Symptomatic impact and anxiety generated by performing pulmonary function tests: Are there differences between patients with fibrotic interstitial lung disease and obstructive airway disease?

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ABSTRACT

INTRODUCTION Pulmonary function tests (PFTs) are a basic tool in the evaluation of respiratory pathology. Understanding how the underlying pathology affects its performance and the levels of dyspnea and anxiety generated in patients remain poorly studied. The aim of this study is to compare PFT performance and dyspnea levels between a group of patients with fibrotic interstitial lung disease (ILD) and a group of patients with obstructive pulmonary disease.

METHODS This was a prospective study conducted between May 2021 and September 2022, with patients who underwent PFT in a level two hospital in Portugal. A questionnaire assessing vital parameters, and dyspnea and anxiety scales was applied. Data obtained before and after performing the tests were compared and analyzed.

RESULTS In all, 80 patients were evaluated, 40 with some form of fibrotic ILD and 40 with obstructive airway disease. A trend towards greater elevation of cardio-respiratory stress, specially through respiratory rate, was found after PFT in the group of patients with ILD. In contrast, a trend towards higher levels of anxiety immediately before PFT was observed in patients with obstructive disease (mostly COPD) compared to that seen in the group of patients with fibrotic ILD. The variables contributing the most to length of stay in the lung function laboratory were: undergoing a bronchodilation test; the number of attempts needed to reach a technically adequate flow-volume curve; the previous degree of dyspnea, heart rate and respiratory rate before the test; and male gender. A diagnosis of fibrotic ILD was also, by itself, a determining factor for a longer stay in the lab.

CONCLUSIONS There are differences in the levels of cardio-respiratory stress, anxiety, and length of stay in the lab to complete PFT between patients with ILD and obstructive airway disease. The awareness for these differences can help to anticipate hazards and allow differentiated approaches to these patients.

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INTRODUCTION

Pulmonary function tests (PFTs) comprise a set of assessments for studying lung function. They may be used in individuals presenting with respiratory symptoms (such as dyspnea or cough) or radiological abnormalities in need of clarification, preoperative evaluation setting or suspected occupational respiratory disease, or for monitoring the disease course and treatment response in patients with known respiratory disease[1,2].

Correct interpretation of PFT requires that the American Thoracic Society (ATS) and European Respiratory Society (ERS) technical standards be met, which demands not only adequate equipment, but also minimally acceptable patient cooperation for protocol required manoeuvres[3]. Thus, obtaining acceptable PFT may prove a challenge, especially in children, older patients, or patients in more severe stages of disease[1]. On the technician's side, explaining the procedure, providing examples and verbal encouragement are essential[2]. However, the type and stage of the respiratory disease in question may potentially influence the difficulty in conducting these tests, which can also lead to patient anxiety and discomfort.

Exertional dyspnea is a common symptom in chronic obstructive airway disease (COPD) and interstitial lung

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disease (ILD). This is a complex symptom, with several associated mechanisms and closely related to exercise tolerance and quality of life. In both nosological groups, depression and anxiety are common[4-8], and may be related with the level of dyspnea/tolerance for exertion, which, in turn, may condition physical and emotional participation in basic activities of daily living[6].

In this study, the authors aimed to evaluate and compare dyspnea and anxiety before and after PFT, the level of heart and respiratory rate, and the delay in performing these tests in a group of patients with either fibrotic ILD or obstructive airway disease (COPD and bronchial asthma).

METHODS

The authors conducted a prospective analytical cross-sectional study, between May 2021 and September 2022, of sequentially enrolled patients who underwent PFT in a lung function laboratory at a level two hospital (hierarchy according to responsibilities and specialties present in the hospital), who had either fibrotic ILD or some form of obstructive airway disease, and agreed to participate in the study.

After obtaining informed consent, a survey (Supplementary file) was applied on the day of the PFT previously requested by the attending pulmonologist. The survey, specially created for this purpose, also evaluated the number of attempts needed to obtain an acceptable output-volume curve, as well as the heart rate and respiratory rate before and immediately after the end of the tests.

