Original Article

Echocardiographic signs of pulmonary hypertension in patients with newly recognized hypersensitivity pneumonitis, prevalence and clinical predictors

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Background: Hypersensitivity pneumonitis (HP) is the third, according to frequency, interstitial lung disease, with the estimated incidence rate of 1–2/100,000. In HP patients, the extensive inflammatory lesions encompassing both small airways and lung parenchyma, as well as subsequent development of lung fibrosis, may result in respiratory insufficiency and secondary pulmonary hypertension (PH). The aim of the present retrospective study was to assess the prevalence of echocardiographic signs of PH and its' clinical predictors, in newly recognized HP patients.

Methods: Consecutive HP patients, recognized in single pulmonary unit between 2005 and 2017, in whom echocardiography was performed at diagnosis, entered the present study. HP diagnosis was verified in every patient according to current diagnostic recommendations. The results of high resolution computed tomography of the chest (HRCT) were re-evaluated by two independent radiologists, blinded to clinical data. Echocardiographic signs of PH were defined as pulmonary artery systolic pressure (PASP) exceeding 36 mmHg. Regression analysis was applied to calculate PH risk, and receiver operator characteristic curves (ROC) were plotted to investigate diagnostic utility of various parameters in PH prediction.

Results: PASP exceeding 36 mmHg was noted in 26 out of 70 patients (37%)—with equal frequency among patients with fibrotic and non-fibrotic HP. Significant predictors of PH on echocardiography were: partial oxygen tension in arterialized capillary blood (PaO2) <69 mmHg, lung transfer capacity for carbon monoxide (TLCO) <42% of predicted, six minutes walking test (6MWT) distance <455 meters, and 6MWT desaturation rate >8%. In case of TLCO <42% of predicted, probability of PH on echocardiography was increased by five-fold, in case of 6MWT desaturation rate >8%—by four fold.

Conclusions: The best predictors of PASP >36 mmHg on echocardiography in HP patients at diagnosis were: TLCO <42% and 6MWT desaturation rate >8%. Neither the presence of lung fibrosis on HRCT, nor the duration of the disease or patients age, were helpful in PH prediction.

Keywords: Hypersensitivity pneumonitis (HP); pulmonary hypertension (PH); lung transfer capacity for carbon monoxide (TLCO)

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Introduction

Hypersensitivity pneumonitis (HP) belongs to the group of interstitial lung diseases with known etiologic factors. The environmental, occupational or hobbyist exposition to organic antigens induces the immunological response, leading in genetically predisposed individuals to chronic inflammatory lung disease (1). Lung biopsy specimens typical of HP, show the features of cellular, bronchiolocentric, lymphocyte - predominant interstitial pneumonia and bronchiolitis, with the presence of poorly formed non-necrotizing granulomas (2). In some patients, chronic inflammation progresses to fibrotic lung disease, with airway centred fibrosis and characteristic bridging fibrosis (2).

Although, HP was previously regarded a rare ILD, nowadays it is usually listed on the third position among interstitial lung diseases, after idiopathic pulmonary fibrosis (IPF) and ILDs in the course of connective tissue diseases or sarcoidosis (3,4).

Recent data indicate growing recognition of HP in many countries, the actual incidence rate is estimated at approximately 1–2/100,000 (5,6).

The diagnostic criteria of HP that have been published recently, include: pulmonary symptoms related to the exposition to responsible antigens and/or the presence of specific serum IgG antibodies (ssIgGs), typical picture of high resolution computed tomography of the chest (HRCT), and increased (>30%) percentage of lymphocytes in bronchoalveolar lavage fluid (BALF) (2). Final diagnosis should be supported by the result of multidisciplinary discussion. Transbronchial lung biopsy (TBLB) is suggested as the procedure of first choice, in the patients with non-fibrotic lung disease (2). In case of diagnostic difficulties, the second line procedures, such as transbronchial cryobiopsy or surgical lung biopsy, may be recommended by multidisciplinary panel to ascertain the diagnosis (2).

