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Determination of the minimal important difference for Dyspnea-12 questionnaire in patients with COPD, after pulmonary rehabilitation.

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The authors contributed to the idea, writing and revising of this paper.

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Abstract

Introduction: The authors of the international task force about the management of Dyspnea recommend assessing sensory and affective components of dyspnea. The Dyspnea-12 questionnaire (D-12) allows to assess both components of dyspnea. D-12 is valid and reliable but its sensitivity to pulmonary rehabilitation was not studied. The aim of this study was to estimate the minimal important difference (MID) for D-12 in COPD patients undergoing a pulmonary rehabilitation program (PRP).

Methods: Severe or very severe COPD patients undergoing a PRP were included. Dyspnea was assessed using D-12, MMRC dyspnea scale, London chest of Activity of Daily Living questionnaire (LCADL). Quality of life was assessed using Saint-George respiratory questionnaire (SGRQ) and COPD assessment Test (CAT); exercise capacity using 6-Minute walk Test (6MWT) and 1-minute sit to-stand test (1STST).

The MID was evaluated using distribution and anchor-based methods.

Results: Sixty patients (age: 64.4 ± 8.2 ; FEV1 (%): 28.6 ± 8.1) were included. At the end of the PRP, patients had significantly decreased their dyspnea measured with D-12, MMRC, LCADL (D-12: 23.9 ± 8.9 to 17.6 ± 9.4 ; MMRC: 3 ± 0.7 to 2.2 ± 1.1 , LCADL: 38 ± 13.9 to 31.6 ± 11 ; $p < 0.0001$). Using the distribution-based analysis, MID of -2.67 (standard error of measurement) or -4.45 (standard deviation) was found. According to methodology, we could only use SGRQ as anchor. With SGRQ as anchor, the receiver operating characteristic curve identified MID for the change in Dyspnea-12 at -6.1 (sensitivity: 58%, specificity: 79%). The correlation with SGRQ was modest ($r=0.33$), so the calculated MID should be interpreted with caution.

Conclusion: D-12 is a good tool to assess the decrease of dyspnea after PR. We propose MID of -6 points. However, Future estimates of MID for the D-12 should use anchors that are more strongly correlated with it.

ClinicalTrials.gov identifier: NCT02656667

Key words: dyspnea; pulmonary rehabilitation; COPD; evaluation; minimal important difference

Accepted Article

Introduction

Dyspnea is a common and distressing symptom (1). It is the most important complaint reported by patients with chronic obstructive pulmonary disease (COPD) (1). Many patients consult their general practitioner or pulmonologist because of dyspnea sensation. It is predictor of risk of hospitalization (2,3), risk of death (4,5) and decrease quality of life (6–8).

The evaluation of dyspnea is essential for the management of COPD patients, and the knowledge about dyspnea mechanisms since ten years brings to evaluate dyspnea according 3 domains : the domain of the symptom impact of dyspnea (on activity of daily living or quality of life), the domain of the affective (or emotional) distress, and the domain of the sensory-perceptual (or physical) experience (9). For the domain of symptom impact, the London Chest of Activity of Daily Living questionnaire (LCADL) and the Modified Medical Research Council dyspnea scale (MMRC) are validated and sensitive tools (10–14), with MID determined (15–17), which allows the clinical interpretation of the evolution of impact of dyspnea in response to intervention (18).

Dyspnea-12 is a validated tool for many chronic pulmonary diseases (19–23)(24) which allows to measure sensory and emotional domains of dyspnea. It is also validated in French language (14). However, no MID has been determinate. MID is an important interpretation criterion, because it is considered to be the minimal necessary and important change to reflect clinical improvement for the patient (25). The determination of the MID for Dyspnea-12 questionnaire could help the interpretation of the evolution of dyspnea after pulmonary rehabilitation.

The aim of our study was to identify the MID for the Dyspnea-12 using anchor-based and distribution-based methods.