Assessment of dyspnea

To assess dyspnea four questionnaires/scales were used:

- Modified Medical Research Council Dyspnea Scale (mMRC), validated for the Portuguese language, applied before PFT. Originally validated for assessing disability in COPD[9], it is currently one of the most used tools for grading exertional dyspnea in chronic respiratory patients.
- Modified Borg scale, applied before and after the PFT. This scale is widely used to assess perceived exertion[10].
- Visual analogue dyspnea scale, applied before and after PFT.
- University of California, San Diego Shortness of Breath Questionnaire (UCSDSOBQ), consisting of 24 items for classification (0–5) of the degree of dyspnea according to the limitation imposed on the performance of various daily tasks and activities, completed before PFT[11].

Assessment of anxiety

To assess anxiety two scales were used:

- Hospital Anxiety and Depression Scale (HADS), consisting of 7 related specific questions (scored from 0–3)[12], completed immediately before undergoing PFT.
- Generalized Anxiety Disorder Assessment (GAD-7), comprising 7 items (score: 0–3) portraying various daily situations and reaction frequency[13], completed immediately before undergoing PFT.

Statistical analysis

Descriptive analysis of the studied variables was performed by obtaining frequencies for categorical variables, and means/medians and standard deviations/interquartile ranges for quantitative variables. Comparison was made between the obstructive airway disease group and the fibrotic ILD group, and between some predefined subgroups within those: asthma vs COPD, fibrotic ILD with 'usual interstitial pneumonia' (UIP) pattern (by histology or identified on high-resolution chest CT) vs 'non-UIP' pattern. Comparison of variables between groups was performed and tested using Fisher's exact test/ Pearson's chi-squared test, Wilcoxon's test/Welch's two sample t-test and Kruskal-Wallis's rank sum test.

We used the total time that the patient remained in the lung function laboratory to complete the examination as a result (dependent variable) of the variables under study and applied multiple linear regression and regression with automatic selection (stepwise). Some correlated variables from the set of independent variables were excluded from the analysis. A stepwise linear regression was used to identify predictors/associations of 'total time' with the selected independent variables. At each step, variables were added based on p-values, and the AIC was used to set a limit on the total number of variables included in the final model.

Statistical analysis was performed using R version 4.2.2. The level of significance was set at 0.05. The hospital's ethics committee approved this study (Ref 44-05-2022).

RESULTS

A total of 80 patients were evaluated, 40 of them with obstructive airway disease and another 40 with some form of fibrotic ILD. In the first group, 45% of the patients had a diagnosis of COPD (with an overall mean FEV_1 value of 70.18 ± 21.9% of the predicted value, with half of the patients in GOLD stages 3 or 4), while the rest had a diagnosis of bronchial asthma (77.3% of them in GINA treatment 1–3 and 22.7% in steps 4–5). Regarding the patients included in the fibrotic ILD group, the distribution of individual diagnoses was as follows: 35.0% with fibrotic hypersensitivity pneumonitis, 27.5% with idiopathic pulmonary fibrosis (IPF), 12.5% with idiopathic or secondary fibrotic non-specific interstitial pneumonia (NSIP), 10.0% with UIP secondary to rheumatoid arthritis, 7.5% of unclassifiable fibrotic interstitial pneumonia , and 5.0% of patients with chronic silicosis complicated by progressive massive fibrosis. In this group, mean FVC and DLCO values were 77.1 ± 22.1% and 53.6 ± 19.8% predicted, respectively.

The following variables were evaluated: age, gender, diagnosis, lung function, number of attempts, number of acceptable curves, heart and respiratory rates before and after PFT, mMRC, UCSDSOBQ, Borg scale (dyspnea), visual dyspnea scale, GAD7, HADS – dimension of 'anxiety', time spent (minutes) in the room and number of technically acceptable flow-volume curves between the two groups (Table 1).