Current guidelines distinguish two forms of HP, fibrotic and non-fibrotic (2). The terms acute HP and chronic HP have been abandoned, due to less clear prognostic significance (2).

Pulmonary hypertension (PH) is one of the negative prognostic factors in many end-stage lung diseases. The knowledge about incidence of PH in HP, especially at diagnosis, is scarce. Moreover, it is not known if there is any clinical phenotype of HP suggestive for PH on echocardiographic examination.

Therefore, the aim of the present retrospective study was to assess the prevalence of echocardiographic signs of PH and its' clinical predictors, in newly recognized HP patients.

We present the following article in accordance with the STARD reporting checklist (available at https://dx.doi.org/10.21037/jtd-21-130).

Methods

Consecutive patients with HP diagnosed between 2005 and 2017 in the single pulmonary unit, in whom 2D-Doppler echocardiographic transthoracic examination was performed at diagnosis, entered the present study.

The algorithm of HP recognition was based on: positive exposure to organic antigens and/or positive ssIgGs, typical HRCT pattern and increased lymphocytosis in BALF, exceeding 30%. In case of unclear diagnosis, transbronchial lung biopsy or surgical lung biopsy were performed. The detailed information concerning the applied diagnostic procedures has been published previously (7,8).

2D-Doppler echocardiographic transthoracic examination, was performed with Siemens Acuson, Sequoia, or Toshiba Medical Systems, SSH-880 CV/W1 Artida. Two-dimensional and colour-flow guided continuous-wave Doppler transthoracic echocadiography was performed by experienced cardiac sonographers according to current standards. Pulmonary artery pressure was estimated based on the peak tricuspid regurgitation velocity (TRV). The tricuspid regurgitation pressure gradient (TRPG, TVPG) was calculated according to the modified Bernoulli equation: $TRPG = 4 \times (TRV)^2$ and systolic PAP (PASP) was calculated from the equation: PASP = TRPG + estimated right atrial pressure. Probability of PH was defined according to 2009 ESC/ERS guidelines, as most patients have been examined at that period of time (9). According to PASP results the patients were divided into two groups:

(I) PH unlikely: TRV ≤2.8 m/s, PASP ≤36 mmHg,
(II) PH possible or likely TRV 2.9–3.4 m/s, PASP 37–50 mmHg or TRV >3.4 m/s, PASP >50 mmHg.

Additionally, pulsed-wave Doppler was used to measure pulmonary artery acceleration time (AcT), defined as the interval between the onset of systolic pulmonary arterial flow and peak flow velocity.

The results of HRCT were re-evaluated retrospectively by two independent radiologists, blinded to clinical data. For the purposes of CT scan analyses, each lung was divided into the upper, central, and lower fields. From each lung field a transverse scan with the highest intensity of lesions was chosen in accordance by two radiologists. Qualitative

and quantitative assessment was performed within the lung window using a 0-1-2 scale to evaluate pulmonary lesions (ill-defined centrilobular nodules, ground glass opacities, mosaic attenuation and/or air trapping). 0= no radiological signs in both lungs, 1= the changes identified in 1–3 lung fields, 2= the changes identified in 4–6 lung fields. Degree of lung fibrosis was coded as: 0= no fibrosis, 1= reticular and/or bronchiectatic fibrosis, 2= honeycombing.

Plethysmography was performed with Master Screen Body/Diffusion by Jaeger (Germany 2002), according to ERS/ATS recommendations (10). The values of pulmonary function indices were reported as percentages of predicted values, according to ERS reference equations (11). For FEV1 and FVC – Falaschetti reference equations have been used (12). Lung transfer capacity for carbon monoxide (TLCO), was examined with the single breath method, using helium gas as a marker (13). The results were expressed as a percentage of predicted values, with correction for haemoglobin.