Materials and Methods

Study population

This observational prospective study was a part of a larger trial (ESNM study) (26). Patients routinely admitted to the pulmonary rehabilitation unit of Centre Hospitalier des Pays de Morlaix (Morlaix, France) were eligible for the study, if they had severe or very severe COPD diagnosed according to American Thoracic Society (ATS)/ERS criteria (27) at admission (forced expiratory volume in 1 s (FEV1) <50% predicted value). Exclusion criteria were previous pneumonectomy or lobectomy in the past 6 months, incapacity to follow a standard rehabilitation programme (locomotor deficits,

acute cardiac failure and acute exacerbation of COPD at the beginning of the programme) and the absence of written informed consent. The study was approved by the ethics board (CPP Ouest 6 – CPP 907, n°2015-A00815-44) in November 2015. This study was registered on clinicaltrial.gov as NCT02656667 number. Written informed consent was obtained from all patients.

Study design

The main purpose of this study was to determine a MID for the Dyspnea-12 questionnaire after pulmonary rehabilitation. All patients followed 3-weeks comprehensive inpatient pulmonary rehabilitation program 5 days a week. Before and after the program, the evaluation included an evaluation of dyspnea (with Dyspnea-12 questionnaire, MMRC, LCADL) as well as exercise capacity (6-Minute walk Test (6MWT) and 1-Minute Sit To Stand Test (STST1)), inspiratory and quadriceps muscle strength, spirometry with plethysmography, health-related quality of life (St.George's Respiratory Questionnaire; SGRQ, COPD Assessment Test (CAT)), anxiety and depression (Hospital Anxiety and Depression Scale) (respectively HADS-A and HADS-D), and an educational diagnosis.

The standardized rehabilitation program was conducted during 3 weeks, 5 days per week and included aerobic exercise performed on treadmill (thirty minutes per day each), ground-based outdoor walking training, strengthening of lower and upper limb muscles groups, therapeutic educational program, aerobic gymnastic in groups, smoking cessation program and socio-psychological and dietary advices. Patients had Neuromuscular Electrical Stimulation (NMES) or cycle ergometer training to perform quadriceps strengthening. All sessions were supervised by a physiotherapist.

The Dyspnea-12 questionnaire

Dyspnea-12 is a 12-item questionnaire rated on a 4-point Likert scale (none (score 0), mild (score 1), moderate (score 2) or severe (score 3)) which provides an assessment of dyspnea severity. The D-12 allows the identification of two subdomains: sensory-perceptual or physical domain (items 1–7, score range 0–21) and affective (or emotional) domain (items 8–12, score range 0–15).

The overall score ranges between 0 and 36 and separate subdomain scores may also be calculated (19,28); higher scores indicate worse dyspnea. Yorke et al. (19)

recommend the use of the focal period “these days” reflecting breathlessness experienced in daily life;

Dyspnea-12 has shown good test properties with high internal consistency, validity, and test-retest reliability over 2 weeks (14,29). Dyspnea-12 questionnaire is a short and simple tool.

Statistical analysis

Statistical analyses were performed using SPSS 20 statistical software (SPSS Inc., Chicago, IL, USA) and graphpad prism 5.

All results were presented as mean \pm standard deviation (SD) or median with interquartile range (Q1-Q3) for the quantitative variables. The qualitative variables were expressed in percentages. The effect of pulmonary rehabilitation on dyspnea and functional parameters was analysed using paired t-test or Wilcoxon’s test (in case of non-normal distribution). Correlations were analysed using Pearson’s or Spearman’s rank correlation coefficient (in case of non-normal distribution). We used linear regression to compare change in D-12 with other outcomes measures.

For comparison, a p-value of <0.05 was considered as statistically significant.

The analysis of the MID for Dyspnea-12 was based on the use of distribution-based and anchor-based methods.

For the distribution-based method, we use the 2 standard methodologies

- The standard deviation (SD) method: $0.5 \times SD$
with $SD = SD$ pre-rehabilitation
- Standard Error of the Measure (SEM): $SD \times \sqrt{1 - (\text{test} - \text{retest})}$
With $SD = SD$ pre-rehabilitation, Test-retest: ICC = 0,91 (30)

For the anchor-based method, MMRC, CAT, LCADL, SGRQ, 6MWT were used as anchors. For anchor-based estimation of the MID, we used the change from baseline variables that correlated with the change in D-12 score from baseline to the end of the pulmonary rehabilitation program with a correlation coefficient of at least 0.3 and a p-value <0.05 as recommended (25). Then, we used the sensitivity- and specificity-based approach with receiver operating characteristic curves to determine the best cut-off for the change in D-12 score with the established MID for the

different anchors. A MID was estimated if area under the curve >0.7 using the ROC curve (31).

