.2–11.5 × 10<sup>3</sup>                            | 4.7–11 × 10<sup>3</sup>                                | 0.9                   |
| Mean ± SD            | 6.7 ± 2.8 × 10<sup>3</sup>                            | 6.8 ± 1.6 × 10<sup>3</sup>                            |                       |
| Platelets (mm<sup>3</sup>) |                                                    |                                                        |                       |
| Range                | 150–320 × 10<sup>3</sup>                             | 150–430 × 10<sup>3</sup>                               | 0.5                   |
| Mean ± SD            | 270 ± 69.2 × 10<sup>3</sup>                           | 249.3 ± 72.2 × 10<sup>3</sup>                          |                       |
| ESR (mm/h)           |                                                      |                                                        | 0.04*                 |
| Range                | 34–98                                                | 20–66                                                 |                       |
| Mean ± SD            | 73.8 ± 24.4                                          | 40.5 ± 11.8                                           |                       |
| Positive rheumatoid factor |                                                 |                                                        | 0.3                   |
| 1 (20)               | 2 (5.8)                                              |                                                        |                       |
| Positive ANA         | 5 (100)                                              | 22 (64.7)                                             | 0.1                   |
| Positive ACL         | 3 (60)                                               | 7 (20.5)                                              | 0.09                  |
| Complement           | 4 (80)                                               | 9 (28.4)                                              | 0.03*                 |
| Positive antitopiomerase |                                                  |                                                        | 0.02*                 |
| 0                    | 19 (55.8)                                            |                                                        |                       |
| Positive antitopoiomerase |                                                  |                                                        | 0.002***              |
| 5 (100)              | 8 (23.5)                                             |                                                        |                       |
| DLCO                 |                                                      |                                                        |                       |
| 5 (100)              | 3 (8.8)                                              |                                                        | 0.0001***             |
| Acrosclerosis        | 3 (60)                                               | 16 (47)                                               | 0.4                   |
| Pulmonary fibrosis   | 2 (40)                                               | 5 (14.7)                                              | 0.2                   |

ACL, anticardiolinin antibodies; ANA, antinuclear antibody; DLCO, diffusing lung capacity of carbon monoxide; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; PAH, pulmonary arterial hypertension; WBC, white blood cell.

<sup>a</sup>$z^2$-test or Student’s $t$-test.

* $P<0.05$, significant; ** $P<0.001$, highly significant; *** Very highly significant.

### Table 4 Comparison of ECHO features in scleroderma patients with and without pulmonary arterial hypertension

|                      | Scleroderma patients with PAH ($N=5$, 12.8%) [N (%)] | Scleroderma patients without PAH ($N=34$, 87.2%) [N (%)] | $P$ value<br><sup>a</sup> |
|----------------------|------------------------------------------------------|--------------------------------------------------------|------------------------|
| Pulmonary artery systolic pressure (mmHg) |                                                      |                                                        | <0.0001***             |
| Range                | 37–63                                                | 15–29                                                  |                       |
| Mean ± SD            | 49.2 ± 10.1                                          | 21.4 ± 3.5                                            |                       |
| Degree of pulmonary hypertension |                                                  |                                                        |                       |
| Mild                 | 2 (40)                                               | 0                                                      |                       |
| Moderate             | 2 (40)                                               | 0                                                      | <0.0001***             |
| Severe               | 1 (20)                                               | 0                                                      |                       |
| Right ventricular dilatation |                                                  |                                                        | <0.01*                |
| Valvular thickening  | 2 (40)                                               | 4 (11.8)                                              | 0.1                   |
| Aortic thickening    | 1 (20)                                               | 5 (14.7)                                              | 0.5                   |
| Degree of tricuspid regurge |                                                |                                                        |                       |
| Mild                 | 3 (60)                                               | 5 (14.7)                                              |                       |
| Moderate             | 2 (40)                                               | 1 (2.9)                                               | <0.0001***             |
| Severe               | 0                                                    | 0                                                      |                       |
| Pericardial effusion | 3 (60)                                               | 11 (32.4)                                             | 0.2                   |
| Ejection fraction    |                                                      |                                                        |                       |
| Range                | 45–80                                                | 45–86                                                 | 0.7                   |
| Mean ± SD            | 62.4 ± 15.5                                          | 60.7 ± 13.2                                           |                       |

ECHO, echocardiogram; PAH, pulmonary arterial hypertension.

