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Impact of pulmonary rehabilitation in patients with interstitial lung disease in Singapore

Dear Editor,

Interstitial lung diseases (ILD) encompass a heterogeneous group of lung parenchymal disorders.[1] ILD-related symptoms impact significantly on quality of life (QoL).[2] Dyspnoea is the most important factor determining health-related QoL in ILD; contributing factors include reduced exercise capacity, loss of mental well-being and social isolation.[3]

Pulmonary rehabilitation (PR) in ILD can improve exercise capacity without major adverse outcomes.[4,5] The King's Brief Interstitial Lung Disease (KBILD) questionnaire was developed by Birring et al. as an ILD-specific tool for patient assessment, and measures performance across psychological; breathlessness and activity; and chest symptoms domains.[6] The KBILD questionnaire has been validated in various European settings.[7] In Singapore, data on PR are scarce and no disease-specific instrument for ILD has been studied. We describe a single-centre, prospective, observational study examining characteristics and outcomes of ILD patients who have and have not undergone PR. We also describe the use of the KBILD questionnaire in measuring patient-reported outcomes. We obtained the KBILD and permission for its use from Professor Birring in October 2018.

An ILD clinic was established in Singapore General Hospital in 2012. Patients evaluated at this clinic who were aged above 21 years old, diagnosed with any ILD of any severity, and willing to give informed consent were enrolled into a prospective database for our study that was approved by institutional review board.

The KBILD was first administered in English to all ILD patients seen on either their first or second visit after 17 October 2018. Patients who could not self-administer the KBILD in English were assisted by a translator. The same translator would assist during repeat visits. Follow-up intervals and management decisions were decided by the managing physician. All patients were offered PR. Patients who agreed to PR were assessed by a physiotherapist and a 6-minute walk test (6MWT) was conducted if there were no contraindications. Thereafter, patients were assigned to twice-weekly outpatient PR sessions for 6–8 weeks or home-based exercises. A repeat KBILD questionnaire was administered at subsequent clinic visits. Patients who completed outpatient PR underwent a repeat 6MWT. The primary outcome measure was the KBILD score. Secondary outcome measures included 6MWT distances for patients who completed outpatient PR. Statistical analysis was performed using Stata version 15.0 (StataCorp LLC, College Station, US).

From 17 October 2018 to 31 December 2019, repeat KBILD scores were obtained for 74 patients; 7 who did not provide consent were excluded. Participants' mean age was 65.8 years and 58.1% were men. There were 86.5% patients having dyspnoea at presentation and the median modified medical research council (MMRC) score was 1. The characteristics and KBILD scores of these subjects are described in Table 1.

There were 19 patients who completed at least 1 session of PR. Of these, 8 completed 6–8 weeks of twice-weekly outpatient PR and 55 patients declined PR. In the 19 patients who attended PR, KBILD psychological, dyspnoea and chest symptoms scores improved by a mean of 7.3, 8.1 and 1.5 points, respectively. The differences in the change in KBILD scores between visits for patients who participated in PR and patients who declined were statistically significant.

As the PR and non-PR groups were unbalanced, 19 subjects who underwent PR were randomly matched by sex for 19 controls in a case-control model. There continued to be no significant differences between cases and controls in terms of demographics, comorbidities, pulmonary function, diagnoses or treatments received. The 8 patients who completed the 6MWT before and after PR showed a mean improvement in the 6MWT distance of 45.6m.

To the best of our knowledge, we describe the first Singapore study in ILD patients where PR improves exercise tolerance, symptoms, and QoL measured, using a patient-reported instrument. The minimal clinically important difference (MCID) in the KBILD is a change of 5 points in the total score, and 6, 7 and 11 points for psychological, breathlessness, and chest symptoms domains, respectively.[8] Our patients who participated in PR showed an improvement in total, dyspnoea and psychological symptoms scores that were greater than the MCID. Patients who underwent a 6MWT before and after PR demonstrated an improvement in 6MWT distances that was greater than the MCID, which has been established to be 24–45m.[9] The use of systemic corticosteroids, steroid-

Table 1. Clinical characteristics, lung function and KBILD scores of patients followed up at an interstitial lung disease clinic in Singapore, grouped by participation in pulmonary rehabilitation