Results

Between June 8th, 2016 and April 13th, 2018, 60 patients were included. The characteristics of included patients are reported in table 1.

After the pulmonary rehabilitation program, significant improvements were found for dyspnea (D-12, MMRC, LCADL), exercise capacity (6MWT, STST1), quadriceps strength, inspiratory muscles strength (PImax), quality of life (SGRQ, CAT), anxiety and depression (HADS-A, HADS-D) (table 2).

The correlation between the different anchors and D-12 are mentioned in table 3. The evolution of D-12 was significantly weakly correlated with the evolution of all anchors (table 3); however, the area under the curve was only >0.7 for SGRQ.

As only the change in SGRQ had a correlation coefficient ≥ 0.3 ($r= 0,333$, $p= 0,0114$) (figure 1) and an area under the curve (AUC) >0.7 using the ROC curve (AUC: 0,75; CI 95%: [0,58-0,91]) (figure 2), it was used as anchor to estimate the MID for Dyspnea-12.

For D-12, the ROC curve (figure 2) indicated a cut-off value of -6 for the MID, with sensitivity of 58% and specificity of 79%.

The different MID estimates using distribution-based and anchor-based methods are summarized in table 4.

Discussion

The aim of this study was to estimate the MID for Dypnea-12 questionnaire after pulmonary rehabilitation.

We show that Dyspnea-12 questionnaire is responsive to change after pulmonary rehabilitation. The estimates for the MID for Dyspnea-12 score ranged from $-2,67$ to $-4,45$ according the distribution-based method and -6 according the anchor-based method.

The present study used both distribution-based and anchor-based methods, according to the recommendations for determining MID (25). Both approaches measure a quantifiable change in outcomes. The distribution based methods compare the change in the outcome evaluated (here D-12) to some measure of

variability (standard deviation) and reliability (standard error of the measurement) (32,33); then, each method (standard error of the measurement and standard deviation) produces a MID different from the other (32). And on another hand, these methods provide a value indicating a statistical difference, but this may not be perceivable by the patient (34). However, in a “reported outcome patient” point of view, anchor-based method seems to be more centered on patient: anchor-based allows to rely a comparison of the change in outcome evaluated (Dyspnea-12) with another outcome (the anchor: SGRQ), which showed an established association (34). Indeed, dyspnea and quality of life are correlated and Dyspnea impact on quality of life for the patients.

We found a difference of estimates for MID between both methods. Then we proposed a MID of – 6 points for Dyspnea-12. However, because of the weak correlation between the evolution of D-12 and the evolution of SGRQ, we must be very cautious, and this suggestion must be validated with other future studies.

It is important to determine MID for dyspnea because this is the cardinal symptom and the most common in patients with COPD (35–38), and the measure of dyspnea is often a tool used as endpoint to evaluate many treatments as pulmonary rehabilitation. Dyspnea is the major symptom reported by the patients and decreasing dyspnea is one of the main objectives of pulmonary rehabilitation and globally the main objective of many treatments for patients with COPD. Often, dyspnea is measured at effort with Borg Scale, but it is not so easy to evaluate the evolution of dyspnea in the same conditions. Admittedly, many tests allow to evaluate dyspnea at a standardised level of exertion, and this point is important because measuring breathlessness at standardised exertion is of fundamental importance for assessing symptom severity (39): the endurance shuttle walk test (40), the cycloergometer endurance test (41), 3-min step test and 3-min constant-rate shuttle walk test (42,43). The best test to compare dyspnoea at the same level of exertion would be the cycloergometer endurance test (constant work rate exercise test), because we can measure dyspnoea at isotime and isowork between the beginning and the end of the pulmonary rehabilitation programme (41). However, dyspnea is often measured at effort and at the end of the 6-minute walk test (because this test is always performed and easy to perform during pulmonary rehabilitation), but with this test, the measure of dyspnea is not realized at the same

level of intensity, because the distance performed often increase after the pulmonary rehabilitation program. Then, dyspnea is not evaluate in the same conditions of exertion.

