

Exercise training in interstitial lung disease: lumping or splitting?

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In 1952, Alvan Barach, a New York physician, wrote, 'It may seem unusual perhaps to suggest exercise to these breathless people, but in fact it is one of the ways by which they can restore physical fitness'.¹ Since then, pulmonary rehabilitation (PR) has proven its worth as a high-value treatment for COPD,² improving exercise capacity, quality of life and muscle strength while also reducing hospital admissions.^{3–6} The usefulness of PR in other respiratory conditions, including interstitial lung disease (ILD), has been assumed because of the shared presence of deconditioning, fatigue, dyspnoea, exercise intolerance and impaired quality of life, factors known to be amenable to exercise training.

ILD includes a heterogeneous group of disorders, with severity and prognosis that vary both between subtypes and at an individual level. The basis of exercise training as a treatment modality may therefore be less straightforward than in other pulmonary disorders. People with COPD often present with a long history of physical inactivity and activity levels are typically reduced even in early disease.⁷ Patients with ILD may have a shorter period prior to presentation and a more rapid trajectory of lung function decline than other chronic lung conditions with less time for deconditioning to develop. In addition, some will be receiving systemic corticosteroid therapy known to have important effects on muscular function⁸ and important systemic effects may be present, including rheumatological conditions, direct muscle involvement in connective tissue diseases and pulmonary hypertension limiting cardiac output. These all may limit the potential for gains in function.⁹

The research literature to support PR in ILD is relatively modest, with only weak recommendations in international guidelines for considering exercise training in ILD.^{10–11} There remain questions about

the value of exercise training-based interventions in ILD in relation to both disease aetiology and severity. In *Thorax*, Dowman *et al*¹² report a randomised, controlled, assessor-blinded trial assessing the effectiveness of PR in 142 stable patients with exertional dyspnoea and a variety of ILD aetiologies. These were considered in three specific categories—asbestosis (n=22), idiopathic pulmonary fibrosis (IPF) (n=61) and connective tissue disease-related (CTD-ILD) (n=23). Participants were randomised to receive a supervised 8 week exercise training programme, including aerobic and resistance training alongside the educational component of PR, or usual care including weekly telephone support. Six-minute walking distance, quality of life and strength measures were performed at baseline, 9 weeks and 6 months.

Following the PR programme, exercise capacity and health status had improved compared with usual care, though whole group improvement in 6 min walking distance, the primary endpoint, was below the minimum clinically important difference for ILD, suggesting that benefits of PR in terms of exercise capacity in this group are relatively modest. By 6 months, measures in the PR arm had returned to baseline though the control arm had deteriorated further with a 21 m difference in exercise capacity persisting. The use of a priori categories allows subgroup analysis and suggests heterogeneity in the response to exercise training in distinct ILD subtypes. Thus, differences in exercise capacity compared with controls were most notable in the asbestosis and IPF groups but were limited in the CTD-ILD group, where both treatment arms displayed a similar small increase in walk distance. PR did improve health status in the CTD-ILD group. Given the relatively small sample size, it is important not to overgeneralise from these comparative findings. However, they do suggest that lumping ILD together in trials to evaluate PR runs a risk of obscuring effects in specific populations. Patients, of course, have the disease that they have, so the comparisons between conditions are of limited relevance for guiding clinical practice.

As in other respiratory diseases, Dowman *et al*¹² found that baseline

clinical variables were poorly predictive of the response to exercise training, and this work provides no basis for using pulmonary function markers of severity to exclude individuals with ILD from exercise training. In fact, those most limited at baseline tended to have the greatest short-term benefit from PR, a pattern that is also recognised in COPD¹³ and has been noted previously in ILD.¹⁴ On the other hand, those with the best preserved physiology were more likely to have long-term gains in exercise capacity. This, and the overall shorter duration of benefit, probably reflects the fact that progression of the underlying lung disease is a more powerful factor in functional capacity in ILD than in COPD.

Naturally those individuals able to progress their exercise intensity during the PR programme gained the greatest benefit. Whether this lack of progression is simply a marker of disease severity or a modifiable factor should be the focus of future work. It is important to recall that those with more advanced ILD often have few treatment options and exercise training may provide one modality to preserve the individual's current level of function to avoid future decline. In such a situation, realistic expectations should be set for the expected gains and what should be considered to be programme 'success'. In this study, the asbestosis group in particular showed a significant decline in exercise capacity with time, which was avoided by the provision of exercise training.

Interestingly there was no significant improvement in quadriceps strength following exercise training in any ILD subtype studied. This raises questions about the training intensity provided, which may have been insufficient, and may need to be tailored to this particular patient group who were entered into a standardised PR programme where patients with COPD likely make up the majority of participants. Also lacking were measures of physical activity, which are known to be reduced in ILD.^{15–16} Although limited data are available, evidence exists to suggest that this parameter is responsive to exercise training in this population.^{17–18} Interestingly, although impaired quadriceps strength and endurance in ILD have been observed, these parameters were not independently associated with exercise capacity, which was determined by lung function measures.¹⁹ The drop-out rate of the study was reassuringly similar to that seen in other chronic lung diseases and we should avoid therapeutic nihilism that patients with a steeper trajectory of decline may not

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adhere to a programme of PR as this did not appear to be the case.

