Pulmonary Arterial Hypertension in Systemic Lupus Erythematosus: Prevalence and Predictors

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ABSTRACT. ***Objective.*** Pulmonary arterial hypertension (PAH) prevalence has been reported to be between 0.5% and 17% in systemic lupus erythematosus (SLE). This study assessed PAH prevalence and predictors in an SLE cohort.

Methods. The Borg dyspnea scale, DLCO, N-terminal pro–brain natriuretic peptide (NT-proBNP), and Doppler echocardiographic (DE) were performed. An echocardiographic Doppler exercise test was conducted in selected patients. When DE systolic pulmonary arterial pressure was ≥ 45 mmHg or increased during exercise > 20 mmHg, a right heart catheterization was performed. Hemodynamic during exercise was measured if rest mean pulmonary arterial pressure was < 25 mmHg.

Results. Of the 203 patients with SLE, 152 were included. The mean age was 44.9 ± 12.3 years, and 94% were women. Three patients had known PAH. The algorithm diagnosed 1 patient with chronic thromboembolic pulmonary hypertension and 5 with exercise-induced pulmonary artery pressure increase (4 with occult left diastolic dysfunction). These patients had significantly more dyspnea, higher NT-proBNP, and lower DLCO.

Conclusion. These data confirm the low prevalence of PAH in SLE. In our cohort, occult left ventricular diastolic dysfunction was a frequent diagnosis of unexplained dyspnea. Dyspnea, DLCO, and NT-proBNP could be predictors of pulmonary hypertension in patients with SLE. (J Rheumatol First Release December 15 2015; doi:10.3899/jrheum.150451)

Key Indexing Terms:

PULMONARY ARTERIAL HYPERTENSION — SYSTEMIC LUPUS ERYTHEMATOSUS

DLCO — N-TERMINAL PRO–BRAIN NATRIURETIC PEPTIDE

DOPPLER ECHOCARDIOGRAPHIC — RIGHT HEART CATHETERIZATION

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Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease that is often accompanied by severe pulmonary and heart complications. Pulmonary arterial hypertension (PAH), Group 1 of pulmonary hypertension (PH) classification, is one of them[1]. This condition is a precapillary PH attributable to extensive vascular remodeling of the small arteries, ultimately causing right ventricular failure and death[2]. Intensive immunosuppressive and pulmonary vasodilator therapies have shown promising results treating this complication. In fact, some studies have revealed 1-year survival of 94% in SLE-associated PAH (SLE-PAH), higher than in scleroderma PAH (SCL-PAH; 82%)[3,4].

The prevalence of SLE-PAH has not been well established. Epidemiological studies published in the last few years have estimated a prevalence between 0.5–17.5%[5,6]. This wide prevalence is explained by the patient's selection criteria, the lack of a standard definition for PAH, and the different PH diagnostic approaches [Doppler echocardiography (DE) or right heart catheterization (RHC)].

Predictors in SCL-PAH, such as dyspnea, DLCO, and N-terminal pro–brain natriuretic peptide (NT-proBNP), have

also been studied in SLE-PAH[3]. A combination of these predictors could be helpful for early diagnosis and treatment of this complication. With the aim of assessing SLE-PAH prevalence in our SLE cohort and to detect possible new cases, we carried out a prospective study using an algorithm based on these PAH predictors.

MATERIALS AND METHODS

Patients. Our study was performed between November 2010 and February 2012 in a cohort of patients diagnosed with SLE [American College of Rheumatology (ACR) criteria][7] by a multidisciplinary medical team including lung specialists, rheumatologists, and cardiologists with expertise in SLE and PAH. The following exclusion criteria were applied: presence of known significant heart disease (systolic dysfunction defined as left ventricle ejection fraction < 50%, more than mild diastolic dysfunction, more than mild mitral or aortic valve disease, cardiomyopathy, and pericardial disease), existence of restrictive lung disease [total lung capacity (TLC) or forced vital capacity (FVC) ≤ 70% of predicted value], or obstructive lung disease [forced expiratory volume in 1 s (FEV1) ≤ 60% of predicted value]. Patients with mental or physical limitations who could not undertake the tests were also excluded. The hospital's ethics committee approved the study and informed consent was obtained from each patient during the first visit.