Six minutes walking test (6MWT) was performed on a corridor, with baseline and sixth minute room air oxygen saturation, according to ATS guidelines (14).

Serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) was assessed with Elecsys proBNP II, Cobas e411, Roche Diagnostics GmbH, Germany.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Bioethical Committee, National Tuberculosis and Lung Diseases Research Institute (NP.: 14/2019) and informed consent was taken from all the patients.

Statistical analysis

All analyses were performed with R version 3.6.0—a software environment for statistical computing and graphics (https://www.r-project.org/). Continuous variables were presented as means and standard deviations, categorical ones—as percentages of the entire population studied. Distributions' normality and homogeneity of variance of continuous variables in different groups were checked with Shapiro-Wilk test and F test, respectively. T-Student test (T-St) or U Mann-Whitney test (M-W), were used for comparison of the two groups. Categorical variables distribution was compared with Pearson's test, with its modifications if applicable. Correlations were analysed with Spearman's rank order test or Pearson's test.

Youden method was used to calculate cut off values of parameters with the highest specificity and sensitivity for echocardiographic PH prediction. Regression analysis (odds ratios and 95% confidence intervals) was applied to assess the best predictors of PH on echocardiography. A receiver operator characteristic curves were plotted for selected predictive parameters.

Results

Seventy patients with newly recognized HP entered the study. The population characteristics are presented in *Table 1*.

In 26 out of 70 patients (37%), PASP exceeding 36 mmHg was noted, in 5 of 70 (7%) PASP exceeded 50 mmHg.

RV was significantly larger and AcT significantly shorter in the patients with PASP >36 mmHg, comparing to those with PASP ≤36 mmHg (*Table 2*).

Demographic and clinical data as well as plethysmography, TLCO and walking test results in the groups of patients with PASP >36 mmHg and with PASP ≤36 mmHg were compared in *Table 3*.

6MWT walking distance (6MWD) was significantly shorter in the patients with PASP >36 mmHg, comparing to those with PASP ≤36 mmHg (mean values 441.23 meters and 511.98 meters, respectively, P=0.006), and desaturation rate on exertion – significantly higher (mean values 11.08% and 5.77% respectively, P=0.001).

Significant correlations were found between TVPG and 6MWD (*Figure 1*), as well as between TVPG and desaturation rate on exertion (*Figure 2*).

Analysis of respiratory indices revealed significantly lower TLCO % pred. in patients with PASP >36 mmHg, comparing to those with PASP ≤36 mmHg, (mean values: 41.08% and 52.64%, respectively, P=0.002). The correlation between TVPG and TLCO% pred. is presented on *Figure 3*.

Arterialised capillary blood gas analysis revealed significantly lower partial oxygen tension (PaO_2) in patients with PASP >36 mmHg, comparing to the remaining ones (mean values: 62 and 72.68 mmHg, respectively, P=0.0002). The correlation between TVPG and PaO_2 is presented on *Figure 4*.

The prevalence of fibrotic HP on HRCT was equal in patients with PASP >36 mmHg and those with PASP ≤36mmHg (66% and 61%, respectively) (*Table 4*). Nevertheless, in 5 patients with PASP >50 mmHg—all presented with lung fibrosis: stage 1, in 2 cases; stage 2, in 3 cases. The presence and extension of ground glass

Table 1 Characteristics of study population

Variables	Mean ± SD
Age at diagnosis (years)	52.63±11.75
Males/females (No.)	35/35
Duration of symptomatic disease (months)	34.04±40.49
Exposure to No. (%)	
Hay and products	32 [46]
Poultry	22 [31]
Pigeons	15 [21]
Others	18 [26]
HRCT	
Fibrotic HP	45 [64]
Non-fibrotic HP	25 [36]
TLC (% pred)	88.58±23.54
VC (% pred)	81.52±20.8
TLCO (% pred)	48.34±34
PaO_2 (mmHg)	68.7±11.7
$PaCO_2$ (mmHg)	36.67±67
6MWD (meters)	485.7±106.3
6MWT desaturation (%)	7.7±7.07
NT-proBNP (pg/mL)	139.53±296.49