These data support the conclusion that PR should be offered as a standard aspect of care in the management of stable patients with ILD who are limited by their condition. Of note, fewer than half of the individuals screened proceeded to enrolment in the study—predominantly because they declined to participate rather than clinical unsuitability. Whether this was related to the PR programme or a reluctance to participate in research is unclear. The manner in which PR is presented to patients will influence uptake. Clinicians advising patients with ILD can now more confidently recommend PR. The majority of patients enrolled in PR programmes will have COPD, but current British Thoracic Society quality standards for PR²⁰ require that ‘pulmonary rehabilitation programmes accept and enrol patients with functional limitation due to other chronic respiratory diseases (for example bronchiectasis, ILD and asthma) if referred’. Reassuringly, data from the Royal College of Physicians COPD audit confirm that only 6% of programmes in the UK report that they exclusively accept individuals with this diagnosis.²¹

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REFERENCES

- Casaburi R. A brief history of pulmonary rehabilitation. *Respir Care* 2008;53:1185–9.
- Zoumot Z, Jordan S, Hopkinson NS. Emphysema: time to say farewell to therapeutic nihilism. *Thorax* 2014;69:973–5.
- McCarthy B, Casey D, Devane D, *et al.* Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2015;(2):CD003793.
- Nici L, Donner C, Wouters E, *et al.* American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med* 2006;173:1390–413.
- Dodd JW, Hogg L, Nolan J, *et al.* The COPD assessment test (CAT): response to pulmonary rehabilitation. A multicentre, prospective study. *Thorax* 2011;66:425–9.
- Griffiths TL, Burr ML, Campbell IA, *et al.* Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *Lancet* 2000;355:362–8.
- Shrikrishna D, Patel M, Tanner RJ, *et al.* Quadriceps wasting and physical inactivity in patients with COPD. *Eur Respir J* 2012;40:1115–22.
- Hanada M, Sakamoto N, Ishimatsu Y, *et al.* Effect of long-term treatment with corticosteroids on skeletal muscle strength, functional exercise capacity and health status in patients with interstitial lung disease. *Respirology* 2016;21:1088–93.
- Hansen JE, Wasserman K. Pathophysiology of activity limitation in patients with interstitial lung disease. *Chest* 1996;109:1566–76.
- Bradley B, Branley HM, Egan JJ, *et al.* Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. *Thorax* 2008;63:v1–58.
- Raghu G, Collard HR, Egan JJ, *et al.* An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011;183:788–824.
- Dowman LM, McDonald CF, Hill CJ, *et al.* The evidence of benefits of exercise training in interstitial lung disease: a randomised controlled trial. *Thorax* 2017;72:610–9. doi:10.1136/thoraxjnl-2016-208638.
- Boutou AK, Tanner RJ, Lord VM, *et al.* An evaluation of factors associated with completion and benefit from pulmonary rehabilitation in COPD. *BMJ Open Respir Res* 2014;1:e000051.
- Ferreira A, Garvey C, Connors GL, *et al.* Pulmonary rehabilitation in interstitial lung disease: benefits and predictors of response. *Chest* 2009;135:442–7.
- Dale MT, McKeough ZJ, Munoz PA, *et al.* Physical activity in people with asbestos related pleural disease and dust-related interstitial lung disease: An observational study. *Chron Respir Dis* 2015;12:291–8.
- Nakayama M, Bando M, Araki K, *et al.* Physical activity in patients with idiopathic pulmonary fibrosis. *Respirology* 2015;20:640–6.
- Dale MT, McKeough ZJ, Munoz PA, *et al.* Exercise training for asbestos-related and other dust-related respiratory diseases: a randomised controlled trial. *BMC Pulm Med* 2014;14:180.
- Ryerson CJ, Cayou F, Topp F, *et al.* Pulmonary rehabilitation improves long-term outcomes in interstitial lung disease: a prospective cohort study. *Respir Med* 2014;108:203–10.
- Mendoza L, Gogali A, Shrikrishna D, *et al.* Quadriceps strength and endurance in fibrotic idiopathic interstitial pneumonia. *Respirology* 2014;19:138–43.
- British Thoracic Society. Quality standards for pulmonary rehabilitation in adults. *British Thoracic Society Reports* 2014;6(2):1–29. <https://www.brit-thoracic.org.uk/document-library/clinical-information/pulmonary-rehabilitation/bts-quality-standards-for-pulmonary-rehabilitation-in-adults/> (accessed 28 Jan 2017).
- Royal College of Physicians and British Thoracic Society. *Pulmonary Rehabilitation: Time to breathe better*. London, Royal College of Physicians: Nov 2015. <https://www.rcplondon.ac.uk/projects/outputs/pulmonary-rehabilitation-time-breathe-better> (accessed 28 Jan 2017).