Study design. The initial screening algorithm was based on DE and the evaluation of dyspnea, NT-proBNP, and DLCO (Figure 1). Dyspnea was scored using the Borg scale and the New York Heart Association (NYHA) functional classification for PAH. All patients took lung function tests and the following variables were chosen: TLC, FVC, FEV1, FEV1/FVC, and DLCO. Other data were also collected: demographic data, cumulative SLE clinical manifestations, autoantibody profile, treatments received, complications, Katz index severity[8], and accumulated damage index [Systemic Lupus International Collaborating Clinics (SLICC)/ACR/damage index (DI)][9].

DE and RHC. Two cardiologists with expert knowledge in DE carried out a full examination of patients while at rest using standard acoustic windows. Exercise DE (EDE) was performed by one of these cardiologists. Systolic pressure of the pulmonary artery (sPAP) was estimated using the simplified Bernoulli equation [sPAP right ventricular systolic pressure ($4V^2$) + 5 mmHg, where "V" is the maximum tricuspid regurgitation velocity (m/s) and "5 mmHg" is the assigned pressure in right atrium]. In cases where the sPAP could not be quantified, pulmonary acceleration time was determined using pulsed Doppler technique. A pulmonary acceleration time < 100 ms was considered the threshold for suspected PH. When it was not possible to estimate both values, sPAP was regarded as normal if right cavities were not dilated[10]. PH was considered likely when sPAP value was ≥ 45 mmHg (Figure 1, Group 1). PH was considered possible when sPAP value was > 35 and < 45 mmHg (Figure 1, Group 2) or sPAP value was ≤ 35 mmHg and at least 1 PH suggestive variable was found (right heart cavities enlargement, unexplained dyspnea, DLCO value < 65%, or NT-proBNP value ≥ 395 pg/ml; Figure 1, Group 3). PH was considered unlikely when sPAP value was ≤ 35 mmHg and no other PH-suggestive variables were found (normal right heart cavities, no dyspnea, DLCO ≥ 65%, and NT-proBNP < 395 pg/ml; Figure 1, Group 4).

We considered right heart cavities dilatation if right atrium longitudinal diameter was > 53 mm, mid-right ventricular diastolic diameter > 35 mm, or if they were larger than left heart cavities (operator interpretation). Groups 2 and 3 underwent EDE. The test involved subjecting the patient to a workload that increased by 25 watts (W) every 2 min until reaching the maximum tolerated effort. In the minute prior to a further load increase, measurements of echocardiograph variables, heart frequency, and blood pressure were taken. PH was suspected when rest sPAP increased by more