HRCT, high resolution computed tomography of the chest; HP, hypersensitivity pneumonitis; TLC, total lung capacity; VC, vital capacity; TLCO, lung transfer capacity for carbon monoxide; PaO_2, partial oxygen tension measured in arterialized capillary blood; $PaCO_2$, carbon dioxide tension measured in arterialized capillary blood; 6MWT, six minutes walking test; 6MWD, six minutes walking test distance; NT-proBNP, serum N-terminal pro-B-type natriuretic peptide; SD, standard deviation.

opacities, ill-defined centrilobular nodules and mosaic lung attenuation pattern on HRCT were not helpful in predicting PH on echocardiography.

According to ROC analysis, the highest diagnostic utility for prediction of PASP>36 mmHg was combined with PaO_2 <69 mmHg, TLCO <42% pred., 6MWD <455 meters, and 6MWT desaturation rate >8% (*Table 5*, *Figure 5*).

Univariate analysis, documented that all the above mentioned parameters were the significant predictors of PASP >36 mmHg (*Table 6*). Risk of PH on echo was increased five-fold in case of TLCO <42% pred., four-fold—in case of exercise desaturation >8%, three-fold—in case of 6MWD <455 meters and two-fold—in those with PaO_2 <69 mmHg.

Discussion

Echocardiography is considered the best non-invasive method to screen for PH associated with lung diseases (15). Symptomatic patients with high probability of PH on echocardiography, should be considered as candidates to right heart catheterization (RHC), especially when their future management would be influenced by RHC results (15). RHC is particularly indicated in case of: referral for lung transplantation, inclusion in clinical trials or planned PH-dedicated therapy (15). Nevertheless, most patients with ILD at the time of diagnosis, would not profit from RHC, and thus the accepted method of PH evaluation is echocardiography.

Majority of published data documenting PH prevalence in the early period of interstitial lung diseases, concern sarcoidosis and IPF. In PULSAR study, based on echocardiography and RHC, PH was found in 3% of

Table 2 Echocardiographic data in HP patients with signs of PH comparing to those without PH

Parameter	PASP >36 mmHg	PASP ≤36 mmHg	P	Test type
TVPG (mmHg)	40.22±10.07	24.66±4.1	0.000000002	M-W
AcT (ms)	80.48±9.74	117.3±21.44	0.000000002	M-W
RV (mm)	27.26±3.55	25.07±4.32	0.03	T-St
LV (mm)	45.56±5.03	46.09±5.69	0.69	T-St

HP, hypersensitivity pneumonitis; PH, pulmonary hypertension; PASP, pulmonary artery systolic pressure; TVPG, trans-tricuspid valve gradient; AcT, pulmonary artery acceleration time; RV, right ventricle diameter; LV, left ventricle diameter; M-W, U Mann-Whitney test; T-St, T Student test.

Table 3 Clinical data, plethysmography results, 6MWT, NT-proBNP and arterialized capillary blood gas analysis in HP patients with echocardiographic signs of PH comparing to those without echocardiographic signs of PH

Parameter	PASP >36 mmHg	PASP ≤36 mmHg	P	Test type
Duration of symptomatic disease (months)	39.37±40.5	30.77±40.6	0.16	M-W
Age at diagnosis (years)	55.56±9.22	50.84± 12.83	0.1	T-St
TLC (% pred)	81.81±24.05	92.93±22.43	0.055	T-St
VC (% pred)	74.04±19.14	86.11±20.65	0.016	T-St
TLCO (% pred)	41.08± 16.58	52.64±13.67	0.002	T-St
TLC%/TLCO%	2.26± 0.86	1.79±0.52	0.008	M-W
VC%/TLCO%	2.09±0.8	1.72±0.54	0.06	M-W
PaO_2 (mmHg)	62±8.82	72.68±11.88	0.0002	T-St
$PaCO_2$ (mmHg)	37.5±3.91	36.18±4.51	0.22	T-St
6MWD (meters)	441.23±86.01	511.98±109.21	0.006	T-St
6MWT desaturation (%)	11.08±7.59	5.7±5.97	0.001	M-W
NT-proBNP (pg/mL)	226.43±449.1	85.2±114.36	0.23	M-W

