Utility of rehabilitation prior to bronchoscopic lung volume reduction: *post hoc* analysis of the VENT trial

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Pulmonary rehabilitation is an essential tool for patients with severe COPD. Given the only modest improvements in exercise capacity, mandatory requirements for rehabilitation before bronchoscopic lung volume reduction should be reconsidered. https://bit.ly/3Mheiu7

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Abstract

Background and objective Rehabilitation programmes are a valuable treatment modality for patients with COPD to increase exercise capacity and quality of life. The utility of pulmonary rehabilitation prior to bronchoscopic lung volume reduction (BLVR) is unclear.

Methods We performed a *post hoc* analysis of the Valve for Emphysema Palliation Trial (VENT) trial, the first multicentre randomised trial comparing the safety and efficacy of BLVR. Patients completed a pulmonary rehabilitation programme prior to BLVR over 6–10 weeks and maintained by daily practice, consisting of endurance training, strength training and upper/lower limb exercise. Lung function and exercise parameters (6-min walk distance (6MWD)) were assessed before and after rehabilitation and we tried to identify predictors for pulmonary rehabilitation benefit.

Results Lung function and exercise capacity of 403 patients (mean±SD age 63.3±7.4 years, 37.5% female, mean±SD forced expiratory volume in 1 s 30.1±7.6 L) were analysed. Exercise capacity significantly improved from 331.6±98.8 m to 345.6±95.3 m ($p<0.001$) in 6-min walk testing (6MWT), with 40.3% showing clinically meaningful improvements. Patients also experienced less dyspnoea after 6MWT, while pulmonary function parameters did not change significantly overall. Patients with lower exercise capacity at screening (6MWD <250 m) benefited more from pulmonary rehabilitation. The indication and prerequisites for BLVR were still present in all patients after pulmonary rehabilitation.

Conclusion The national mandatory requirements for rehabilitation prior to BLVR, which apply to all COPD patients, should be reconsidered and specified for COPD patients who really benefit.

Introduction

COPD remains a major healthcare issue with a global impact, currently being the fourth leading cause of death worldwide [1]. The high impact of morbidity and mortality associated with COPD includes a significant economic burden, with COPD accounting for >50% of the direct costs of respiratory disease, and an impact on productivity at work and home. At an individual level, the rapid downward spiral of symptom-induced inactivity, muscle deconditioning and subsequent weakness associated with the disease affects quality of life, with reduced social interaction, depression and in many cases death [2]. In its more severe manifestation, emphysema, pathological damage to the lung parenchyma and destruction of elastin leads to air trapping and hyperinflation of the lungs and is the main mechanism of exertional dyspnoea [3, 4].

Medical management of COPD involves multiple strategies, starting with smoking cessation, pulmonary rehabilitation and self-management, vaccination, pharmacological therapy to improve airflow, reduce

symptoms and exacerbations and minimise infections. Oxygen supplementation is required for hypoxaemic patients and long-term noninvasive ventilation is offered to patients with hypercapnia and respiratory failure [1]. Pulmonary rehabilitation programmes improve exercise tolerance, complementing pharmacotherapy, to reverse systemic musculoskeletal dysfunction in severe COPD patients [5]. For patients with advanced emphysema refractory to medical management, the next steps are noninvasive and invasive surgical options in appropriately selected patients. Hyperinflation is addressed by several techniques of lung volume reduction [6–9].

Patients being considered for interventions such as bronchoscopic lung volume reduction (BLVR) or lung volume reduction surgery (LVRS) must be clinically stable to safely undergo the procedure. Clinical trials evaluating BLVR required pulmonary rehabilitation prior to randomisation to maximise function prior to intervention [6, 7]. Currently, health insurance companies worldwide require mandatory pulmonary rehabilitation prior to BLVR, not only with the idea that this may improve the general condition before BLVR as a safety measure, but also to prevent patients from needing interventional therapy after conservative treatment options have been exhausted. Despite this requirement, to our knowledge, there are no data available that prove the benefit of pulmonary rehabilitation before BLVR [10]. This requirement can affect both the timing of the procedure and the willingness to receive this guideline-recommended noninvasive therapy [1]. Furthermore, this creates disparity issues in countries or regions where pulmonary rehabilitation is not easily accessed. Finally, in a setting where pulmonary function may improve following BLVR, enabling more vigorous cardiac and peripheral muscle training, it is unclear whether it is justified to make pulmonary rehabilitation a mandatory prerequisite in the pre-procedural setting.

