Pulmonary rehabilitation is effective in patients with tuberculosis pulmonary sequelae

To the Editor:

We read with interest the study reported by Collin *et al.* [1], who carried out a survey on organisation and priorities of national tuberculosis (TB) programmes in Europe. With an estimated annual incidence of 10 million cases, TB is considered one of the three global infectious disease priorities, together with HIV/AIDS and malaria. However, TB incidence has significantly declined in the general European population during the past two decades, with a relative increase in vulnerable groups [2, 3].

Traditional TB control is focused on the rapid diagnosis and effective treatment of infectious cases, in order to break the transmission chain, and to cure individual patients. As TB mainly affects low income countries, little research has been conducted to determine whether medical interventions should be considered complete when a patient is "successfully treated" [4], or if potential sequelae should be investigated and pulmonary rehabilitation (PR) performed.

Although mainly focused on chronic obstructive pulmonary disease (COPD), the American Thoracic Society (ATS)/European Respiratory Society (ERS) rehabilitation guidelines discuss the potential usefulness of PR in other respiratory diseases. TB is not mentioned, although recent evidence shows that obstructive and/or restrictive functional sequelae could occur, potentially affecting quality of life (QoL) [5, 6]. To date, no guidance on indications and procedures for TB sequelae is available [5].

We retrospectively investigated if patients with sequelae detected after anti-TB treatment had any benefits from PR in a low TB incidence setting.

Patients with a history of pulmonary TB and successful treatment, admitted between 2004 and 2017 in the PR reference centre of Tradate, Italy, were selected for the study. The institutional ethical committee approved the study (2215 CE, June 19, 2018).

Only patients with clinical stability and able to perform >80% of the training sessions with a physiotherapist, as well as 6-min walking test (6MWT) before and after PR, were selected. The following information was collected:

1) Clinical data (*i.e.* anthropometric data, medical history, comorbidities and concomitant medications);
2) Lung function tests based on ATS guidelines at admission and pre-discharge [7], using a body plethysmograph (Masterlab Body; Jaeger, Würzburg, Germany) and ERS predicted values [8];
3) Diffusing capacity of the lung for carbon monoxide according to the ATS/ERS guidelines [9] (MasterScreen PFT System; Jaeger, VIASYS Healthcare, Hoechberg, Germany);
4) Arterial blood gases from radial artery (ABL 820 Radiometer Medical, Brønshøj, Denmark) in patients breathing room air in the sitting position for at least 20 min;
5) Overnight oximetry monitoring (Nonin Handheld 8500; Nonin, Tilburg, the Netherlands);
6) 6MWT;
7) Symptoms (Borg dyspnoea and fatigue scores before and after the 6MWT).

Patients underwent a comprehensive 3-week PR programme including: specialist nurse training (inhalation techniques and/or oxygen-therapy when prescribed); 18 aerobic-training sessions by cycle ergometer supervised by a respiratory therapist (five sessions per week, 30 min each: 5 min warm-up, 20 min training

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The majority of patients completing anti-tuberculosis treatment have sequelae and benefit from pulmonary rehabilitation http://ow.ly/WyOH30nFQLV

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TABLE 1 Clinical characteristics and pulmonary function in patients admitted between January 1, 2004 and December 31, 2017