6MWT, six minutes walking test; NT-proBNP, serum N-terminal pro-B-type natriuretic peptide; HP, hypersensitivity pneumonitis; PH, pulmonary hypertension; PASP, pulmonary artery systolic pressure; TLC, total lung capacity; VC, vital capacity; TLCO, lung transfer capacity for carbon monoxide; PaO_2, partial oxygen tension measured in arterialized capillary blood; $PaCO_2$, carbon dioxide tension measured in arterialized capillary blood; 6MWD, six minutes walking test distance; M-W, U Mann-Whitney test; T-St, T Student test.

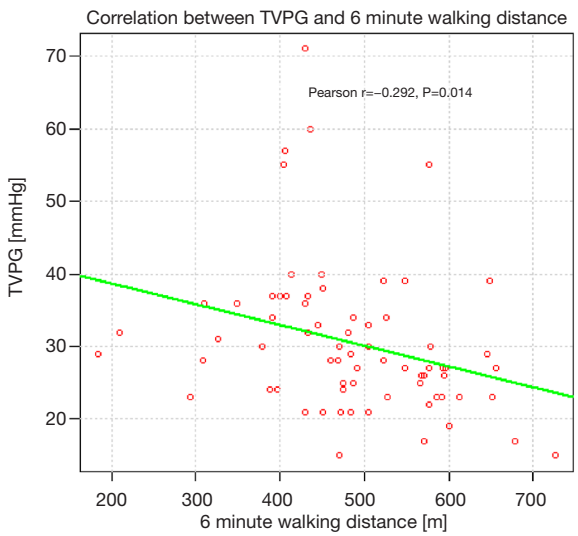

Figure 1 Correlation between TVPG and 6MWD in 70 HP patients. 6MWD, six minutes walking distance; HP, hypersensitivity pneumonitis.

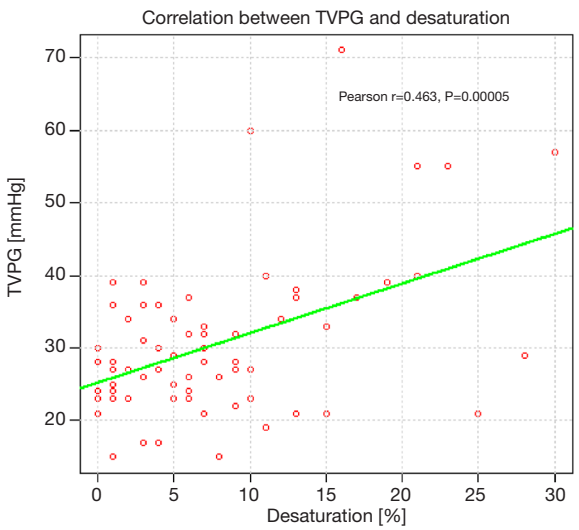

Figure 2 Correlation between TVPG and desaturation rate on 6MWT in 70 HP patients. 6MWD, six minutes walking distance; HP, hypersensitivity pneumonitis.