We evaluated the impact of pulmonary rehabilitation prior to BLVR through a *post hoc* analysis of data from the Valve for Emphysema Palliation Trial (VENT) [7, 11], the first multicentre randomised clinical trial comparing the safety and efficacy of endoscopic lung volume reduction with Zephyr valves in heterogeneous emphysema *versus* medical treatment. All enrolled patients underwent a detailed rehabilitation programme before being randomised to either the treatment or control group.

Methods

A total of 492 patients with severe emphysema were randomised in the study with a United States cohort of 321 patients [7] and a European cohort of 171 patients [11].

The inclusion and exclusion criteria have been published previously [12] and are summarised here: age 40–75 years, diagnosis of heterogeneous emphysema, forced expiratory volume in 1 s (FEV_1) 15–45% predicted, total lung capacity (TLC) >100% pred, residual volume (RV) >150% pred, body mass index (BMI) $\leqslant 31.1\ kg \cdot m^{-2}$ (men) or $\leqslant 32.3\ kg \cdot m^{-2}$ (women), partial pressure of carbon dioxide (P_{aCO_2}) <50 mmHg and partial pressure of oxygen (P_{aO_2}) >45 mmHg on ambient air, and post-rehabilitation 6-min walk distance (6MWD) $\geqslant$140 m. Patients with diffusion capacity of the lung for carbon monoxide (D_{LCO}) <20% pred, presence of giant bullae or α-antitrypsin deficiency, previous thoracotomy, excessive sputum, severe pulmonary hypertension, active infection or unstable cardiac conditions were excluded.

Study design

Patients signed an institutional review board- or ethics committee-approved informed consent form before undergoing the screening evaluations. Prior to randomisation, patients who had not completed pulmonary rehabilitation within the previous 60 days underwent 6–8 weeks of pulmonary rehabilitation and optimised medical management at the discretion of the treating physician within the context of the Global Initiative for Chronic Obstructive Lung Disease guidelines [1]. Patients who had recently (within the last 60 days) completed pulmonary rehabilitation and provided documentation of the rehabilitation programme were eligible for baseline testing.

The rehabilitation programme offered two visits at the rehabilitation centre per week with a minimum attendance requirement of 75% and included lower and upper limb endurance training as well as a lower and upper limb strength training with the following components.

1) Lower limb endurance training: on a treadmill, on an exercise bicycle or both, depending on the treating therapist's assessment of individual circumstances.
2) Upper limb endurance training: exercises using some form and level of resistance for each hand (*e.g.* dumbbells or TheraBands).
3) Lower and upper limb strength training: exercises involving some form and level of resistance (*e.g.* dumbbells or TheraBands).

Following completion of the in-clinic pulmonary rehabilitation programme, the patients were encouraged to follow a home maintenance programme at least twice a week. The programme consisted of the following components.

1) Lower limb endurance training (walking for 20–30 min substituted for treadmill or exercise bicycle).
2) Upper limb endurance training (as recommended by pulmonary rehabilitation therapist, intended to be similar to in-clinic programme).
3) Lower and upper limb strength training (as recommended by pulmonary rehabilitation therapist, intended to be similar to in-clinic programme).

Patients who successfully completed their pulmonary rehabilitation programme underwent baseline assessments and, if they continued to meet all protocol entry criteria, were randomised 2:1 to either the treatment or control group. Evaluations performed at screening and repeated after pulmonary rehabilitation were supplemental oxygen use, vital signs, electrocardiogram, spirometry, body plethysmography, D_{LCO}, P_{aO_2}, P_{aCO_2}, oxygen saturation and 6-min walk test (6MWT).

Subjects randomised to the treatment group underwent Zephyr valve placement procedure; these data have been published previously [7, 11] and are not the subject of this article. The data presented here are for the impact of pulmonary rehabilitation on aspects of lung function measures and exercise capacity.