<sup>a</sup>$z^2$-test or Student’s $t$-test.

* $P<0.01$, significant; ** $P<0.0001$, very highly significant.
and laboratory parameters. Among all factors, type of limited scleroderma, Raynaud’s phenomenon, and reduced complement \((P < 0.04, 0.01,\) and \(0.01,\) respectively) were associated significantly with the occurrence of PAH in scleroderma, but long disease duration and activity index of the disease \((P = 0.001\) and \(0.001,\) respectively) were highly significantly associated with the occurrence of PAH, whereas both positive anticentromere and reduced DLCO were very highly significantly associated with the occurrence of PAH in scleroderma \((P = 0.0001\) and \(0.0001,\) respectively) \((Table 5).\)

Table 6 summarizes the clinical data, laboratory features, and PASP in scleroderma patients with PAH.
**Discussion**

**Prevalence of pulmonary hypertension**

Scleroderma is an autoimmune disease with multiple organ involvement. Some of these patients may have variable degrees of PH [18]. Doppler echocardiography is the most widely available technology among the noninvasive imaging methods. Echocardiography provides both estimates of pulmonary artery pressure and an assessment of cardiac structure and function. These features justify its application as the most commonly used screening tool in patients with suspected PAH [19]. In the present study, Doppler echocardiography was used as a screening tool for the detection of PH in scleroderma patients. In our scleroderma patients, Doppler echocardiography could detect elevated PASP in 12.8% of patients, degree of PH, right ventricular dilatation, valvular thickening, tricuspid regurge, and even pericardial effusion with or without symptom onset. Scleroderma patients with PAH showed greater positive anticientromere antibody (100%) and reduced complement (80%) in comparison with scleroderma patients without PAH.

Our result is in agreement with the following studies: in prospective studies using the right heart catheterization for diagnosis, the prevalence of SSc-PAH is between 7.8 and 12% [20,21]. With an estimated US prevalence of SSc of about 240 cases per million and a conservative PAH prevalence of 10% among these patients, the estimated overall prevalence of SSc-PAH is around 24 individuals per million, which represents 5–10 times the number of patients affected by idiopathic PAH [22]. In the French PAH registry, connective tissue disease (mainly represented by SSc) accounts for 15.3% of PAH cases [23]. Probably because of a higher prevalence of SSc in the USA [24], the proportion of SSc-PAH is at least 30% of patients with PAH, as indicated by one single large registry [25].

**Subsets of systemic sclerosis at risk of pulmonary arterial hypertension**

In our study, patients with scleroderma-PH were predominantly women ranging in age from 16.5 to 32 years. In the present study, Raynaud’s phenomenon was found in four adult-onset scleroderma patients with PH (80%). Raynaud’s phenomenon is part of a systemic vascular response that includes a decrease in the size of the pulmonary capillary bed, which may in turn result in muscular necrosis and secondary inflammation [26].

This study also reported that Raynaud’s phenomenon, decreased DLCO, and anticientromere were associated with an increased OR (OR = 2.85, 6.15, and 7.001, respectively), and were considered as significant independent predictors of PAH in scleroderma (P < 0.01, <0.0001, and <0.0001, respectively). Also, in the current study, disease duration, disease activity, and limited scleroderma were associated with an increased risk for PAH (OR = 3.58, 8.09, and 8.28, respectively), and were associated significantly with the occurrence of PAH in scleroderma (P < 0.01, <0.001, and <0.04, respectively) in the linear regression analysis.

These are in agreement with the following studies that found that several clinical markers are associated with an increased risk of developing PAH in the setting of SSc, including limited skin involvement [27], disease duration greater than 10 years [27], late age of onset of SSc, severity [28] or duration [29] of Raynaud’s phenomenon, and reduced nail-fold capillary density [27,30]. Several investigators have emphasized