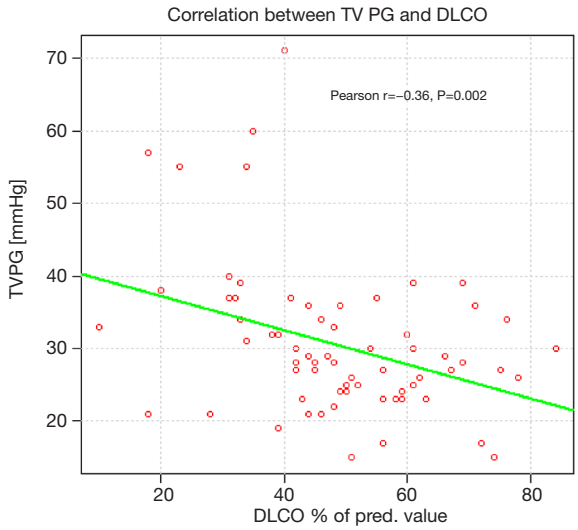

Figure 3 Correlation between TVPG and TLCO in 70 HP patients. TLCO, lung transfer capacity for carbon monoxide; HP, hypersensitivity pneumonitis.

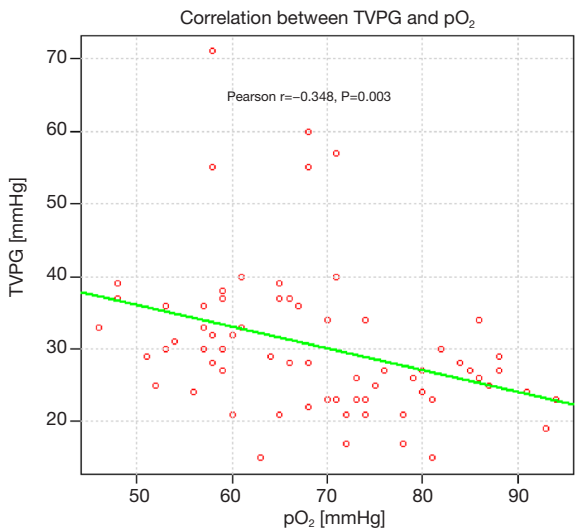

Figure 4 Correlation between TVPG and PaO_2 in 70 HP patients. PaO_2, partial oxygen tension; HP, hypersensitivity pneumonitis.

patients with sarcoidosis (16). ARTEMIS-IPF study confirmed the presence of Group 3 PH on RHC in 14% of IPF patients with mild-to moderate restriction (17).

However, there is not much data in literature, concerning PH prevalence, in HP. The first report was published in 2012 by Koschel *et al.*, who found PASP >50 mmHg on echocardiography in 19% of fibrotic HP patients (18). The epidemiological study of Walscher *et al.* published recently, documented PH in 9.5% of consecutive HP patients, but PH definition was based on medical diagnosis only (19).

We found PASP >36 mmHg in 37% of HP patients at diagnosis, and PASP >50 mmHg in 7%. PASP >50 mmHg was diagnosed exclusively in fibrotic HP, and concerned 11% of the group.

Thus, based on our observations, and the data of Koschel *et al.* (18), we presumed, that highly probable diagnosis of PH on echocardiography (PASP >50 mmHg) may concern 11–19% of patients with fibrotic HP at diagnosis.

The only report concerning hemodynamic evaluation of PH in HP was published by Oliveira *et al.*, who documented mPAP ≥25 mmHg in 25 out of 50 consecutive patients with fibrotic HP (50%), but severe PH (mPAP >35 mmHg) was noted in 10% only (20).

The discrepancies between researchers concerning PH frequency in HP, could have been caused by different characteristics of study groups, e.g., the number of patients with fibrotic HP included, time from disease onset to diagnosis, and the patients' age. Nevertheless, time from first symptoms to diagnosis was not significantly different in our group of patients with PASP >36 mmHg, comparing to those with PASP ≤36 mmHg. Likewise, no significant differences of patients age at diagnosis were noted between the two groups.

Clinical profile of our HP patients with PASP >36 mmHg, showed significantly decreased exercise capacity (decreased walking distance, increased desaturation rate) and significantly lower resting PaO_2 comparing to those with PASP ≤36 mmHg. This was the result of impaired lung diffusion capacity. Mean TLCO% pred. was 41.08% in those with PASP >36 mmHg and 52.64% pred. in the remaining ones.