Statistical analysis

All analyses have been performed using IBM SPSS (version 28; IBM Corporation, Somers, NY, USA). Data are presented as mean±SD or median (minimum–maximum and interquartile range). Frequency data are presented as n (%). Comparison of clinical data between pre- and post-rehabilitation was performed by two-sided t-test for paired data.

6MWT data were only compared pre- and post-rehabilitation when complete datasets were available (Borg dyspnoea pre and post score, fatigue pre and post score, 6MWD). In addition, subgroup analyses were performed for patients with a 6MWD increase after pulmonary rehabilitation equal to or greater than the minimal clinically important difference (MCID) of 26 m [13] *versus* <26 m and a screening 6MWD <250 m *versus* ⩾250 m. A multiple linear regression analysis was performed to identify predictors for 6MWD increase after pulmonary rehabilitation according to clinical relevance for the following parameters: age, BMI, sex, FEV_1, RV, forced vital capacity (FVC), TLC, RV/TLC, D_{LCO}, P_{aCO_2}, P_{aO_2} and all parameters of 6MWT (Borg scores, 6MWD).

Due to the explorative nature of the study, p-values were interpreted descriptively. No adjustment for multiple testing was performed. p-values <0.05 were considered statistically significant.

Results

Patient selection and characteristics

Of 492 subjects enrolled in the VENT study (n=171 European cohort, n=321 USA cohort), we excluded subjects who did not complete pulmonary rehabilitation (n=35) or did not perform a screening evaluation.

Finally, 403 patients were included in the analysis (table 1). The mean 6MWD before pulmonary rehabilitation in the group with complete datasets for 6MWT (n=350) was 331.6±98.8 m (median 326.0 m, min 100 m, max 715 m).

Outcome after pulmonary rehabilitation

After completion of pulmonary rehabilitation, all patients underwent reassessment of lung function and exercise capacity (table 2). Lung function parameters like FEV_1 (no change) and RV (+0.01 L) did not significantly change after rehabilitation overall. The 6MWD increased significantly by 14.0 m (p<0.001), but less than the MCID of 26 m [13], and patients suffered from less dyspnoea after 6MWT: Borg dyspnoea post-6MWT decreased from 4.5±2.1 points to 4.3±2.2 points (p=0.018). 40.3% (141 out of 350) achieved the MCID for 6MWT. P_{aCO_2} worsened minimally (+0.4 mmHg; p=0.038) after rehabilitation.

Predictors of success of pulmonary rehabilitation

The group of patients that reached MCID for 6MWD after pulmonary rehabilitation also showed a statistically significant increase of FVC (from 64.8±14.8% to 67.0±15.2%; p=0.009), but not of other lung function parameters. The dyspnoea pre score decreased from 1.4±1.5 points to 1.1±1.4 points (p=0.046). When comparing the patient group with 6MWD increase ⩾26 m *versus* <26 m, no statistically significant differences in screening parameters (lung function, blood gas) were detected, but patients with 6MWD increase ⩾26 m had lower 6MWD at screening (298.4±95.4 *versus* 354.0±94.9 m; p<0.001).

TABLE 1 Baseline characteristics

	Subjects	Baseline values
Age (years)	403	63.3±7.4
Sex (female)	403	154 (38.2)
BMI (kg·m^{-2})	403	24.4±3.9
Final treatment group		
Treatment (*versus* control)	403	270 (67)
Target lobe		
Right upper lobe	403	207 (51.4)
Right lower lobe	403	52 (12.9)
Left upper lobe	403	91 (22.6)
Left lower lobe	403	53 (13.2)
Blood gas		
P_{aO_2} (mmHg)	398	66.9±13.1
P_{aCO_2} (mmHg)	399	39.1±6.8
Lung function		
FEV_1 (L)	396	0.9±0.3
FEV_1 (%)	393	30.1±7.6
RV (L)	396	4.9±1.2
RV (%)	396	225.6±52.4
FVC (L)	392	2.6±0.8
FVC (%)	392	66.1±15.5
TLC (L)	396	7.6±1.5
TLC (%)	391	126.4±16.1
D_{LCO} (%)	399	33.1±10.2
Symptoms and exercise capacity		
6MWD (m)	397	329.4±100.5
6MWT dyspnoea pre[#]	380	1.2±1.5
6MWT dyspnoea post[#]	381	4.6±2.2
6MWT fatigue pre[#]	368	1.1±1.5
6MWT fatigue post[#]	370	3.1±2.3