| Table 6 Cases of scleroderma patients with pulmonary arterial hypertension |
|---|
| Age (years), type, and disease duration | Extrapulmonary manifestations | Investigations | PASP (mmHg), degree of PAH |
| Female, 34 years, limited, and 17.5 years | Raynaud’s phenomenon, sclerodactyly | ESR (70 mm/h), positive ANA, positive pulmonary fibrosis, positive anticientromere, positive anticyclic citrulline, hypocomplement, right ventricular dilatation, pericardial effusion, mild tricuspid regurge | 42, mild |
| Female, 50 years, limited, and 18 years | Raynaud’s phenomenon, arthritis, sclerodactyly, arthralgia, tendon friction rub | ESR (80 mm/h), positive ANA, positive anticientromere, acrosclerosis, pericardial effusion, reduced DLCO, mild tricuspid regurge | 37, mild |
| Female, 45 years, limited, and 16 years | Arthritis, telangiectasia, sclerodactyly, tendon friction rub | ESR (89 mm/h), positive ANA, positive anticientromere, positive anticyclic citrulline, hypocomplement, acrosclerosis, pericardial effusion, mild tricuspid regurge, right ventricular dilatation, pulmonary fibrosis, reduced DLCO | 54, moderate |
| Female, 50 years, limited, and 33 years | Arthritis, Raynaud's phenomenon, telangiectasia, sclerodactyly, esophageal dysmotility | ESR (54 mm/h), positive ANA, positive anticientromere, hypocomplementemia, reduced DLCO, moderate tricuspid regurge | 63, severe |
| Female, 30 years, diffuse, and 5 years | Arthritis, Raynaud's phenomenon, telangiectasia, sclerodactyly, tendon friction rub | ESR (98 mm/h), positive ANA, positive anticientromere, positive anticyclic citrulline, hypocomplement, acrosclerosis, moderate tricuspid regurge, pulmonary fibrosis, acrosclerosis, reduced DLCO | 50, moderate |

ANA, antinuclear antibody; DLCO, diffusing lung capacity of carbon monoxide; ESR, erythrocyte sedimentation rate; PAH, pulmonary arterial hypertension; PASP, pulmonary artery systolic pressure.
the pivotal role of an isolated reduction in DLCO or a progressive decrease in DLCO as an independent predictor for subsequent PAH [28].

Multiple registries describe SSc populations worldwide. The South Australian Scleroderma Register, a population-based cohort of 374 living and 234 deceased SSc patients, showed that isolated PH occurs as a late-stage complication about 20 years after the onset of scleroderma. Isolated PH was the most common in those with lcSSc, and was predicted by multiple telangiectasia, reduced nail-fold capillary density, digital ulceration, and gross reduction of DLCO [27]. No dcSSc patient in this cohort developed PAH.

A registry created by the European League Against Rheumatism Scleroderma Trials and Research (EUSTAR) group suggests that the autoantibody profile has a better predictive value for the development of PAH than traditional clinical risk factors. They compared the risks of lung complications on the basis of clinical findings versus the presence of autoantibodies in 3656 patients (87% of women, 1349 dcSSc, 2101 lcSSc) from 102 centers in 30 countries [3]. The frequency of PH, diagnosed by echocardiography, was similar between dcSSc and lcSSc (22.3 and 20.5% of patients, respectively). However, the PAH surrogate in this study [PH with no pulmonary fibrosis (PF)] occurred more in lcSSc than in dcSSc (9.2 vs. 5.9%); conversely, PF, which was more common, occurred more frequently in dcSSc versus lcSSc (53.4 vs. 34.7%). PH without PF was more prevalent in those with anticentromere versus anti-Scl-70 antibodies (13 vs. 5%) [3]. Female patients were almost twice as likely to be anticentromere antibody positive as male patients (26.3 vs. 50.3% in the lcSSc group). An important caveat is that this study includes no catheterization data. Nonetheless, SSc-PAH is more common in patients with lcSSc [formerly called CREST (calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome] and in those with anticentromere antibodies [31].

Conclusion

PAH is an aggressive and malignant manifestation of vasculopathy in SSc that causes considerable morbidity and mortality, and necessitates early diagnosis and intervention. Efficacious therapeutic interventions for PAH are available and can be used alone or in combination to mitigate disease progression. The patients with SSc are at a significantly increased risk of developing PAH compared with the general population. Echocardiography should be performed routinely once a year (as a screening tool) and consideration should be given to screening PAH, especially in female patients with a long duration of scleroderma, positive anticientromere antibodies, decreased DLCO, and low level of complement, as they are significant predictors of PH in scleroderma.

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Conflicts of interest

There are no conflicts of interest.

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