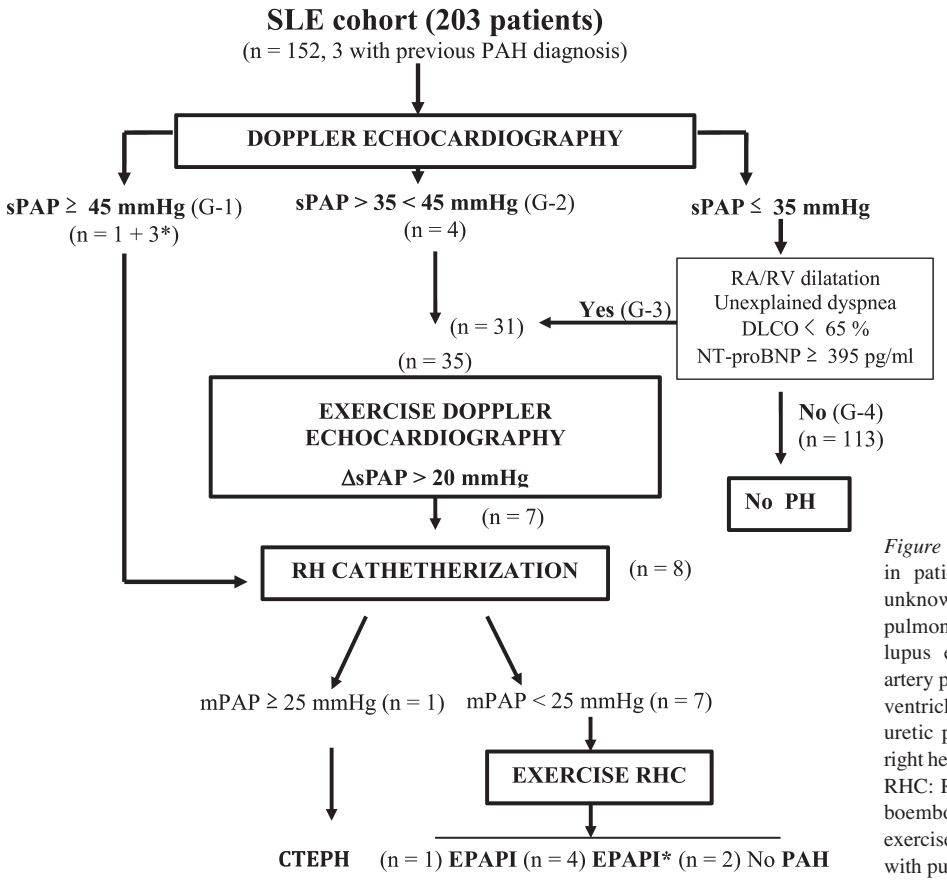

Figure 1. Screening algorithm for diagnosis of PAH in patients with SLE. 3*: Three patients with unknown left heart diseases were excluded. PAH: pulmonary arterial hypertension; SLE: systemic lupus erythematosus; sPAP: systolic pulmonary artery pressure; G: group; RA: right atrial; RV: right ventricle; NT-proBNP: N-terminal pro–brain natriuretic peptide; PH: pulmonary hypertension; RH: right heart; mPAP: mean pulmonary arterial pressure; RHC: RH catheterization; CTEPH: chronic thromboembolic pulmonary hypertension; EPAPI*: exercise-induced pulmonary artery pressure increase with pulmonary artery wedge pressure < 20 mmHg.

than 20 mmHg at maximum tolerated exercise[11]. A Philips iE33 Ultrasound (Philips Healthcare) was used for DE at rest and during exercise. For this last purpose, it was connected to a semirecumbent cycle ergometer (bicycle ergometer, angio with echo cardiac stress table, Lode BV) tilted to the left by 20–30º. Images obtained from echocardiography were saved in digital format and interpreted by 2 blinded observers. Intraobserver and interobserver concordance when determining rest sPAP, and intraobserver concordance for exercise sPAP were established using the concordance correlation coefficient ρ_c[12] on a randomized sample of 40 and 12 cases, respectively. Patients diagnosed with significant respiratory or left heart disease during selection and screening stages were not included in the algorithm.

The remaining patients suspected of having PH underwent RHC. RHC procedure was carried out by doctors specialized in hemodynamic, following the standard technique using Swan-Ganz catheter. The following variables were recorded during catheterization: mean right atrial pressure, sPAP, pulmonary artery diastolic pressure, mean pulmonary arterial pressure (mPAP), and pulmonary artery wedge pressure (PAWP). Cardiac output (CO) was measured using the thermodilution method and cardiac index was determined as CO ÷ body surface area (l/min/m^2). Pulmonary vascular resistance (PVR) was calculated as (mPAP – PAWP ÷ CO) × 80 (dyne·s·cm^{-5}).

PH was diagnosed when mPAP during catheterization was ≥ 25 mmHg. It was considered to be precapillary when PAWP was ≤ 15 mmHg and postcapillary PH when PAWP was > 15 mmHg. In cases in which mPAP was < 25 mmHg, hemodynamic was evaluated during exercise. Exercise test during RHC (ERHC) was carried out with the patient in supine position using a cycle ergometer attached to the hemodynamic examination table. The protocol involved 25-W load increases every 2 min until the patient's level of tolerance was reached. Hemodynamic variables were measured prior to each load increase. In our protocol, when at maximum effort mPAP was ≥ 30 mmHg, exercise-induced PAP increase (EPAPI) was established. EPAPI with PAWP < 20 mmHg, and PVR > 80 dyne·s·cm^{-5} was considered early or latent pulmonary vascular disease, and EPAPI with PAWP ≥ 20 mmHg was considered occult left ventricular filling dysfunction[13].

