

pulmonary disease patients.

## A pilot study in Portugal

### Cantar em doentes com doença pulmonar obstrutiva crônica: um estudo-piloto em Portugal

Chronic obstructive pulmonary disease (COPD) is a disorder characterized by airflow limitation that is not fully reversible. The severity and magnitude of the symptoms increase as the disease progresses, leading to significant disability and a negative effect on quality of life.<sup>1-3</sup> Despite optimal treatment with pharmacological agents, classic pulmonary rehabilitation and oxygen, many patients continue to be symptomatic.<sup>3</sup>

It is well known that respiration is an essential factor for singing and that this technique involves strong fast inspirations, followed by extended, regulated expirations, which require accurate control of breathing.<sup>1,2,4-6</sup>

The objective of this study was to investigate the effects of weekly singing classes on maximal respiratory pressures, spirometric measurements, parameters in six-minute walk test (6MWT), maximum expiration breathing time and health-related quality of life (QoL) in patients with COPD.

Patients with COPD who were attending a maintenance pulmonary rehabilitation program (90 min, twice a week) at the Physical Medicine and Rehabilitation Department in Pedro Hispano Hospital were invited to participate in the study. They had to have been diagnosed with COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD). All subjects had to have been in a stable clinical condition for at least 6 weeks before admission to the study and to have signed a written informed consent at their initial visit.

Demographics, height, weight and clinical history were recorded. All patients initially completed plethysmography (FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, TLC and RV); maximal inspiratory and expiratory pressures at the mouth level (MIP, MEP); assessment of QoL employing Saint George's Respiratory Questionnaire (SGRQ), COPD Assessment Test (CAT) and EuroQoL Test; Hospital Anxiety and Depression Scale (HADS); London Chest Activity of Daily Living Scale (LCADL) and Medical Research Council Dyspnoea Questionnaire (mMRC) for dyspnea; six minutes walk test (6MWT) with documentation of time taken to recover oxygen saturation, Modified Borg dyspnea score and heart rate following the test.

Maximum expiration breathing time was always assessed by the same researcher.

The patients were enrolled in weekly classes lasting approximately 1 h, for 10 weeks. The classes were coordinated by a singing teacher and a physiotherapist. The patients participated in the classes as a group and the activities included the following:

- (a) Relaxation exercises of neck and upper and lower limb muscles, conducted by a physiotherapist (10–15 min);
- (b) Vocalization exercises, led by the singing teacher, as a preparation for singing (15 min);

The songs increased in difficulty as the sessions progressed and the patients were instructed to practice the songs at home during the week.

The final evaluation of the patients was performed after 10 sessions. If episodes of acute exacerbations occurred, the final assessment was performed only after a minimum of 3 weeks of clinical stability.

The components of the final evaluation were the same as those for the initial assessment. On final evaluation patients also responded to a questionnaire drawn up by the researchers (Fig. 1).

The study took place between February and May 2013 (10 sessions). Eight patients were selected to participate in the study but two of them were subsequently excluded.

Two patients were dropped from the study because they did not attend at least 7 sessions.

The results are listed in Tables 1 and 2.

Despite the small number of patients it is possible to observe that the FEV<sub>1</sub> improved from 1.15 L (45%) to 1.21 L (47%) for Patient 1, remained the same in Patients 2 and 3 (33 and 34%) and got worse in Patient 4 (54–51%).

No significant differences were observed in relation to residual volume (RV) and total lung capacity (TLC). In terms of maximum expiratory pressures (MEP) we found an improvement after singing lessons in only three of the patients. Patient 3 was the only patient who experienced a COPD exacerbation during study time and was the only patient not to improve MEP.

When analyzing the results for the 6-minute walk test (6MWT) we observed an increase in the distance travelled by Patient 2 and Patient 3 (60 m for Patient 2 and 99 m for Patient 3) and a decrease for Patient 1 and 4. Only Patient 4 had final oxygen saturations below 90% when the test was performed after the singing lessons (before the program only three patients had oxygen saturation below 90%). The expiratory time decreased in all patients tested.

In terms of quality of life questionnaires (Table 2) we found that there were no major differences between the pre- and post-singing session results.

When analyzing the answers to the questionnaire prepared by the researchers we found that all patients reported improvement in lung function control, reduced anxiety and more self-esteem after the singing lessons. In addition, all patients reported a feeling of well-being and recorded the experience as very pleasant.