Data are presented as n, mean±SD or n (%). BMI: body mass index; P_{aO_2}: partial pressure of oxygen; P_{aCO_2}: partial pressure of carbon dioxide; FEV_1: forced expiratory volume in 1 s; RV: residual volume; FVC: forced vital capacity; TLC: total lung capacity; D_{LCO}: diffusion capacity of the lung for carbon monoxide; 6MWD: 6-min walk distance; 6MWT: 6-min walk test. [#]: dyspnoea and fatigue were measured pre- and post-exertion using the modified Borg 0–10 scale.

TABLE 2 Lung function measures before and after pulmonary rehabilitation

	Subjects	Before rehabilitation	After rehabilitation	p-value
FEV_1 (L)	395	0.89±0.27	0.89±0.27	0.192
FEV_1 (%)	391	30.09±7.59	29.86±7.59	0.256
FVC (L)	391	2.62±0.79	2.65±0.79	0.178
FVC (%)	391	66.13±15.05	67.07±15.05	0.080
RV (L)	394	4.86±1.19	4.87±1.15	0.724
RV (%)	393	225.18±52.29	226.33±49.31	0.576
RV/TLC (%)	394	63.5±8.7	63.4±8.4	0.744
TLC (L)	394	7.64±1.48	7.68±1.45	0.194
TLC (%)	385	126.34±16.20	126.72±16.87	0.597
6MWD (m)	350	331.6±98.8	345.6±95.3	**<0.001**
6MWT dyspnoea pre[#]	350	1.2±1.3	1.2±1.3	0.585
6MWT dyspnoea post[#]	350	4.5±2.1	4.3±2.2	**0.018**
6MWT fatigue pre[#]	350	1.1±1.5	1.1±1.5	0.378
6MWT fatigue post[#]	350	3.2±2.3	3.1±2.3	0.455
P_{aO_2} (mmHg)	395	67.0±13.1	67.6±13.2	0.164
P_{aCO_2} (mmHg)	398	39.0±6.8	39.4±7.0	**0.038**

Data are presented as n or mean±SD, unless otherwise stated. Statistically significant results are written in bold type. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; RV: residual volume; TLC: total lung capacity; 6MWD: 6-min walk distance; 6MWT: 6-min walk test; P_{aO_2}: partial pressure of oxygen; P_{aCO_2}: partial pressure of carbon dioxide. [#]: dyspnoea and fatigue were measured pre- and post-exertion using the modified Borg 0–10 scale.

Patients with a screening 6MWD <250 m (n=74) improved significantly from 203.5±38.4 m to 244.2 ±60.7 m (p<0.001) in 6MWT and showed also an increase of FVC (59.3±13.4% to 61.8±14.5%; p=0.042) without improvement of other lung function parameters. In contrast, patients with a screening 6MWD ⩾250 m (n=276) did not improve significantly in terms of exercise capacity (366.0±80.0 m to 372.8 ±83.9 m; p=0.065). As expected, patients with screening 6MWD <250 m were older, had worse lung function (lower FEV_1, lower FVC, higher RV) and blood gas compared to patients with screening 6MWD ⩾250 m.

The regression analysis revealed the 6MWD prior to pulmonary rehabilitation (p<0.001, b= −0.543) (figure 1) and D_{LCO} (p=0.025, b=0.132) (figure 2) as predictors for therapy success in terms of exercise capacity improvement.

Discussion

To our knowledge, this is the first study to evaluate the effects of pulmonary rehabilitation in patients that are candidates for BLVR. We have shown, in a large cohort of 403 patients with severe COPD and emphysema, that pulmonary rehabilitation has no effect on pulmonary function in accordance with existing data, while it improves exercise capacity, particularly in patients with lower 6MWD at screening. After pulmonary rehabilitation, all patients still had the indication and prerequisites for BLVR.