Statistical analysis. Continuous variables are expressed as means with their corresponding SD and categorical variables as percentages. Continuous variables were compared with the Mann-Whitney U test. Categorical variables were compared with the chi-squared or Fisher's exact test. A p value < 0.05 was considered significant. PAH prevalence was calculated as the ratio between the number of patients diagnosed during the study and those already known, and all participants involved in the study. The SPSS version 20 (SPSS Inc.) was used to analyze the data.

RESULTS

Study population. One hundred sixty-one patients from the cohort of 203 patients agreed to participate in our study. Nine were excluded: 2 could not undergo the tests (1 had Down syndrome and the other was functionally handicapped by his right hip), 5 had respiratory disease, and 2 left heart disease. Finally, 3 of the remaining 152 patients had been previously diagnosed with SLE-PAH. These 3 patients presented with exercise dyspnea, and the European Cardiology Society/European Respiratory Society guidelines[2] were followed to reach the diagnosis. Accordingly these tests were performed: echocardiography, pulmonary function tests, NT-proBNP, V/Q scan, and RHC. The clinical characteristics of the 152 patients are displayed in Table 1.

Rest and EDE findings. Of the 149 patients finally included in the algorithm, sPAP could not be recorded in 24 patients (16%) because of lack or poor quality of tricuspid regurgitation signal. Because of absence of right heart enlargement, sPAP was considered normal in these 24 patients. In addition, a good signal to measure pulmonary acceleration time was achieved in 15 of the 24 patients, which was found to be normal in all cases. Intraobserver and interobserver concordance for rest sPAP were 0.99 and 0.96, respectively. As shown in Figure 1, 4 patients were classified in Group 1 (3 with mitral and aortic valve disease were excluded from the algorithm and the posterior analysis), 4 in Group 2, 31 in Group 3, and 113 in Group 4. In agreement with the algorithm, 35 patients required EDE, which was considered positive in 7 cases. The EDE intraobserver concordance for maximum peak effort sPAP was 0.97. The patients with a positive EDE showed higher rest sPAP, NT-proBNP, and dyspnea score (Table 2).

Rest and exercise catheterization findings. Eight patients selected by ED and EDE required RHC for PH confirmation. Only 1 patient was finally diagnosed as precapillary PH

Table 1. Systemic lupus erythematosus cohort clinical characteristics (n = 152). Values are mean ± SD or %.

Characteristics	Values
Age, yrs	44.90 ± 12.33
Age at diagnosis, yrs	30.7 ± 12.16
Female	94
White	87
Antiphospholipid syndrome	14
Raynaud phenomenon	44
Smoker or ex-smoker	35
Systemic hypertension	26
Anti-DNA antibody	63
Anti-RNP antibody	41
Antiphospholipid antibody	36
Hydroxychloroquine therapy	82
Prednisone therapy	84
Immunosuppressant therapy	46
SLICC	1.09 ± 1.6

SLICC: Systemic Lupus International Collaborating Clinics Index.

Table 2. Exercise Doppler echocardiogram findings. Values are mean ± SD unless otherwise specified.

Variables	Positive Exercise Echocardiography, n = 7	Negative Exercise Echocardiography, n = 28	p
Load, watts	58 ± 11	59.6 ± 3.7	NS
Heart rate, beats/min	124 ± 6.3	137.6 ± 3.7	NS
Exercise time, min	6.8 ± 1.1	6.3 ± 0.5	NS
FVC, % predicted	94 ± 14	98 ± 18	NS
DLCO, % predicted	61 ± 20	60 ± 10	NS
sPAP, mmHg	31 ± 5	23 ± 5	< 0.02
ΔsPAP, mmHg	30 ± 12	10 ± 5	< 0.03
NT-proBNP, pg/ml	307 ± 369	199 ± 392	< 0.006
Dyspnea, Borg scale	3.1 ± 0.90	1.4 ± 1	< 0.001

FVC: forced vital capacity; NT-proBNP: N-terminal pro-brain natriuretic peptide; sPAP: systolic pulmonary arterial pressure; ΔsPAP: increase in sPAP during the exercise; NS: not significant.

