



Objectively identified comorbidities in chronic obstructive pulmonary disease: impact on pulmonary rehabilitation outcomes

To the Editor:

Pulmonary rehabilitation (PR) is a comprehensive intervention recognised as a core component in the treatment of patients with chronic obstructive pulmonary disease (COPD) [1]. Comorbidities are highly prevalent in patients with COPD entering PR [2–4], which may be associated with the change in exercise performance and health status after PR [3–5]. Nonetheless, previous studies used self-reported and/or chart-based comorbidities, and only the impact of individual comorbidities or arbitrarily grouped comorbidities were studied [3, 4].

VANFLETEREN *et al.* [2] identified five clusters based on the presence of 13 objectively diagnosed comorbidities in patients with COPD. The aims of the present study were: 1) to investigate the impact of 13 individual objectively identified comorbidities on changes in functional exercise performance and health status following PR in patients with COPD; and 2) to investigate the impact of the five comorbidity clusters on these changes.

Patients adhered to the following inclusion criteria: Global Initiative for Chronic Obstructive Lung Disease grades 2–4 [6], 40–80 years of age, clinically stable state, and a smoking history of ≥ 10 pack-years or relevant occupational exposure. Patients were considered ineligible if they had any disease and/or condition that could compromise the initial assessments. All participants gave written informed consent, and the study was approved by the local ethics and review boards (MEC 10-3-067). The baseline data from this study have been published before [2].

Participants enrolled in an 8-week inpatient (5 days-week⁻¹) or 14-week outpatient (3 days-week⁻¹) comprehensive PR programme [7]. During initial evaluation, 13 comorbidities were diagnosed using objective measures and according to international criteria, and five comorbidity clusters were identified. Further details can be found in VANFLETEREN *et al.* [2]. Self-reported comorbidities were assessed using the Charlson comorbidity index [8]. The total score on this index was not adjusted for age and did not include COPD as comorbidity, as previously suggested [3, 4].

Functional exercise capacity (the 6-min walk test and the constant work rate cycling test (CWRT), performed on a cycle ergometer) and health status (St. George's Respiratory Questionnaire (SGRQ)) were assessed before and after PR. An improvement in: the 6-min walking distance (6MWD) of ≥ 30 m [9]; the CWRT time of ≥ 100 s [10]; and a decrease in SGRQ total score of ≥ 4 [11] were considered clinically relevant. Logistic regression models adjusted for age, sex, forced expiratory volume in the 1 s (FEV₁) and the baseline 6MWD, CWRT time or SGRQ total score were used to identify the predictive role of comorbidities on meaningful improvements following PR. Statistical significance was considered at $p < 0.01$.

255 patients with COPD were recruited, but 42 patients were ineligible [2]. 213 participants (59% male, mean age 64 ± 7 years, mean FEV₁ $51 \pm 17\%$ predicted) started PR, of which 19 (9%) participants dropped out. No differences were found between patients who dropped out and patients who completed the programme. The proportion of patients undergoing inpatient or outpatient rehabilitation was comparable between clusters ($p = 0.37$).

The mean change (95% CI) for 6MWD, cycle endurance time, and health status scores were 30 m (23–38 m), 202 s (155–248 s) and -4.0 (-6.0 – -2.0), respectively, and proved to be clinically meaningful and statistically significant. Logistic regression models revealed that none of the 13 objectively diagnosed comorbidities changed the likelihood for a clinically meaningful change in 6MWD, CWRT time or SGRQ total score following PR (fig. 1). When the number of objectively identified comorbidities (none, 1 and >1) were taken into account in logistic regression models, none of the analyses reached statistical significance (fig. 1). Similar results were found for the total score in the Charlson index (0, 1 or ≥ 2 points). With the “less comorbidity” cluster as reference, none of the clusters had a significantly different likelihood to achieve the minimal