The authors of the task force about assessment and management of dyspnea (1) mentioned that dyspnea must be evaluated according 3 domains: the sensory domain of dyspnea, the emotional domain of dyspnea and the impact of dyspnea in activity of daily living or quality of life. Dyspnea-12 questionnaire is an instrument which allows the measure of emotional and sensory domains of dyspnea (29). It is the first tool which allows the evaluation of emotional and sensory domains of dyspnea in daily living, independently of physical activity. In our study, both emotional and sensory domains decrease significantly after a pulmonary rehabilitation program. However, at this time, the MID for Dyspnea-12 was not determined. MID was proposed for the measure of the impact of Dyspnea in activity of daily living. Two instruments allow to evaluate the impact of dyspnea in activity of daily living: the MMRC scale and the LCADL questionnaire. The MID for the MMRC is -1 point and the MID for the LCADL is – 3 points (15,17). Then our study allows to propose a MID for dyspnea-12. In clinical practice, the practitioner has now different tools to measure and track the evolution of dyspnea in all domains of dyspnea.

The multidimensional dyspnea profile questionnaire (44) is an other instrument which could measure sensory and emotional domains of dyspnea. These 2 instruments are complementary, MDP seems to be more appropriate to measure dyspnea at exertion and Dyspnea-12 was constructed to measure dyspnea in daily living (45) and is well correlated with anxiety (46). And on an other hand, the MID for the MDP is not determined at this time.

Our study remains some limits: only severe or very severe COPD patients were included in this study. Then, the MID could be different with less severe stages of COPD. Lastly, in our study, we did not used a global rating of change, which could be useful as anchor.

To our knowledge, this is the first study to determine MID for Dyspnea-12. To know the MID of this instrument will help the clinician to identify which patients decrease or not their dyspnea sensation in daily living. And on an other hand, the MID could be used to determine the sample size for futures studies, which would use Dyspnea-12 as endpoint.

In conclusion, Dyspnea-12 is a good tool to assess the decrease of dyspnea after PR. We propose MID of -6 points for Dyspnea-12 questionnaire. However, this is the first estimate of MID for D-12 and our results will need confirmation in other futures studies.

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Disclosure of interest:

The authors report no conflict of interest.

Data availability statement

Data are available on request to the corresponding author

References:

1. Parshall MB, Schwartzstein RM, Adams L, Banzett RB, Manning HL, Bourbeau J, et al. An official American thoracic society statement: Update on the mechanisms, assessment, and management of dyspnea. *Am J Respir Crit Care Med.* 2012;185(4):435–52.
2. Ong KC, Earnest A, Lu SJ. A multidimensional grading system (BODE index) as predictor of hospitalization for COPD. *Chest.* 2005;128(6):3810–6.
3. Lange P, Marott JL, Vestbo J, Nordestgaard BG. Prevalence of night-time dyspnoea in COPD and its implications for prognosis. *Eur Respir J.* 2014;43(6):1590–8.
4. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med.* 2004 Mar;350(10):1005–12.
5. Berraho M. Dyspnea: A strong independent factor for long-term mortality in the elderly. *J Nutr Heal Aging.* 2013;17(10):908–12.
6. Curtis JR, Martin DP, Martin TR. Patient-assessed health outcomes in chronic

lung disease: what are they, how do they help us, and where do we go from here? *Am J Respir Crit Care Med.* 1997;156(4 Pt 1):1032–9.