It is worth to notice that despite relatively mild decrease of mean lung volumes in our study group (TLC 88.58% pred., VC 81.52% pred.), mean TLCO% pred. was disproportionally low (48% pred.). According to the opinion of pulmonary specialists in DELPHI study, low TLCO at diagnosis in the patient with ILD presenting with HRCT signs of small airways disease, is very suggestive of HP diagnosis (21). The other authors documented that significant TLCO increase may be achieved during immunosuppressive therapy in HP patients, resulting in the large clinical benefit (22,23).

In our study group, optimal predictors of PH on echocardiography, were PaO_2 <69 mmHg, 6MWD <455 meters, TLCO <42% pred. and 6MWT desaturation rate >8%.

Table 4 HRCT findings in HP patients with echocardiographic signs of PH comparing to those without the echocardiographic signs of PH

HRCT type of changes/intensity	PASP >36 mmHg 27 cases, n			PASP ≤36 mmHg 43 cases, n			P
	Score 0	Score 1	Score 2	Score 0	Score 1	Score 2	
Centrilobular nodules	17	8	2	22	15	6	0.56
Ground glass opacities	5	12	10	8	22	13	0.82
Mosaic lung attenuation	5	12	10	7	22	14	0.86
Lung fibrosis	9	11	7	16	17	10	0.47

HRCT, high resolution chest computed tomography; HP, hypersensitivity pneumonitis; PH, pulmonary hypertension; PASP, pulmonary artery systolic pressure.

Table 5 The utility of various parameters for prediction of PH on echocardiography in 70 HP patients—ROC analysis

Parameter	AUC	95% CI	P	Optimal cut off	Spec	Sens	PPV	NPV
PaO_2, mmHg	0.756	0.642–0.756	0.0096	69 mmHg	0.64	0.81	0.57	0.85
TLCO (% pred.)	0.723	0.587–0.723	0.037	42%	0.89	0.62	0.76	0.80
6MWD meters	0.726	0.603–0.726	0.026	455 meters	0.8	0.69	0.67	0.81
6MWT desat (%)	0.732	0.608–0.732	0.027	8%	0.77	0.58	0.6	0.76
TLC/DLCO	0.692	0.558–0.692	0.07	1.72	0.64	0.77	0.57	0.82
VC/DLCO	0.636	0.499–0.636	0.21	1.69	0.59	0.62	0.47	0.72

PH, pulmonary hypertension; HP, hypersensitivity pneumonitis; ROC, receiver operator characteristic curve; AUC, area under the curve; spec, specificity; sens, sensitivity; PPV, positive predictive value; NPV, negative predictive value; PaO_2, partial oxygen tension measured in arterialized capillary blood; TLCO, lung transfer capacity for carbon monoxide; 6MWD, six minutes walking test distance; 6MWT, six minutes walking test; TLC, total lung capacity.

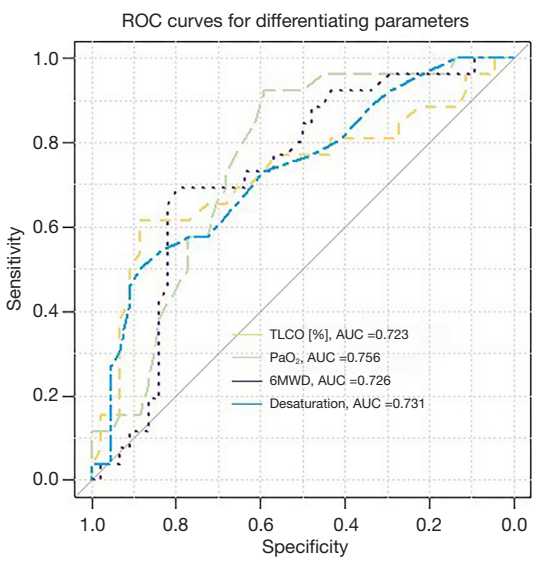

Figure 5 Diagnostic utility of various parameters for prediction of PASP >36 mmHg on echocardiography in 70 HP patients—ROC analysis. PASP, pulmonary artery systolic pressure; HP, hypersensitivity pneumonitis; ROC, receiver operator characteristic curve.