The rehabilitation programme offered to the VENT study cohort included the typical guideline-based aspects of pulmonary rehabilitation programmes [14], including endurance training as well as strength training with upper and lower limb exercises. The American Thoracic Society and European Respiratory Society [14] recommend pulmonary rehabilitation programmes to last a minimum of 8 weeks to achieve effects on exercise performance and quality of life, while studies report different time spans of pulmonary rehabilitation programmes of 4–52 weeks [15]. Based on the observed significant improvement for 6MWD, we assume that the pulmonary rehabilitation programme offered to the VENT cohort was efficient, especially as the programme was based on the National Emphysema Treatment Trial (NETT) programme, with the same content and duration. Our patient cohort is an exemplary cohort for BLVR, but may have more severe lung function impairment and hyperinflation than usual COPD patient cohorts studied in pulmonary rehabilitation trials, and therefore have less benefit from pulmonary rehabilitation.

The reported benefits of pulmonary rehabilitation include reduced hospital admissions, reduced dyspnoea, and improved exercise capacity, limb muscle strength and quality of life [14]. Patients with hyperinflation also benefit from pulmonary rehabilitation with clinically meaningful improvements in 6MWD and St George's Respiratory Questionnaire (SGRQ) [16, 17]. A large review by the Cochrane Collaboration [15]

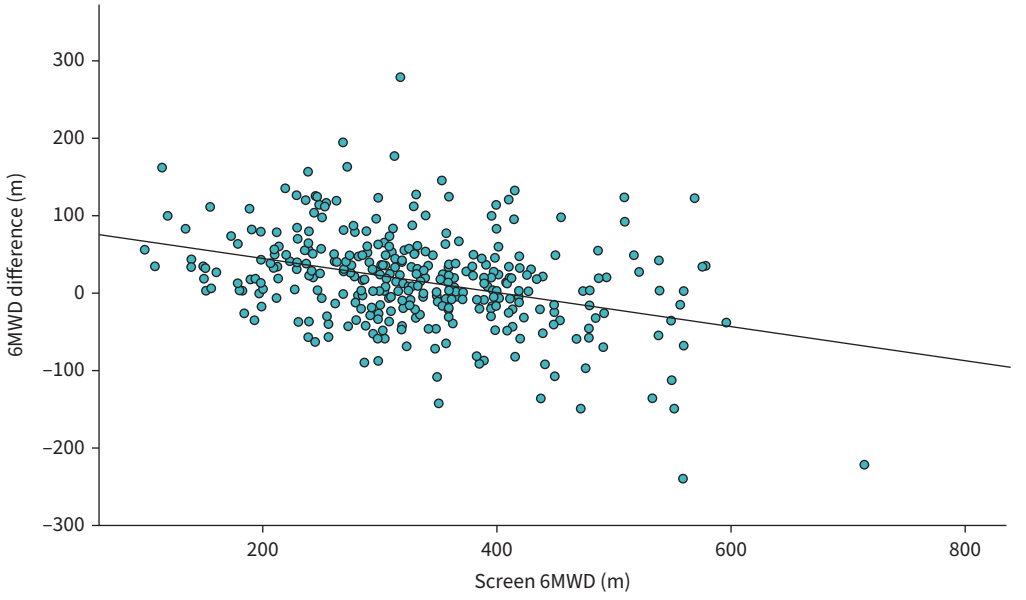

FIGURE 1 Scatter plot of 6-min walk distance (6MWD) at screening and change in walking distance after pulmonary rehabilitation.