Table 1. Description of the characteristics studied in the two groups*

Characteristics	n	Overall (N=80)	Obstructive airway disease (N=40)	ILD (N=40)	p[a]
Gender	80				0.3
Female		39 (49%)	22 (55%)	17 (42%)	
Male		41 (51%)	18 (45%)	23 (57%)	
Age (years)	80	63 (13)	57 (11)	69 (11)	**<0.001**
FEV_1/FVC	80	72 (12)	66 (11)	78 (9)	**<0.001**
FEV_1	80	74 (24)	70 (22)	78 (25)	0.12
FVC	80	79 (21)	82 (20)	77 (22)	0.3
DLCO-SB	68	60 (21)	67 (20)	54 (20)	**0.007**
KCO	68	77 (20)	79 (21)	76 (18)	0.6
Spirometry	80	42 (53%)	18 (45%)	24 (62%)	0.14
Plethysmography	80	38 (48%)	22 (56%)	16 (40%)	0.14
BD test prescribed	80	36 (45%)	24 (60%)	12 (30%)	**0.007**
DLCO prescribed	80	69 (86%)	29 (72%)	40 (100%)	<0.001
Number of attempts	78	3.96 (1.62)	3.63 (1.05)	4.28 (1.97)	0.3
Number of acceptable curves	78				**0.004**
2		8 (10%)	0 (0)	8 (20%)	
3		67 (86%)	37 (97%)	30 (75%)	
4		3 (3.8%)	1 (2.6%)	2 (5.0%)	
Unknown		2	2	0	
HR before PFT	80	80 (13)	81 (12)	80 (14)	0.9
HR after PFT	77	83 (13)	83 (12)	84 (14)	0.8
RR before PFT	80	20.3 (4.5)	19.0 (3.0)	21.6 (5.4)	**0.010**
RR after PFT	77	22.2 (5.8)	20.2 (3.5)	24.3 (6.9)	**0.002**
mMRC	80	1.18 (0.99)	0.50 (0.68)	1.85 (0.77)	**<0.001**
UCSDSOBQ	80	22 (23)	21 (22)	24 (23)	0.5
Borg before PFT	80	1.16 (1.48)	1.10 (1.57)	1.23 (1.39)	0.4
Borg after PFT	80	2.62 (2.10)	2.36 (1.90)	2.88 (2.28)	0.4
Visual scale before PFT	80	1.38 (1.60)	1.28 (1.57)	1.48 (1.65)	0.6
Visual scale after PFT	80	3.05 (2.28)	2.78 (2.15)	3.33 (2.40)	0.3
HADS	80	5.0 (3.5)	5.6 (3.7)	4.5 (3.2)	0.2
GAD7	80	6.5 (5.3)	7.0 (5.7)	5.9 (4.8)	0.4
Lab time	78	25 (8)	25 (6)	26 (10)	0.4

*Data are given either as n (%) or mean (SD). a Pearson's chi-squared test. Welch's two sample t-test. Wilcoxon's rank sum test. FEV_1/FVC: forced expiratory volume/forced vital capacity. DLCO: diffusing capacity of the lungs for carbon monoxide. KCO: carbon monoxide transfer coefficient BD: bronchodilation. HR: heart rate. RR: respiratory rate. mMRC: modified medical research council dyspnea scale. UCSDSOBQ: University of California, San Diego shortness of breath questionnaire. HADS: hospital anxiety and depression scale. GAD7: generalized anxiety disorder assessment.

The group with fibrotic ILD had a lower median age (p<0.001), a lower DLCO (p<0.05) and a higher FEV_1/FVC value (p<0.001). Post PFT heart rate, respiratory rate, and severity of dyspnea by visual analogue scale, also tended to be higher in this group.