(Figure 1, Group 3 and Table 3); posterior studies using pulmonary gammagraphy, computed tomography lung angiogram, and pulmonary angiography classified this PH as chronic thromboembolic pulmonary hypertension (CTEPH). The remaining patients, with mPAP < 25 mmHg, needed ERHC for diagnosis. Exercise hemodynamic was normal in 2 patients (1 in Group 2 and 1 in Group 3). Five patients had increased mPAP and were classified as EPAPI, 1 patient belonged to Group 3 with PAWP < 20 mmHg (mPAP 34 mmHg, PAWP 13 mmHg, and PVR 198 dyne·s·cm^{-5}), and 4 patients (1 in Group 1, 3 in Group 3) with PAWP > 20 mmHg (Figure 1). A V/Q scan was performed in the patient with EPAPI and PAWP < 20 mmHg, ruling out chronic pulmonary thromboembolic disease.

Patients with PH. In our SLE cohort, the prevalence of PAH plus CTEPH was 2.6% (3 patients with known PAH and 1 with CTEPH). Five patients (3%) were classified as EPAPI, corresponding to possible early PAH in 1 patient and occult left heart dysfunction in 4. There was no difference in age, time of disease evolution, age at diagnosis, and clinical characteristics for patients with PAH and CTEPH, and patients in the miscellaneous group (PAH, CTEPH, and EPAPI) in comparison with the remaining cases without PH (Table 4). In the PAH and CTEPH groups, there were more patients with antiphospholipid syndrome (APS), antiphospholipid antibodies, and a higher mean SLICC/ACR/DI, although the differences were not significant (Table 4). The analysis between groups found possible predictors of PAH and CTEPH: unexplained dyspnea according to the Borg scale, low DLCO, and elevated NT-proBNP (Table 4).

DISCUSSION

Our article describes the results of a screening algorithm for patients with SLE-PAH based on the dyspnea score, DLCO, NT-proBNP, and DE. This algorithm also included RHC and exercise tests such as EDE and ERHC. This comprehensive approach, although it detected 1 CTEPH and 5 EPAPI, did not identify any additional patients with PAH besides the previously diagnosed. The low SLE-PAH prevalence contrasts with other previous studies performed only with ED[5], which may have overestimated the real prevalence by failure in pre/post-capillary discrimination. A Chinese study carried out with DE, from an online registry of 1934 patients with SLE, found a prevalence of 3.8%. The authors excluded heart and respiratory diseases, and PAH was defined as sPAP > 40 mmHg in 2 ED[14]. Left heart disease, with its multiple causes [diastolic dysfunction, myocarditis, ischemic heart disease, valvular dysfunction (Libman-Sacks endocarditis)], is one of the main differential diagnoses of SLE-PAH[15,16]. In our manuscript, 3 patients were excluded because of left heart disease by rest echocardiography, and 4 patients (57%) after ERHC showed an elevation of PAWP > 20 mmHg, being diagnosed of occult left ventricular filling dysfunction. A similar finding was described in patients with connective tissue disease (predominantly systemic sclerosis) where ERHC revealed an elevation of PAWP > 20 mm Hg in 33% of patients with EPAPI[17]. Therefore, exercise hemodynamic measurements are of incremental value for left heart diastolic dysfunction detection and may provide a window into earlier diagnosis of this condition. SLE-PAH prevalence assessment also required differentiating PAH from other causes of precapillary PH associated with SLE[16]. In this regard, 4 patients with chronic interstitial pneumonia and 1 with shrinking lung syndrome were excluded from the screening algorithm.

Although the aim of our study was to describe SLE-PAH predictors, it was problematic to draw definite conclusions because of the few cases found. However, an approach to these predictors was performed by collecting cases in a PAH and CTEPH group, and in a miscellaneous group. Unexplained dyspnea, measured on the Borg scale, stood out particularly in the study of predictors. Occult left ventricular filling dysfunction was the most frequent cause of this symptom. In PAH, CTEPH, and EPAPI cases, Borg scale score was ≥ 2, and functional class (NYHA) of patients was mostly II (Table 4). These data contrast with Prabu, *et al*[18],

Table 3. Clinical, echocardiographic, and hemodynamic data of patients with pulmonary hypertension and with exercise-induced PAP increase.