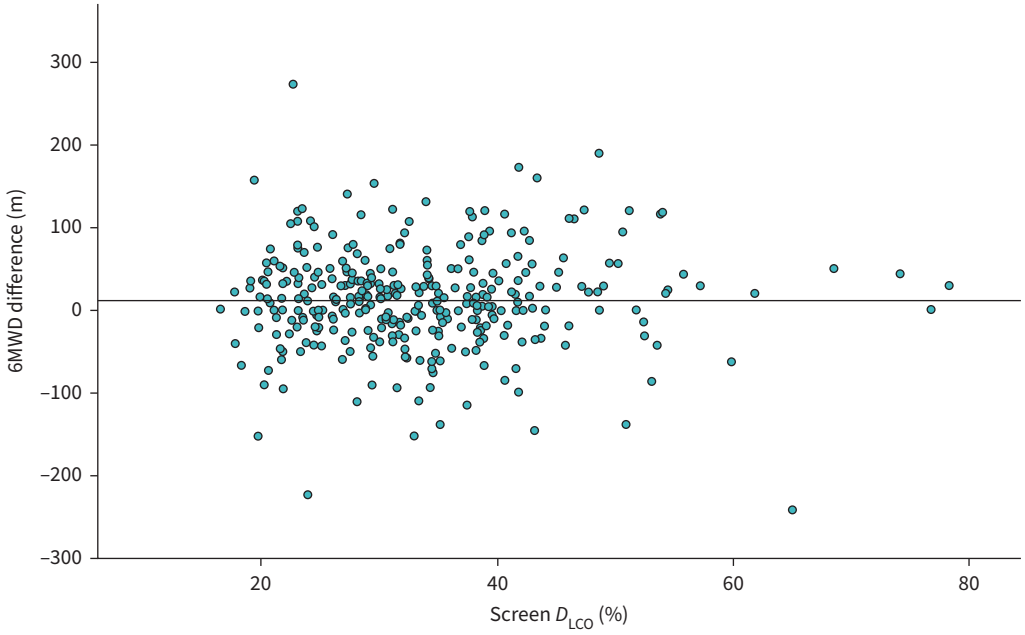

FIGURE 2 Scatter plot of diffusion capacity of the lung for carbon monoxide (D_{LCO}) at screening and change in 6-min walk distance (6MWD) after pulmonary rehabilitation.

looking at 65 studies and 3822 participants to assess effects of pulmonary rehabilitation on COPD patients showed that pulmonary rehabilitation programmes provide clinically meaningful improvements for quality of life, SGRQ (mean difference (MD) total –6.9 points) and exercise capacity (MD +43.9 m). Only a few studies evaluated effects of pulmonary rehabilitation on lung function, and the changes reported were small (FEV_1 increase from 57.3% to 60.8% after 3 years [16]; FEV_1 decline of 18±22 mL per year over 7 years [17]; FEV_1 increase from 47.3±9.4% to 55.6±9.0% after 12 weeks [18]). Consistent with these effects, pulmonary function parameters did not improve overall after pulmonary rehabilitation in the presented trial, while exercise capacity increased. The overall improvement in exercise capacity of 14 m was less in our patients than the reported MCID for 6MWD of 25–54 m [13, 19]; 40.3% achieved the MCID for 6MWD of 26 m [13].

Improvements in exercise capacity were accompanied by a minimal increase of P_{aCO_2}, which was not clinically significant. Patients may have exhausted their ventilatory reserve by overexerting themselves.

The regression analysis and subgroup analyses showed that patients with reduced exercise capacity at screening were responders for pulmonary rehabilitation in terms of improved 6MWD. One can imagine that patients with more limited exercise capacity and quality of life may have a higher motivation and potential to improve their training state. Supervised training and professional guidance have greater effects in patients who are severely limited by dyspnoea at rest, as this was the parameter that improved in the 6MWT, and pulmonary rehabilitation programmes may help these patients more than patients that have already good skills in breathing manoeuvres and exercise training.

In addition, D_{LCO} was shown as a significant, but very weak predictor for pulmonary rehabilitation benefit. In emphysema patients, diffusion capacity correlates with emphysema extent, so it seems logical that better diffusion capacity directly and indirectly may allow for better exercise performance. It should be noted that this regression analysis was only carried out with a few parameters and, for example, parameters such as depression or quality of life were not included at all, although they could certainly explain a part of the rehabilitation outcome.

Our findings are in contrast to other studies that tried to identify prognostic features for pulmonary rehabilitation success and dropout in COPD patients. The baseline state was evaluated as a poor predictor for pulmonary rehabilitation response, although dyspnoea symptom scores were positively associated with pulmonary rehabilitation outcome, and younger age, current smoking and lower health status were negatively associated with pulmonary rehabilitation outcome [20, 21].

Although prediction of pulmonary rehabilitation success needs further evaluation, the findings are encouraging for physically impaired COPD patients and may indicate that it could be useful to perform pulmonary rehabilitation before BLVR in patients with more impaired, but still preserved, exercise capacity. However, one must bear in mind that this does not fully reflect the real-world setting, where patients with a 6MWD <140 m (excluded from the VENT trial!) are also often treated with BLVR and are severely impaired in their ability to walk. Further studies are needed to evaluate which patients benefit most from pulmonary rehabilitation and if there is a 6MWD threshold that has to be taken into account.