Regarding dyspnea, the baseline mMRC level was

Table 2. Description of variables by subgroups according to diagnosis*

Characteristics	n	Overall (N=80)	Non UIP (N=22)	UIP (N=18)	COPD (N=19)	Asthma (N=21)	p[a]
Gender	80						0.031
Female		39 (49%)	12 (55%)	5 (28%)	7 (37%)	15 (71%)	
Male		41 (51%)	10 (45%)	13 (72%)	12 (63%)	6 (29%)	
Age (years)	80	63 (13)	65 (12)	73 (9)	60 (8)	54 (12)	**<0.001**
FEV_1/FVC	80	72 (12)	75 (9)	83 (6)	58 (8)	73 (8)	**<0.001**
FEV_1	80	74 (24)	71 (27)	88 (18)	59 (21)	80 (18)	**<0.001**
FVC	80	79 (21)	74 (25)	81 (17)	75 (18)	88 (21)	0.10
DLCO-SB	68	60 (21)	57 (19)	50 (21)	59 (19)	75 (19)	0.004
KCO	68	77 (20)	78 (15)	73 (21)	69 (21)	89 (17)	0.033
Spirometry	80	42 (53%)	11 (50%)	13 (76%)	6 (32%)	12 (57%)	0.058
Plethysmography	80	38 (48%)	11 (50%)	5 (28%)	13 (72%)	9 (43%)	0.059
BD test prescribed	80	36 (45%)	10 (45%)	2 (11%)	11 (58%)	13 (62%)	**0.007**
DLCO prescribed	80	69 (86%)	22 (100%)	18 (100%)	15 (79%)	14 (67%)	**<0.001**
Number of attempts	78	3.96 (1.62)	3.73 (1.08)	4.94 (2.58)	3.72 (0.89)	3.55 (1.19)	0.3
Number of acceptable curves	78	2.94 (0.37)	2.95 (0.38)	2.72 (0.57)	3.00 (0.00)	3.05 (0.22)	0.032
HR before PFT	80	80 (13)	81 (16)	79 (11)	79 (13)	82 (12)	>0.9
HR after PFT	77	83 (13)	85 (15)	82 (11)	82 (14)	84 (11)	0.9
RR before PFT	80	20.3 (4.5)	23.1 (6.2)	19.8 (3.8)	20.0 (2.7)	18.1 (3.0)	**0.002**
RR after PFT	77	22.2 (5.8)	26.4 (7.8)	21.8 (4.7)	21.3 (3.5)	19.2 (3.3)	**<0.001**
mMRC	80	1.18 (0.99)	1.82 (0.73)	1.89 (0.83)	0.74 (0.73)	0.29 (0.56)	**<0.001**
UCSDSOBQ	80	22 (23)	27 (25)	19 (21)	26 (25)	16 (19)	0.3
Borg before PFT	80	1.16 (1.48)	1.50 (1.22)	0.89 (1.53)	0.87 (1.14)	1.31 (1.89)	0.2
Borg after PFT	80	2.62 (2.10)	3.36 (2.52)	2.28 (1.84)	2.32 (1.48)	2.40 (2.25)	0.5
Visual Scale before PFT	80	1.38 (1.60)	1.86 (1.67)	1.00 (1.53)	1.00 (1.11)	1.52 (1.89)	0.2
Visual Scale after PFT	80	3.05 (2.28)	3.73 (2.60)	2.83 (2.09)	2.68 (1.42)	2.86 (2.69)	0.5
HADS	80	5.0 (3.5)	5.4 (3.9)	3.4 (1.5)	5.9 (3.7)	5.3 (3.7)	0.2
GAD7	80	6.5 (5.3)	6.2 (5.6)	5.6 (3.6)	7.3 (4.8)	6.9 (6.5)	0.7
Lab time	78	25 (8)	28 (10)	24 (9)	25 (6)	24 (6)	0.3

*Data are either given as n (%) or median (interquartile range). **a** Pearson's chi-squared test. Kruskal-Wallis's rank sum test. Fisher's exact test.

significantly higher in the fibrotic ILD patients (p<0.001). The UCSDSOBQ and Borg scale values also tended to be higher in this group of patients compared to patients with obstructive airway disease. No statistically significant differences were found between subgroups: asthma versus COPD and UIP versus non-UIP (Table 2).

In the anxiety assessment, there were no statistically significant differences between groups. However, the analysis by subgroups showed a trend towards a higher level of anxiety in the subgroup of patients diagnosed with COPD, compared to the other groups of patients (Table 2).

Total time in the respiratory function laboratory was significantly impacted by the performance of a bronchodilation test (p<0.001), the number of attempts needed to achieve a technically adequate flow-volume curve (p<0.001), the visual analogue dyspnea scale value before the test (p<0.001), UCSDSOBQ score (p<0.05), heart and respiratory rates before the test (p<0.001), and male gender (p<0.05). A diagnosis of fibrotic ILD was also a determining factor (p<0.05) (Table 3).

Table 3. Study of determining variables for time in the respiratory function laboratory