	All n=74	Declined to participate in PR n=55	Participated in PR n=19	*P* value
Demographics				
Age, mean (SD), years	65.8 (10.6)	64.4 (10.7)	69.9 (9.3)	0.05
Male sex, no. (%)	43 (58.1)	29 (52.7)	14 (73.7)	0.110
Race, no. (%)				
Chinese	59 (79.7)	45 (81.8)	14 (73.7)	0.292
Malay	6 (8.1)	5 (9.1)	1 (5.3)	
Indian	8 (10.8)	5 (9.1)	3 (15.8)	
Others	1 (1.4)	0 (0.0)	1 (5.3)	
Non-smoker, no. (%)	42 (56.8)	34 (61.8)	8 (42.1)	0.226
Ex-smoker, no. (%)	21 (28.4)	13 (23.6)	8 (42.1)	
Smoker, no. (%)	11 (14.9)	8 (14.6)	3 (15.8)	
Symptoms at baseline				
Cough, no. (%)				
Not at all/ rarely	24 (32.4)	20 (36.4)	4 (21.1)	0.489
Occasionally but not bothersome	31 (41.9)	21 (38.2)	10 (52.6)	
Most days	19 (25.7)	14 (25.6)	5 (26.3)	
Severe and interferes with activity	0 (0)	0 (0)	0 (0)	
Dyspnoea, no. (%)	64 (86.5)	45 (81.8)	19 (100.0)	0.056
MMRC score, no. (%)				
0	10 (14.3)	8 (15.7)	2 (10.5)	0.403
1	35 (54.7)	26 (57.8)	9 (47.4)	
2	14 (21.9)	8 (17.8)	6 (31.6)	
3	4 (6.3)	3 (6.7)	1 (5.3)	
4	1 (1.4)	0 (0)	1 (5.3)	
MMRC, median (IQR)	1 (0,3)	1 (0,3)	1 (1,2)	0.314
Comorbidities				
Diabetes mellitus, no. (%)	23 (31.1)	16 (29.1)	7 (36.8)	0.572
Hypertension, no. (%)	34 (46.0)	22 (40.0)	12 (63.2)	0.110
Hyperlipidaemia, no. (%)	43 (58.1)	31 (56.4)	12 (63.2)	0.788
Ischaemic heart disease, no. (%)	17 (23.0)	11 (12.6)	6 (31.6)	0.349
Asthma, no. (%)	2 (2.5)	2 (3.6)	0 (0)	0.399
Pulmonary physiology				
Baseline FVC, mean (SD), L	2.18 (0.61)	2.19 (0.61)	2.15 (0.61)	0.793
Baseline FVC % predicted, mean (SD)	71.5 (15.0)	71.4 (14.8)	71.5 (16.1)	0.993
Baseline FEV1, mean (SD), L	1.89 (0.50)	1.90 (0.51)	1.88 (0.50)	0.867
Baseline FEV1 % predicted, mean (SD)	86.8 (18.7)	86.4 (18.9)	87.6 (18.5)	0.826
Baseline DLCO, mean (SD), mM/min/kPa[a]	4.93 (2.23)	5.05 (2.34)	4.55 (1.86)	0.443
Baseline DLCO, % predicted, mean (SD)[a]	60.0 (15.0)	61.0 (15.8)	57.3 (12.5)	0.395
Baseline TLC, mean (SD), L	3.80 (0.83)	3.81 (0.86)	3.76 (0.75)	0.848
Baseline TLC % predicted, mean (SD)[b]	79.1 (15.9)	80.2 (16.7)	75.3 (12.5)	0.310

CTD-ILD: connective tissue disease related interstitial lung disease; DLCO: diffusing capacity for carbon monoxide; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; HP: hypersensitivity pneumonitis; LAM: lymphangioleiomyomatosis; MMRC: minimal clinically important difference; PR: pulmonary rehabilitation; SD: standard deviation; TLC: total lung capacity

[a] Missing data: 10

[b] Missing data: 14

Table 1. Clinical characteristics, lung function and KBILD scores of patients followed up at an interstitial lung disease clinic in Singapore, grouped by participation in pulmonary rehabilitation (Cont'd)