Despite the requirement of pulmonary rehabilitation prior to BLVR, to our knowledge, there are no data available that prove the benefit of pulmonary rehabilitation before BLVR. However, data are available for patients undergoing LVRS. Debigaré *et al*. [22] showed that patients undergoing pulmonary rehabilitation before LVRS achieved significant improvements in 6MWD, quality of life, peak work rate, peak oxygen consumption, endurance time and muscle strength in home-based exercise training, although there was no improvement in lung function. Similar findings were reported in the NETT programme which included 1218 emphysema patients who underwent pulmonary rehabilitation before LVRS with significant improvements for 6MWD (76 feet≙23 m), quality of life (SGRQ −3.5 points) and dyspnoea [23]. Apart from a slight decrease in hyperinflation (RV/TLC decrease of 0.6%), no improvement in lung function was observed (FEV_1 −0.1±3.7%, RV/TLC −0.6±5.1%). Patients who had previously undergone pulmonary rehabilitation had smaller improvements. ∼10% of patients improved by pulmonary rehabilitation were no longer willing to undergo LVRS (which does not mean that they were no longer eligible). The authors of NETT concluded that pulmonary rehabilitation is important in the preparation and selection of patients for LVRS, as exercise levels improved significantly [23].

While we agree with the assumption that some patients will reach a general condition through pulmonary rehabilitation in which they are better equipped and fit enough for BLVR, it is worth noting that benefits of pulmonary rehabilitation diminish after 6-12 months if there are no maintenance strategies [19] and patients will probably revert to their pre-pulmonary rehabilitation status; however, BLVR will have been delayed. Conversely, the improvement in lung function after BLVR improves the dominant ventilatory limitation to exertion present in COPD and likely results in more effective cardiac and peripheral muscle training. The greater ability and willingness to participate in pulmonary rehabilitation following BLVR plausibly results in greater improvements in exercise capacity and quality of life, with longer-lasting effects.

Finally, the inability of some patients to participate effectively in pulmonary rehabilitation due to disabling symptoms or frailty which may be improved with BLVR, or due to limited access to pulmonary rehabilitation facilities in certain countries or geographic regions, would eliminate this potential treatment option, and increase treatment disparities in the setting of mandatory pulmonary rehabilitation requirement.

The effect of the timing of pulmonary rehabilitation, if better pre- or post-BLVR, should be assessed in future studies. It is also important to identify the group of COPD patients who will benefit most from pulmonary rehabilitation, so that individualised recommendations can be made. Until then, it should be up to the treating physician to recommend pulmonary rehabilitation before or after BLVR, depending on the individual patient's general condition and circumstances.

The main limitation of this study is that assessing the benefit of pulmonary rehabilitation was not the primary objective and end-point of this study. Data for 6MWD and other parameters were incomplete, and may have influenced the results. However, this was a prospective study with parameters collected under strict study conditions, so the results appear to be reliable.

What this study cannot answer is whether pulmonary rehabilitation has an influence on the outcome of BLVR. This needs to be addressed in future studies.

Conclusion

Supervised pulmonary rehabilitation prior to BLVR in patients with emphysematous COPD resulted, overall, in modest improvements in exercise capacity and dyspnoea. These findings challenge the recommendation that all patients being considered for BLVR should undergo pulmonary rehabilitation. Patients with low but preserved exercise capacity may benefit most from pulmonary rehabilitation prior to BLVR and the general condition in these patients may be improved as a safety measure. The idea of preventing patients from needing interventional therapy after pulmonary rehabilitation should be discarded, as none of the patients improved to the point where BLVR was no longer possible or necessary. Finally, our data suggest that pulmonary rehabilitation prior to BLVR procedures may not be a critical prerequisite in all patients.

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Data availability statement: The data will be made available on reasonable request from the corresponding author.