TLCO <42% pred. increased probability of PASP >36 mmHg by five-fold, and 6MWT desaturation rate >8% by four-fold.

According to Oliveira *et al.* PaO_2 and FVC were the independent predictors of PH at RHC, nevertheless, this group was composed of patients with much more advanced lung disease, mean FVC was 59% pred. (20).

We previously found FVC/TLCO index and TLC/TLCO index as significant predictors of PH on echocardiography in the group of 93 patients with various interstitial lung diseases (ILDs), nevertheless we failed to demonstrate the utility of these parameters in PH prediction in the present group of patients (24).

What may be interesting, NT-proBNP serum level was not helpful in PH prediction, neither in our study group, nor in the study of Oliveira *et al.* (20). According to our observations, serum NT-proBNP increase is a late sequel of right heart dysfunction in group 3 PH, thus it is not helpful in PH screening at the time of ILDs recognition.

We are the first authors who investigated the relationship

Table 6 Risk of PH on echocardiography—univariate analysis

Variable	Cut off	RR	95% CI	P
TLCO (% pred.)	42	5.42	2.82–7.43	0.00005
PaO_2 (mmHg)	69	2.22	1.57–2.56	0.00069
6MWD (meters)	455	3.38	2.08–4.26	0.00013
6MWT desat %	8	4.4	2.03–6.77	0.00085

PH, pulmonary hypertension; TLCO, lung transfer capacity for carbon monoxide; PaO_2, partial oxygen tension measured in arterialized capillary blood; 6MWD, six minutes walking test distance; 6MWT, six minutes walking test; RR, relative risk.

between lung fibrosis and echocardiographic signs of PH. HRCT analysis revealed that fibrotic HP was equally frequent among patients with PASP >36 mmHg and those with PASP ≤36 mmHg. Moreover 9 patients without lung fibrosis had PASP ≥36 mmHg, and 10 patients with advanced lung fibrosis (honeycombing) had no echocardiographic signs of PH. Thus, lung fibrosis was not a good predictor of PH on echocardiography, if PASP of 36 mmHg was considered as cut off value. Nevertheless, PASP >50 mmHg was observed exclusively among fibrotic HP patients. Unfortunately, PASP >50 mmHg was a rare finding in our study group (7%), despite the fact that fibrotic lung disease was frequent (64% of patients). Therefore the role of lung fibrosis as PH predictor has not been confirmed.

The limitations of our study concerned mostly its' retrospective character. Our clinical practice is to perform echocardiographic examination in HP at diagnosis, but occasionally, initial echocardiography was lacking due to technical reasons. Therefore some of the patients diagnosed with HP in between 2005 and 2017, were not included into the present study. Moreover patients with echocardiographic PASP >50 mmHg, RHC was not performed to confirm PH diagnosis. Nevertheless this concerned only 5 patients, and in 3 of them—advanced fibrotic HP, with honeycombing-was diagnosed.

Conclusions

We found echocardiographic signs of PH in 37% of HP patients at diagnosis, but most of them presented with moderately increased PASP. PH probability was significantly increased in patients with PaO_2 <69 mmHg, TLCO <42% pred., 6MWD <455 meters, and desaturation rate exceeding 8%. The presence of lung fibrosis on HRCT, the duration of the disease, and the patients' age at diagnosis, were not helpful in prediction of PH on echocardiography.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/jtd-21-130). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Bioethical Committee, National Tuberculosis and Lung Diseases Research Institute (NP.: 14/2019) and informed consent was taken from all the patients.

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