The aim of the singing lessons was to improve the quality of life in patients with moderate and severe COPD, by helping them to control daily symptoms that interfere with their quality of life, as suggested in the literature.

Functionally MEP tended to improve MEP, as observed in other studies<sup>1</sup> but these results cannot be considered valid given the low number of patients and the lack of a control group. The expiratory time decreased in all patients tested.

Despite their not having ticked major differences in quality of life questionnaires, the singing program was perceived by patients as a pleasant experience, which is similar to the results found in the literature.<sup>2,5,6</sup>

**Table 1** Respiratory tests before and after the program.

	Patient 1		Patient 2		Patient 3		Patient 4	
Measurements	Patient 1		Patient 2		Patient 3		Patient 4	
	BSP*	ASP**	BSP	ASP	BSP	ASP	BSP	ASP
FEV1 (L)	1.15 (45%)	1.21 (47%)	0.84 (33%)	0.85 (33%)	0.90 (34%)	0.87 (34%)	1.21 (54%)	1.21 (51%)
FEV1/FVC (%)	59	51	53	50	37	40	67	67
TLC (L)	6.14 (101%)	5.95 (98%)	4.72 (96%)	4.70 (95%)	9.38 (154%)	7.66 (126%)	3.90 (92%)	3.90 (92%)
FVC (L)	1.97 (59%)	2.38 (71%)	1.59 (53%)	1.71 (58%)	2.43 (72%)	2.20 (65%)	1.81 (66%)	1.81 (66%)
DLCO/Va (mmol/min/Kpa/L)	95	94	18	16	35	41	79	79
RV (L)	3.95 L (163%)	3.53 L (146%)	3.12 (180%)	2.99 (171%)	6.61 (272%)	5.07 (207%)	2.10 (143%)	2.10 (143%)
MIP	75	78	70	48	89	78	63	53
MEP	86	88	66	89	97	75	111	121
6MWT (O <sub>2</sub> Sat)	92	93	88	93	85	92	89	88
6MWT (final Borg dyspnea)	5	4	3	3	6	4	4	4
6MWT (final HR)	119	105	128	135	105	105	125	120
6MWT (distance/meters)	480	440	360	420	360	459	480	420
Expiratory time (s)	14.9	12.6	14	10	16	13	12.5	8.5

FEV 1: forced expiratory volume in 1 s; FVC: forced vital capacity; TLC: total lung capacity; DLCO/Va: ratio between carbon monoxide diffusing capacity to alveolar volume; RV: residual volume; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; 6MWT (O<sub>2</sub> Sat): oxygen saturation at the end of six minutes walk test; 6MWT (Final Borg Dyspnea): Modified Borg scale for dyspnea at the end of six minutes walk test; 6MWT (Final HR): heart rate at the end of six minutes walk test; 6MWT (distance/meters): distance traveled at the end of six minutes walk test.

\* Before singing program.

\*\* After singing program.

**Table 2** QoL questionnaires before and after the program.

	Patient 1	Patient 2		Patient 3		Patient 4		
Gender/age	Male/68	Female/50		Male/68		Female/42		
Supplementary oxygen?	No	Yes		No		Yes		
Disease/stage	COPD/GOLD III		COPD/GOLD IV		COPD/GOLD IV		COPD/GOLD III	
Measurements	Patient 1		Patient 2		Patient 3		Patient 4	
	BSP <sup>*</sup>	ASP <sup>**</sup>	BSP	ASP	BSP	ASP	BSP	ASP
SGRQ	19	17	22	27	41	49	44	40
CAT	22	19	14	16	22	23	10	25
EuroQoL	7	8	7	8	11	9	28	10
mMRC	1	1	2	2	4	3	2	3
HADS anxiety	7	6	7	7	3	4	10	10
HADS depression	3	1	4	6	2	6	8	5
LCADL	13	17	21	22	19	26	36	33

SGRQ: St. George's Respiratory Questionnaire; CAT: COPD Assessment Test; EuroQoL: questionnaire to measure health status; mMRC: Modified Medical Research Council Dyspnea Scale; HADS Anxiety: Hospital Anxiety and Depression Scale, punctuation for anxiety; HADS Depression: Hospital Anxiety and Depression Scale, punctuation for Depression; LCADL: London Chest Activity of Daily Living Scale.

\* Before singing program.

\*\* After singing program.