Patient	mPAP, mmHg, R/E	PAWP, mmHg, R/E	CO, l/min	PVR, dyne·s·cm^{-5}	NYHA Functional Class	sPAP, mmHg	Dilatation RA/RV
1	58	8	3.7	1081	III	79	Yes
2	44	10	6.5	418	III	50	Yes
3	56	10	5.3	694	III	70	Yes
4	27	11	5.6	254	III	33	No
5	18/34	7/13	4.3	205	II	35	No
6	18/32	11/21	3.8	147	III	35	No
7	17/33	12/22	3.9	103	II	55	Yes
8	17/35	12/24	5.5	73	II	27	No
9	19/36	13/23	4.5	107	II	25	Yes

PAP: pulmonary arterial pressure; mPAP: mean PAP; R/E: rest/exercise; PAWP: pulmonary arterial wedge pressure; CO: cardiac output; PVR: pulmonary vascular resistance; NYHA: modification of the New York Heart Association functional class for pulmonary hypertension; sPAP: systolic PAP; RA/RV: right atrial/right ventricle.

Table 4. Relevant variables of patients with or without pulmonary hypertension, and in the miscellaneous group. Values are mean ± SD or % unless otherwise specified.

Variables	No PH, n = 143	PH*, n = 4	MG**, n = 9	p
Age, yrs	45 ± 12	35 ± 8	45 ± 17	NS
Age at enrollment, yrs	31 ± 12	23 ± 8	32 ± 17	NS
Time since diagnosis, yrs	14 ± 8	10 ± 4	14.3 ± 9	NS
Raynaud phenomenon	42	25	33	NS
APS	15	50	22	NS
aPL	50	75	44	NS
Katz Index	3.2 ± 2	5.8 ± 3	4.2 ± 3	NS
SLICC median	1.09 ± 1.7	2.3 ± 1.3	1.14 ± 1.6	NS
Borg scale	0.68 ± 1.14	3 ± 0.8	2.9 ± 0.8	< 0.000/< 0.000
NT-proBNP, pg/ml	110 ± 184	488 ± 457	474 ± 418	< 0.000/< 0.003
sPAP, mmHg	23.6 ± 5.6	58 ± 20	44.25 ± 20.25	< 0.000/< 0.000
DLCO, % predicted	71 ± 13	58 ± 7	61 ± 5	< 0.05

* PH group: pulmonary arterial hypertension plus chronic thromboembolic pulmonary hypertension. ** MG: pulmonary arterial hypertension plus chronic thromboembolic pulmonary hypertension and exercise-induced PAP increase. PH: pulmonary hypertension; MG: miscellaneous group; APS: antiphospholipid syndrome; aPL: antiphospholipid antibodies; SLICC: Systemic Lupus International Collaborating Clinics Index; NT-proBNP: N-terminal pro-brain natriuretic peptide; PAP: pulmonary arterial pressure; sPAP: systolic PAP; NS: not significant.

who found no differences between patients with SLE with and without PAH in dyspnea score.

To our knowledge, this is the first time that NT-proBNP was included in a systematic screening algorithm for SLE-PAH. Patients with SLE had higher concentrations of NT-proBNP or BNP than controls, which appears to be associated with left atrium diameter[19,20]. The choice of a 395-pg/ml cutoff point was based on 2 studies undertaken on systemic sclerosis in which diagnostic sensitivity and specificity were established between 56–69% and 95–100%, respectively[21,22]. However, other studies have used lower cutoff points to improve sensitivity[23]. In our study, a lower cutoff point, for example ≥ 209 pg/ml, would have selected 6 more cases with possible PH, although these patients had no other features that suggested PH.

Impairment in DLCO in patients with SLE has been correlated with Raynaud phenomenon, anti-U1RNP antibodies, and interstitial lung disease[24]. DLCO with NT-proBNP have also been studied as SLE-PAH independent predictors[25,26]. Recommendations suggest DLCO < 60% as a cutoff for screening patients with SCL-PAH[27]. The choice of a cutoff DLCO < 65% in our algorithm was because of the tendency of patients with SCL-PAH to have lower DLCO than patients with SLE-PAH[3].