Clinical characteristics						
COPD diagnosis	23/43 (54.8%)					
Respiratory failure	18/43 (41.9%)					
Asthma	8/43 (18.6%)					
Bronchiectasis	13/43 (30.2%)					
Interstitial lung disease	2/43 (4.7%)					
Silicosis	1/43 (2.3%)					
OSA	16/43 (37.2%)					
Emphysema	17/43 (39.5%)					
Chronic heart disease	18/43 (41.9%)					
Arterial hypertension	19/43 (44.2%)					
Diabetes	7/43 (16.3%)					
Neoplasia	14/43 (32.6%)					
Chronic hepatitis B	1/43 (2.3%)					
Chronic hepatitis C	4/43 (9.3%)					
Lung surgery						
Therapeutic pneumothorax	6/43 (14.0%)					
Other lung surgical procedures	3/43 (7.0%)					
Patients with airflow obstruction (n=29)	**Nonsmokers (n=6)**	**Smokers (n=23)**	**p-value**			
Respiratory function						
FEV_1 L	0.8 (0.8–0.9)	1.1 (0.9–1.6)	0.03			
FEV_1 %	46.0±11.1	48.3±17.2	0.73			
FVC L	1.7±0.8	2.7±0.9	0.004			
FVC %	69.2±15.1	78.5±18.6	0.20			
FEV_1/FVC	52.1±12.7	45.5±12.7	0.21			
RV %	165.6±37.0	142.7±37.7	0.17			
D_{LCO} %		60.8±22.4				
6MWT						
Distance covered m	364.1±144.1	375.1±121.5	0.83			
Distance % predicted	81.7±31.4	81.5±24.4	0.99			
S_{pO_2} baseline	94.0±1.1	94.2±1.6	0.74			
S_{pO_2} average	90.6±3.9	89.3±3.8	0.40			
S_{pO_2} min	87.8±5.5	86.3±5.1	0.47			
Pulmonary function	**Patients with impaired respiratory pattern# (n=34)**			**Patients with normal respiratory pattern (n=9)**		
	Pre-pulmonary rehabilitation	**Post-pulmonary rehabilitation**	**p-value**	**Pre-pulmonary rehabilitation**	**Post-pulmonary rehabilitation**	**p-value**
Lung function tests						
FEV_1 L	1 (0.8–1.3)	1.1 (0.9–1.4)	<0.0001	2.3 (1.9–2.6)	2.5 (1.9–2.9)	0.21
FEV_1 %	48.3 (38.3–59.6)	53.4 (44.0–65.0)	<0.0001	85.2 (81.0–95.4)	98.1 (85.7–105.6)	0.21
FVC L	2.3±0.9	2.4±0.9	0.09	2.5±0.7	2.8±0.8	0.08
FVC %	73.7±17.7	78.8±16.9	0.003	94.6±16.7	89.5±37.3	0.70
FEV_1/FVC	51.4±15.1	52.4±14.8	0.23	77.6±6.2	81.1±13.8	0.41

Continued

TABLE 1 Continued

Pulmonary function	Patients with impaired respiratory pattern# (n=34)			Patients with normal respiratory pattern (n=9)		
	Pre-pulmonary rehabilitation	Post-pulmonary rehabilitation	p-value	Pre-pulmonary rehabilitation	Post-pulmonary rehabilitation	p-value
RV %	137.1 (111.9–178.9)	147 (106.3–173.6)	0.24	113.9 (92.7–132.6)	106.9 (100.8–124.8)	1.0
D_{LCO} %	60.1±20.5					
BGA						
P_{aO_2}	66.2±7.3	70.9±7.2	0.009	66.3±5.4	84.9±0.8	0.12
P_{aCO_2}	41.6±6.4	39.9±6.0	0.10	39.6±1.0	34.6±2.8	0.16
PH	7.4±0.0	7.4±0.0	0.80	7.5±0.0	7.4±0.0	0.03
S_{aO_2}	94.3 (92.8–95.5)	95.1 (93.1–96.2)	0.01	95.5 (94.1–96.2)	96.8 (96.7–96.8)	0.18
F_{IO_2}	21 (21–21)	21 (21–21)	0.32			
6MWT						
Distance covered m	371±127.5	406±133.5	0.01	407±82.2	466±62.5	0.05
Distance % predicted	82.1±27.5	89.7±28.3	0.01	86.0±20.3	98.4±19.2	0.05
HR baseline	80.3±9.9	81.9±13.6	0.43	75.0±10.2	78.9±9.1	0.40
HR average	102.1±12.6	105.9±13.0	0.03	100.4±7.4	100.5±10.2	0.97
HR max	112.9±14.5	116.7±14.5	0.08	111.5±11.9	111.6±15.1	0.98
S_{pO_2} baseline	94.3±1.7	94.8±1.7	0.10	95.8±0.9	95.9±1.0	0.81
S_{pO_2} average	90 (87–94)	91.5 (88.5–94.5)	0.05	95 (94–96)	96 (94.5–96.0)	1.0
S_{pO_2} min	88 (83–91)	89 (86.0–92.5)	0.05	94 (93–95)	94 (92–95)	0.89
Modified Borg dyspnoea baseline	0 (0–2)	0 (0–1)	0.79	0 (0–1)	0 (0–2)	0.68
Modified Borg dyspnoea final	4 (2–5)	3 (0.5–4.0)	0.006	4 (1–5)	2.5 (1.5–4.5)	0.14
Modified Borg fatigue baseline	0 (0–1)	0 (0.0–0.8)	0.77	0.5 (0–2)	0.8 (0.0–1.5)	0.94
Modified Borg fatigue final	3 (2–5)	2.5 (0–4)	0.009	1 (0–7)	4 (0.5–4.5)	0.77
Spontaneous walking S_{pO_2}						
Initial F_{IO_2}	21 (21–32)	26 (21–30)	0.40			
S_{pO_2} baseline	93.2±1.3	95.2±1.3	0.10			
S_{pO_2} average	89.5 (88.7–91.5)	91.5 (90.7–93.2)	0.04			
S_{pO_2} min	86 (84–89)	89 (87–90)	0.03			