#### Questions

1. Do you think that singing added some benefit to pulmonary rehabilitation? If yes, explain.
2. Did singing lessons were a positive experience?
3. Did singing lessons were a nice experience?
4. Do you think that singing lessons added some benefit to your effort capacity?
5. Do you think that singing lessons added some benefit to your dyspnoea?
6. Do you think that singing lessons added some benefit to your breathing control?
7. Do you think that singing lessons added some benefit to your life satisfaction?
8. What do you think was more important (put in order):
  - the group spending time together
  - the warm up exercises
  - the singing exercises
  - the songs
  - the music
  - the professor
9. Do you sing more at home now?
10. Do you go out more now?
11. Do you think singing lessons improved your self confidence?
12. Do you think singing lessons added some benefit to your anxiety ?
13. Do you think singing lessons had some negative outcome?

**Figure 1** Questionnaire drawn up by the researchers.

All patients said that the project should be continued and expanded.

The present data<sup>2,4</sup> and this study suggest that singing does produce specific benefits and that participation in singing classes should be encouraged where these are available.

## Acknowledgements

We extend our thanks to the singing teacher Vitor Manuel da Silva Sousa for making himself so available and his help in building, implementing and finalizing this project, which otherwise would not have been achieved.

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<http://dx.doi.org/10.1016/j.rppneu.2014.02.009>

## Pleural adenosine deaminase in the diagnostic workup of tuberculous pleural effusion



## Adenosina deaminase do líquido pleural na abordagem diagnóstica do derrame pleural tuberculoso

To the Editor,

Adenosine deaminase (ADA) has been promoted as a quick, efficient and cost-effective method in the diagnosis of tuberculous effusions.<sup>1</sup> However, the predictive parameters of ADA, in the diagnostic workup of tuberculous effusions, depend on the prevalence of the disease in the population<sup>2</sup> and no such analysis has been published in Portugal, a country of intermediate tuberculosis (TB) incidence (25.9 per 100,000 in 2010).<sup>3</sup>

In response to this situation, we carried out a cross-sectional analysis over a 4-year period, beginning in January 2006, in which we evaluated pleural fluid results from all patients admitted to our department with a pleural effusion of unknown etiology. Only the results obtained from the first thoracocentesis were included and samples from empyema were excluded from our analysis. Pleural ADA was measured using Giusti's colorimetric method. Mann-Whitney test was performed to compare medians and a Receiver Operating Curve (ROC) was used to determine the predictive parameters of different cutoffs. Prism 6 from Graphpad Software was used for the statistical analysis.

A total of 107 pleural samples were analyzed, including TB ( $n=20$ ), malignant ( $n=54$ ), parapneumonic ( $n=20$ ) and

idiopathic ( $n=13$ ) effusions. Of the 107 patients, 57.9% were males, median age was 72.5 (interquartile range: 59.7; 80.2) and all the patients were of European ethnicity. TB pleural effusions were found to have the highest median ADA value (98.55 U/L), which were significantly higher than malignant effusions (17.99 U/L) ( $p < 0.0001$ ) – the group with second highest median ADA value. Using the ROC curve we found that an ADA cutoff of 40.5 U/L had the best performance in the diagnosis of pleural TB (see Table 1), with a sensitivity of 95%, specificity of 91.55%, positive predictive value (PPV) of 73.08% and negative predictive value (NPV) of 98.77%. Seven nontuberculous exudates (8.0%) reached the diagnostic cutoff. Using a  $>50\%$  lymphocyte count criteria in the diagnostic workup, only 4.5% nontuberculous exudates were misclassified – 2 malignant (plasmacytoma and lymphoma) and 2 parapneumonic. The association of these two criteria increased specificity (95.40%) and PPV (82.61%). Using an ADA cutoff level of 74.6 U/L and the  $>50\%$  lymphocyte criteria further increased specificity (98.85%) and PPV (93.75%), and only one (1.1%) nontuberculous exudate was misclassified.

The diagnosis of tuberculous pleural effusion is a common diagnostic challenge due to low mycobacterial detection rates and to the frequent need for invasive, sometimes technically difficult, operator dependent techniques like the pleural biopsy or thoracoscopy.<sup>4</sup> In this context, a rational interpretation of pleural fluid characteristics, particularly ADA level and differential leukocyte count, is essential to the diagnostic workup. In our research, an ADA level  $< 40$  U/L can virtually exclude pleural TB with a NPV of 98.7%, while an ADA level  $> 74.6$  U/L with  $>50\%$  lymphocyte has a very high PPV of 93.75 and can thus be used to safely confirm pleural TB with a very small error rate of 1.1%. The