EDE has been used to detect family predisposition for PAH[28] and for early SCL-PAH[11,29,30]. A percentage ranging from 27–50% of patients with SCL-PAH and with normal ED increased sPAP significantly during EDE[11,29,30]. Moreover, in connective tissue disease, sPAP correlation between EDE and ERHC showed good agreement[17]. However, only 11–47% of cases with positive EDE displayed an increase in PVR[17,30]. In our investigation, only 20% of 35 selected patients showed positive EDE, which is possibly associated with the lower PAH prevalence. Another factor that could affect EDE sensitivity was tricuspid insufficiency inappropriate determination because of technical reasons[17]. Nevertheless, in this cohort, only 1 patient had a suboptimal tricuspid regurgitation jet measure. Posterior clinical and echocardiographic followup of this patient did not reveal any increase in symptoms or rest sPAP. Regarding the method, abnormal EDE response in SCL-PAH has been defined by sPAP higher than 40 mmHg during exercise[17], sPAP of 46 mmHg immediately after exercise[31], or postexercise increase in sPAP > 20 mmHg[11]. In any case, the chosen method does not appear to affect the percentage of EDE-positive cases[11,31]. In our study, 5 of 7 patients with positive EDE (72%) showed good ERHC correlation. The discrepancies found in 2 cases between EDE and ERHC could be explained by variations in the patients' clinical conditions from 1 test to another or miscellaneous technical problems. Similar to other scleroderma investigations[11,29], SLE predictors of abnormal EDE response were dyspnea, rest sPAP, and NT-proBNP (Table 2).

Although exercise is excluded from the definition of PH because of the lack of knowledge of pulmonary pressure normal upper limit during effort[2], it is also true that some data suggest the existence of exercise-induced PAH as an early stage in PAH[13]. In fact, Kovacs, *et al*[32] reassessed exercise invasive hemodynamic in 10 patients with borderline SCL-PAH after 1 year, and progression in mPAP and PVR was noted. Further, one-fifth of patients with scleroderma with EPAPI included in the UK PH registry developed resting PAH after 2.3 years[33]. On the other hand, studies with EDE, similar to others carried out with ERHC, suggest an upper limit of normal mPAP at exercise of 30 mmHg at a CO of < 10 l/min or a total PVR at exercise of < 3 Wood units[34]. In our cohort, 1 case classified as EPAPI during ERHC had an

increased mPAP in an amount higher than expected with respect to pulmonary flow (mPAP of 34 mm Hg/CO 8.5 l/min). ERHC can also determine whether pulmonary venous pressure increases. Studies carried out on healthy subjects show that PAWP rarely surpasses 20 mmHg during exercise[12]. Using this cutoff, 4 cases were classified as EPAPI with PAWP > 20 mmHg (left ventricular diastolic dysfunction).

We did not find any significant association with clinical characteristics, SLE damage, or APS, perhaps because of the low number of patients with PAH. This situation contrasts with Li, *et al* and Prabu, *et al* in which pericarditis, pleuritis, anti-RNP APS, and lupus anticoagulant antibody were established as factors associated with the development of SLE-PAH[14,18].

One of the study limitations was that only 1 center participated. Also, a low number of patients were evaluated for low prevalence. However, most of studies about PAH-SLE prevalence have been performed with a similar number of patients[6]. We also have to take into account that the majority of patients in the cohort were mild cases and in remission. EDE and ERHC protocols were similar but not identical, and small variations because of body position may exist. Finally, a diagnostic algorithm like this should be validated; however, the non-detection of new SLE-PAH cases makes that unnecessary.

Our data confirm SLE-PAH low prevalence. Occult left ventricular diastolic dysfunction was a frequent cause of unexplained dyspnea in patients with SLE. Dyspnea, DLCO, and NT-proBNP could be predictor factors of PH and PAH. A screening program for SLE-PAH based on ED, NT-proBNP, DLCO, and EDE does not appear to be cost-effective and should be restricted to patients with SLE and unexplained dyspnea.

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