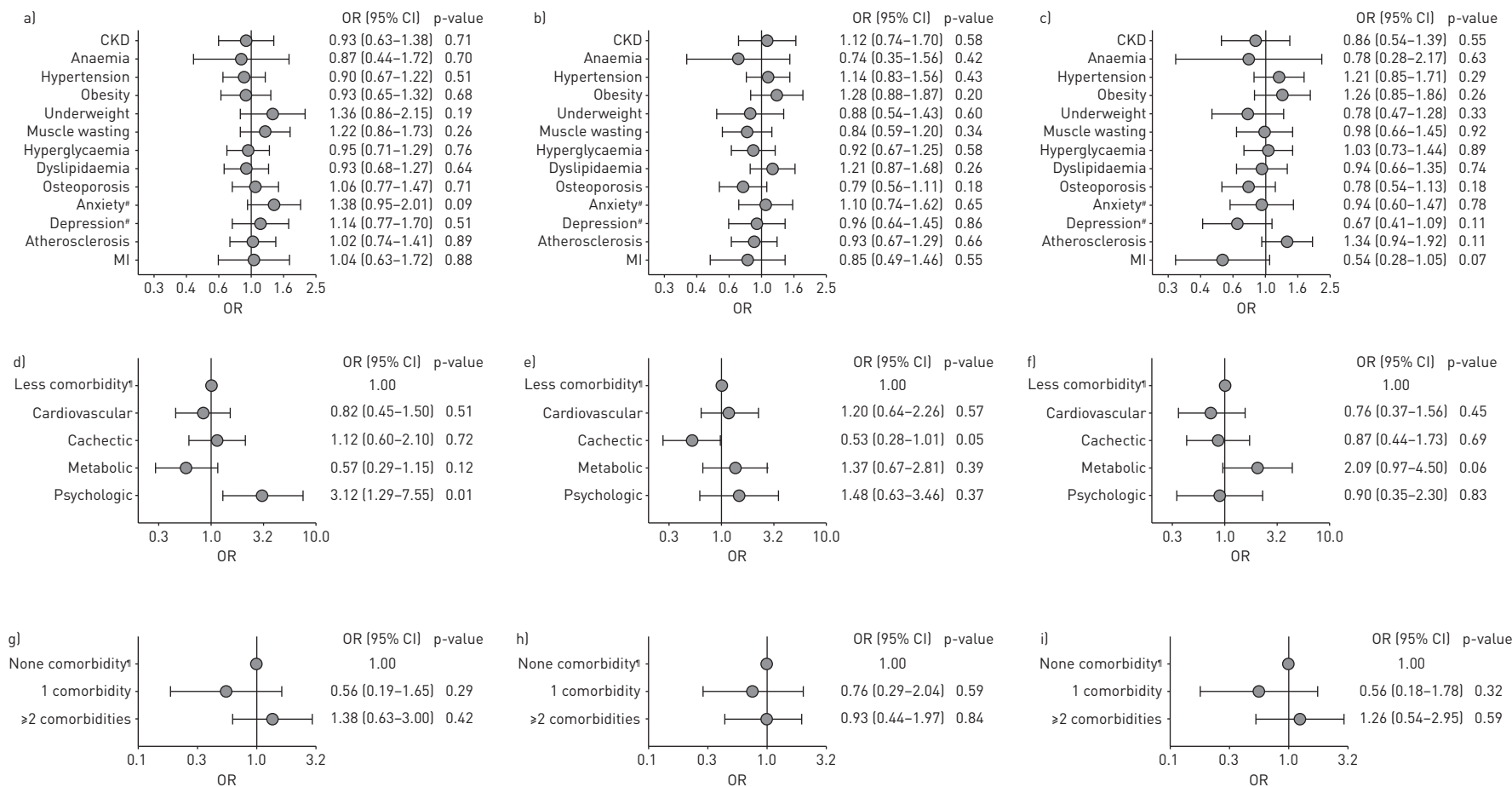


FIGURE 1 Predictive role of individual objectively identified comorbidities (a–c), clusters of objectively identified comorbidities (d–f), and the number of objectively identified comorbidities (h–i) on meaningful improvements, after pulmonary rehabilitation, in: a, d and g) the 6-min walk test (n=187 due to missing data); b, e and h) constant work rate test (n=174 due to missing data); and c, f and g) St. George's Respiratory Questionnaire (n=151 due to missing data). Models adjusted for age, sex, forced expiratory volume in 1 s and the baseline value in each outcome measure. CKD: chronic kidney disease; MI: myocardial infarction. †: participants showing symptoms; ‡: reference.

important change on the different outcomes. Only the “psychologic” cluster had a significantly higher likelihood for clinically meaningful change in 6MWD (fig. 1).

The present study showed that the presence of individual or clusters of objectively identified comorbidities do not, generally, influence the likelihood of having a clinically meaningful change in 6MWD, CWRT time and/or SGRQ total score following PR in patients with COPD. These data emphasise that patients with COPD are still able to obtain significant and clinically relevant improvements in functional exercise capacity and health status after PR, irrespective of the presence of comorbidities.

Osteoporosis, heart disease and metabolic disease have been shown to be positively or negatively associated with changes in 6MWD and SGRQ scores following PR [3, 4]. We were not able to corroborate these findings. In our study, comorbidities were assessed using objective measures, while most previous studies used “self-reports” or data from medical records [3, 4]. Moreover, previous studies used a different threshold to classify an improvement in 6MWD as clinically relevant (*i.e.* 54 m) [3, 4].

Surprisingly, only the “psychologic” cluster was associated with a higher likelihood of achieving meaningful improvements in 6MWD compared to the “less comorbidity” cluster. The “psychologic” cluster is characterised by more baseline symptoms of anxiety and depression [2]. Previously, VON LEUPOLDT *et al.* [12] showed that more symptoms of anxiety and depression are associated with reduced exercise capacity. We believe that more symptoms of anxiety and/or depression may lead to excessive sensitiveness to dyspnoea, which in turn can work as a limiting factor for exercise. As suggested by MAURER *et al.* [13], the multidisciplinary and comprehensive approach adopted in PR programmes may help to desensitise patients who are excessively sensitive to dyspnoea, and this can translate as greater improvements in terms of exercise capacity. A reduction of anxiety and depression symptom scores, commonly achieved after PR, may, in turn, contribute to dyspnoea desensitisation [13].

The presence of common comorbidities in patients with COPD has been used frequently as an exclusion criterion for PR [1]. In the present study, only patients with comorbidities potentially interfering with the safety or usefulness of the programme were excluded, such as unstable heart disease or uncurated malignancies. Our study proves that common comorbidities, in general, do not influence the likelihood of improving following PR. Moreover, exercise has been suggested as the cornerstone of PR in COPD [1], and this strategy has been used as therapy in other chronic diseases as well, such as cardiovascular and metabolic diseases [14, 15]. Therefore, patients with COPD and the above mentioned comorbidities may benefit even more from PR.

The patients included in the current analysis were those referred for PR, which can compromise the generalisability of our findings. Nevertheless, VANFLETEREN *et al.* [2] have previously shown that these patients have similar characteristics compared to patients from other studies. Another possible limitation is that some analyses may be underpowered. Therefore, the current findings are more hypothesis-generating than definitive. Studies with large samples and preferably from different centres are desirable.

In summary, comorbidities do not seem to preclude patients with COPD from obtaining significant and clinically meaningful improvements in functional exercise capacity and health status following PR. Complex patients with COPD and comorbidities should not be withheld from PR.



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Patients with COPD and multiple comorbidities can still benefit from pulmonary rehabilitation

<http://ow.ly/LXAWc>

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