Data are presented as mean±SD or median (interquartile range), unless otherwise stated, COPD: chronic obstructive pulmonary disease; OSA: obstructive sleep apnoea; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; RV: residual volume; D_{LCO}: diffusing capacity of the lung for carbon monoxide; 6MWT: 6-min walk test; S_{pO_2}: peripheral capillary oxygen saturation; BGA: blood gas analysis; P_{aO_2}: partial pressure of arterial oxygen; P_{aCO_2}: partial pressure of arterial carbon dioxide; PH: potential of hydrogen; S_{aO_2}: oxygen saturation in arterial blood; F_{IO_2}: fraction of inspired oxygen: HR: heart rate. #: patients with obstructive or restrictive or mixed pattern.

and 5 min warm-down) at constant load (calculated with Hill equation [10]). Optional PR components included: inspiratory muscle conditioning (using a threshold-loading device [4]), breathing exercises, airways clearance, psychological support (three sessions per week), relaxation (five sessions per week) and nutritional counselling (personalised diet). Patients attended two educational group sessions, managed by a respiratory therapist, on lifestyle, physical activity and maintenance programmes.

A pre-discharge evaluation (including lung function tests, blood gases analysis, 6MWT and symptom assessment) was performed at the end of the PR programme. Pre-PR data were compared with post-PR both in patients with and without functional impairment. QoL data pre- and post-PR was available for two patients only and, then, no data were provided.

Out of 111 patients with previous history of pulmonary TB, admitted between 2004 and 2017, 43 (39%) met the criteria required to be included in the study (*i.e.* >80% of the training sessions and 6MWT before and after PR), whereas 68 (31%) were excluded because data on 6MWT both before or after PR were not available.

43 cases (24 males, median age 75 years) were selected; 54.8% and 41.9% had a diagnosis of COPD and respiratory failure, respectively; 23.3% required long-term oxygen therapy and 31% underwent noninvasive mechanical ventilation. 46.5% were former and 11.6% current smokers. 11 (25.6%), five (11.6%), and 18 (41.9%) cases had an obstructive, restrictive and mixed pattern respectively, whereas nine (20.9%) had normal spirometry (table 1).

Respiratory function was assessed in 20 smokers *versus* nine nonsmokers with airflow obstruction: no major differences were found, with the only exception of forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) absolute values (table 1).

Subjects with impaired lung function showed a significant improvement in 6-min walking distance ($p=0.01$), in final Borg dyspnoea ($p=0.006$) and fatigue ($p=0.009$) scores, as well as of FEV_1 ($p<0.0001$), FVC ($p=0.003$), mean partial pressure of arterial oxygen ($p=0.009$), and median oxygen saturation in arterial blood ($p=0.01$).

Although several co-factors might have contributed, our findings support those of a previous study [6] showing that airway obstruction in patients with a history of TB was not associated with smoking history.

No pre- *versus* post-PR changes were observed among patients with normal respiratory pattern.

Preliminary data suggest that PR is effective in patients with a previous history of TB and with lung function impairment. As more and more countries can potentially manage PR in patients with TB sequelae, well-designed prospective studies are necessary to identify patients needing clinical assessment, as well as to clarify which PR models can be implemented to ensure a functional recovery.

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