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References

1 Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease: 2023 Report. 2023. https://goldcopd.org/2023-gold-report-2/.
2 Halbert RJ, Natoli JL, Gano A, *et al.* Global burden of COPD: systematic review and meta-analysis. *Eur Respir J* 2006; 28: 523–532.
3 Ofir D, Laveneziana P, Webb KA, *et al.* Mechanisms of dyspnea during cycle exercise in symptomatic patients with GOLD stage I chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2008; 177: 622–629.
4 Elbehairy AF, Ciavaglia CE, Webb KA, *et al.* Pulmonary gas exchange abnormalities in mild chronic obstructive pulmonary disease. Implications for dyspnea and exercise intolerance. *Am J Respir Crit Care Med* 2015; 191: 1384–1394.
5 Troosters T, Gosselink R, Janssens W, *et al.* Exercise training and pulmonary rehabilitation: new insights and remaining challenges. *Eur Respir Rev* 2010; 19: 24–29.
6 Fishman A, Martinez F, Naunheim K, *et al.* A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med* 2003; 348: 2059–2073.
7 Sciurba FC, Ernst A, Herth FJF, *et al.* A randomized study of endobronchial valves for advanced emphysema. *N Engl J Med* 2010; 363: 1233–1244.
8 Criner GJ, Sue R, Wright S, *et al.* A multicenter randomized controlled trial of Zephyr endobronchial valve treatment in heterogeneous emphysema (LIBERATE). *Am J Respir Crit Care Med* 2018; 198: 1151–1164.
9 Valipour A, Slebos D-J, Herth F, *et al.* Endobronchial valve therapy in patients with homogeneous emphysema. Results from the IMPACT study. *Am J Respir Crit Care Med* 2016; 194: 1073–1082.
10 Herth FJF, Slebos D-J, Criner GJ, *et al.* Endoscopic lung volume reduction: an expert panel recommendation – update 2019. *Respiration* 2019; 97: 548–557.
11 Herth FJF, Noppen M, Valipour A, *et al.* Efficacy predictors of lung volume reduction with Zephyr valves in a European cohort. *Eur Respir J* 2012; 39: 1334–1342.
12 Strange C, Herth FJF, Kovitz KL, *et al.* Design of the endobronchial valve for emphysema palliation trial (VENT): a non-surgical method of lung volume reduction. *BMC Pulm Med* 2007; 7: 10.
13 Puhan MA, Chandra D, Mosenifar Z, *et al.* The minimal important difference of exercise tests in severe COPD. *Eur Respir J* 2011; 37: 784–790.
14 Rochester CL, Vogiatzis I, Holland AE, *et al.* An official American Thoracic Society/European Respiratory Society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. *Am J Respir Crit Care Med* 2015; 192: 1373–1386.

15 McCarthy B, Casey D, Devane D, *et al.* Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2015; 2015: CD003793.
16 Incorvaia C, Russo A, Foresi A, *et al.* Effects of pulmonary rehabilitation on lung function in chronic obstructive pulmonary disease: the FIRST study. *Eur J Phys Rehabil Med* 2014; 50: 419–426.
17 Foglio K, Bianchi L, Bruletti G, *et al.* Seven-year time course of lung function, symptoms, health-related quality of life, and exercise tolerance in COPD patients undergoing pulmonary rehabilitation programs. *Respir Med* 2007; 101: 1961–1970.
18 Ma Y, Chen Y, Zhang N, *et al.* Efficacy and safety of pulmonary rehabilitation training on lung function, quality of life, and T cell immune function in patients with stable chronic obstructive pulmonary disease: a randomized controlled trial. *Ann Palliat Med* 2022; 11: 1774–1785.
19 Spruit MA, Singh SJ, Garvey C, *et al.* An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med* 2013; 188: e13–e64.
20 Selzler A-M, Simmonds L, Rodgers WM, *et al.* Pulmonary rehabilitation in chronic obstructive pulmonary disease: predictors of program completion and success. *COPD* 2012; 9: 538–545.
21 Garrod R, Marshall J, Barley E, *et al.* Predictors of success and failure in pulmonary rehabilitation. *Eur Respir J* 2006; 27: 788–794.
22 Debigaré R, Maltais F, Whittom F, *et al.* Feasibility and efficacy of home exercise training before lung volume reduction. *J Cardiopulm Rehabil* 1999; 19: 235–241.
23 Ries AL, Make BJ, Lee SM, *et al.* The effects of pulmonary rehabilitation in the National Emphysema Treatment Trial. *Chest* 2005; 128: 3799–3809.