Variables	Multiple linear regression			Stepwise linear regression		
	Beta	95% CI	p	Beta	95% CI	p
Group						
Obstructive disease	-	-		-	-	
Fibrotic interstitial disease	4.1	-0.65–8.8	0.089	4.4	0.94–7.9	**0.014**
Gender						
Female	-	-		-	-	
Male	-2.9	-6.2–0.49	0.092	-3.2	-6.0 – -0.39	**0.026**
Age	-0.09	-0.26–0.07	0.257	-0.11	-0.24–0.03	0.118
FEV1/FVC	-0.14	-0.32–0.04	0.117	-0.17	-0.31 – -0.03	**0.020**
FVC	0.00	-0.08–0.08	0.971			
KCO	-0.04	-0.13–0.05	0.353			
Spirometry	0.71	-2.4–3.8	0.645			
BD test prescribed	9.7	6.6–13	**<0.001**	9.4	6.6–12	**<0.001**
DLCO prescribed	-8.9	-22–4.5	0.189	-7.6	-18–2.8	0.148
Number of attempts	2.0	1.1–3.0	**<0.001**	2.0	1.2–2.9	**<0.001**
Number of acceptable curves	-3.3	-8.2–1.5	0.173	-3.6	-7.9–0.83	0.110
HR before PFT	-0.10	-0.21–0.00	0.058	-0.11	-0.21– -0.01	**0.034**
RR before PFT	0.45	-0.05–0.95	0.077	0.55	0.19–0.91	**0.004**
RR after PFT	0.05	-0.36–0.46	0.790			
mMRC	-0.17	-2.8–2.5	0.897			
UCSDSOBQ	-0.14	-0.26 – -0.02	**0.024**	-0.12	-0.20 – -0.04	**0.003**
Visual Scale before PFT	2.5	1.1–3.8	**<0.001**	2.5	1.5–3.6	**<0.001**
Visual Scale after PFT	0.25	-0.60–1.1	0.553			
HADS	0.07	-0.67–0.82	0.844			
GAD7	-0.01	-0.52–0.50	0.969			

DISCUSSION

Differences were found in some objective measures of cardio-respiratory stress, such as HR and RR, immediately after the end of PFT in the group of patients with fibrotic ILD.

Additionally, this group of patients reported a higher level of dyspnea when assessed by the mMRC scale, and tended to have a higher value on both the Borg scale and on the visual analogue dyspnea scale, which aligns with the fact that dyspnea is a common and intrusive symptom in patients with IPF, fibrotic hypersensitivity pneumonitis and ILD secondary to connective tissue disease[14-16].

Regarding anxiety, a prevalence of up to 31% has been reported in patients with chronic ILD[17] and up to 34% in patients with asthma[18]. In patients with COPD, there have been reports of prevalence reaching as high as 55%[19]. In this study, the COPD subgroup also tended to report higher levels of anxiety.

In patients with fibrotic ILD or obstructive airway disease, both dyspnea and anxiety may profoundly impact the natural course of disease, not only by reducing quality of life measures but also by increasing social isolation, depression, lack of adherence to therapy and risk of hospitalizations and exacerbations[19].

Patients with fibrotic ILD spent a longer time in the laboratory to complete PFT ($p<0.05$) and tended to have a lower number of acceptable curves during their performance.

Although PFTs are an invaluable tool for longitudinal monetarization of these patients, in advanced stages of disease the progressive limitation of their ability to collaborate with the performance of serial PFT may lead to

greater levels of frustration and anxiety while also impairing the tests' reliability and reproducibility.

A better awareness by the clinical staff of specific difficulties in performing PFT imposed by certain diseases and the possibility of improving strategies and providing adequate pulmonary laboratory time, may help to reduce anxiety and discomfort in these patients.

CONCLUSIONS

Obstructive airway diseases and ILD are eminently different in their pathophysiology, clinical repertoire, and natural history. We sought to assess differences imposed by the type of disease on the difficulty in performing PFT and the level of dyspnea and anxiety hence generated.

Despite limitations related to sample size, there was a greater cardio-respiratory stress in patients with fibrotic ILD when compared with patients with obstructive airway disease, objectively assessed by HR and RR immediately after finishing PFT. Similarly, some indicators suggest a higher level of dyspnea after PFT in the former group. A longer time needed to perform PFT as well as a lower number of acceptable curves were also observed in the ILD subgroup. As for anxiety, the subgroup of patients with COPD tended to present with higher levels. The awareness for these differences can help to anticipate hazards and allow differentiated approaches to these patients.

CONFLICTS OF INTEREST

The authors have completed and submitted to ICMJE for Disclosure of Potential Conflicts of Interest and none was reported. C. Cascais Costa reports support for attending Sanofi - Congresso Portugues de Pneumologia 2022, and Linde - Congresso de Pneumologia do Norte 2023. P. G. Ferreira reports receiving consulting fees and honoraria for lectures from Boehringer Ingelheim and also support for attending meetings and/or travel for Boehringer Ingelheim.

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ETHICAL APPROVAL AND INFORMED CONSENT

Ethical approval was obtained from the hospital's ethics committee (Approval number: 44-05-2022; Date: 15 December 2022). Participants provided informed consent.

DATA AVAILABILITY

The data supporting this research are available from the authors upon reasonable request.

PROVENANCE AND PEER REVIEW

Not commissioned; externally peer-reviewed.

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