	All n=74	Declined to participate in PR n=55	Participated in PR n=19	*P* value
Diagnostic procedures				
Bronchoalveolar lavage, no. (%)	28 (37.8)	22 (40.0)	6 (31.6)	0.591
Transbronchial lung biopsy, no. (%)	12 (42.9)	10 (45.5)	2 (33.3)	0.595
Cryobiopsy, no. (%)	1 (8.3)	1 (10.0)	0 (0)	1.00
Surgical lung biopsy, no. (%)	4 (5.4)	3 (5.5)	1 (5.3)	1.00
Final diagnosis				
Idiopathic interstitial pneumonia, no. (%) CTD-ILD HP LAM Unclassifiable	44 (59.5) 24 (32.4) 2 (2.7) 2 (2.7) 2 (2.7)	28 (50.9) 21 (38.2) 2 (3.6) 2 (3.6) 2 (3.6)	16 (84.2) 3 (15.8) 0 (0) 0 (0) 0 (0)	0.209
Ongoing treatments				
Corticosteroids, no. (%)	30 (40.5)	23 (41.8)	7 (36.8)	0.460
Steroid sparing agents, no. (%)	24 (32.4)	18 (32.7)	6 (31.6)	0.582
Opioids, no. (%)	5 (6.8)	3 (5.5)	2 (10.5)	0.382
Long-term oxygen therapy, no. (%)	7 (9.5)	3 (5.5)	4 (21.1)	0.067
KBILD scores				
Baseline total score, mean (SD)	64.1 (14.5)	71.1 (9.4)	43.9 (2.8)	<0.001
Follow-up total score, mean (SD)	64.1 (4.8)	64.9 (5.0)	61.5 (3.0)	0.006
Change in total score, mean (SD)	-0.1 (14.1)	-6.1 (10.9)	17.5 (3.8)	<0.001
Baseline dyspnoea scores, mean (SD) (Questions 1, 4, 11, 13)	12.7 (4.2)	14.9 (2.1)	6.3 (1.1)	<0.001
Follow-up dyspnoea scores, mean (SD) (Questions 1, 4, 11, 13)	13.6 (2.8)	12.9 (2.9)	13.6 (2.2)	0.305
Change in dyspnoea scores, mean (SD) (Questions 1, 4, 11, 13)	0.4 (5.4)	-2.0 (3.8)	7.3 (2.7)	<0.001
Baseline psychological scores, mean (SD) (Questions 3, 5, 6, 8, 10, 12, 14)	33.1 (7.4)	36.6 (4.9)	22.9 (2.2)	<0.001
Follow-up psychological scores, mean (SD) (Questions 3, 5, 6, 8, 10, 12, 14)	32.8 (3.0)	33.4 (3.2)	31.1 (1.7)	0.003
Change in psychological scores, mean (SD)	-0.3 (7.2)	-3.2 (5.9)	8.1 (2.6)	<0.001
Baseline chest symptoms scores, mean (SD) (Questions 2, 7, 9)	15.8 (3.6)	17.1 (3.1)	11.9 (1.4)	0.003
Follow-up chest symptoms scores, mean (SD) (Questions 2, 7, 9)	15.0 (3.0)	15.5 (3.0)	13.4 (2.6)	0.008
Change in chest symptoms scores, mean (SD)	-0.8 (3.9)	-1.6 (4.0)	1.5 (2.7)	0.002

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sparing agents, opioids and long-term oxygen did not differ significantly between study arms, suggesting that observed differences in KBILD scores and 6MWT distances were not due to differences in therapies received. Our study highlighted that there are measurable and important benefits for ILD patients who undergo PR. The study showed that while the KBILD was validated in a culturally distinct population, it remained robust and sensitive to changes in the health status of ILD patients.

There are limitations to our research. Firstly, as a single-centre study, the small sample sizes limit the external applicability of our findings. Secondly, our study did not address barriers and facilitators for PR uptake. A single-centre study within a district general hospital showed that a lack of awareness and low perceived benefits were important barriers to PR,[10] making PR uptake an area for our future research. Thirdly, the KBILD was conceptualised as a self-administered instrument, but some of our patients completed it with assistance from a translator. As the KBILD has yet to be validated for local languages, the current study would not have been possible without translators. A literature review conducted did not identify prior local studies describing the use of KBILD or Saint George's Respiratory Questionnaire in ILD patients. We had chosen the KBILD as it was shorter and easier to administer. Finally, enrolment into PR was low, which may have introduced selection bias, although symptom management was important in improving the QoL of ILD patients. Our study suggests that PR produces measurable improvements based on a patient-reported instrument, and encourages clinicians to continue to refer ILD patients for PR.

Patients who participated in PR demonstrated improvements in KBILD scores and 6MWT distances, consistent with published observations that PR improves QoL and exercise capacity. The KBILD is a robust instrument that has been validated in various European settings. Efforts should be taken to translate and validate it for use in Singapore.

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