7. Chen YW, Camp PG, Coxson HO, Road JD, Guenette JA, Hunt MA, et al. A Comparison of Pain, Fatigue, Dyspnea and their Impact on Quality of Life in Pulmonary Rehabilitation Participants with Chronic Obstructive Pulmonary Disease. *COPD J Chronic Obstr Pulm Dis.* 2018;15(1):65–72.
8. Gruenberger J, Vietri J, Keininger DL. Greater dyspnea is associated with lower health-related quality of life among European patients with COPD. 2017;937–44.
9. Lansing RW, Gracely RH, Banzett RB. The multiple dimensions of dyspnea: review and hypotheses. *Respir Physiol Neurobiol.* 2009;167(1):53–60.
10. Bestall JC, Paul E a, Garrod R, Garnham R, Jones PW, Wedzicha J a. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax.* 1999;54(7):581–6.
11. Mahler D, Wells C. Evaluation of Clinical for Rating Dyspnea. *Chest.* 1988;93(3):580–6.
12. Garrod R, Bestall J, Paul E, Wedzicha J, Jones P. Development and validation of a standardized measure of activity of daily living in patients with severe COPD: The London chest activity of daily living scale (LCADL). *Respir Med.* 2000;94(6):589–96.
13. Garrod R, Paul E a., Wedzicha J a. An evaluation of the reliability and sensitivity of the London Chest Activity of Daily Living Scale (LCADL). *Respir Med.* 2002;96(9):725–30.
14. Beaumont M, Jegou F, Pichon R, Ber L, Péran L, Rogé C, et al. Validation of the French version of the London Chest Activity of Daily Living scale and the Dyspnea-12 questionnaire. *Int J Chron Obstruct Pulmon Dis.* 2018;13:1399–405.
15. de Torres JP. Power of Outcome Measurements to Detect Clinically Significant Changes in Pulmonary Rehabilitation of Patients With COPD*. *Chest.* 2002;121(4):1092–8.
16. Bisca GW, Proença M, Salomão A, Hernandez N a, Pitta F. Minimal detectable change of the London chest activity of daily living scale in patients with COPD. *J Cardiopulm Rehabil Prev.* 2014;34(3):213–6.

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17. Almeida Gulart A, de Araujo CLP, Bauer Munari A, Schneider BF, Dal Lago P, Mayer AF. Minimal important difference for London Chest Activity of Daily Living scale in patients with chronic obstructive pulmonary disease. *Physiother (United Kingdom)*. 2020;107:28–35.
 18. Kon SSC, Canavan JL, Jones SE, Nolan CM, Clark AL, Dickson MJ, et al. Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. *lancet Respir Med*. 2014 Mar;2(3):195–203.
 19. Yorke J, Moosavi SH, Shuldham C, Jones PW. Quantification of dyspnoea using descriptors: development and initial testing of the Dyspnoea-12. *Thorax*. 2010;65(1):21–6.
 20. Yorke J, Swigris J, Russell AM, Moosavi SH, Ng Man Kwong G, Longshaw M, et al. Dyspnea-12 is a valid and reliable measure of breathlessness in patients with interstitial lung disease. *Chest*. 2011;139(1):159–64.
 21. Yorke J, Russell A, Swigris J, Shuldham C, Haigh C, Rochnia N, et al. ASSESSMENT OF DYSPNEA IN ASTHMA: VALIDATION OF THE DYSPNEA-12. *J Asthma*. 2011;48(6):602–8.
 22. Yorke J, Armstrong I. The assessment of breathlessness in pulmonary arterial hypertension: reliability and validity of the Dyspnoea-12. *Eur J Cardiovasc Nurs*. 2014;13(6):506–14.
 23. Tan JY, Yorke J, Harle A, Smith J, Blackhall F, Pilling M, et al. Assessment of Breathlessness in Lung Cancer: Psychometric Properties of the Dyspnea-12 Questionnaire. *J Pain Symptom Manage*. 2017;53(2):208–15.
 24. Aparecida Simsic A, Yorke J, Gatti Regueiro E, Pires Di Lorenzo V, Baddini-Martinez J. Validation of the dyspnoea-12 scale into Portuguese speaking COPD patients. *Clin Respir J*. 2018;12:1942–8.
 25. Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol*. 2008 Feb;61(2):102–9.
 26. Péran L, Beaumont M, Le Ber C, Le Mevel P, Berriet A, Nowak E, et al. Effect of Neuromuscular Electrical Stimulation versus Cycle ergometer training in a pulmonary rehabilitation program on exercise capacity, in severe and very severe COPD. *Eur Respir J*. 2019;54(Suppl. 63):PA1204.
 27. Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global Strategy for the Diagnosis, Management and Prevention of Chronic

- Obstructive Pulmonary Disease, GOLD Executive Summary. *Am J Respir Crit Care Med.* 2012;(C):1–67.
28. Yorke J, Spencer LG, Duck A, Ratcliffe S, Kwong GN, Longshaw MS, et al. Cross-atlantic modification and validation of the a tool to assess quality of life in idiopathic pulmonary fibrosis (ATAQ-IPF-cA). *BMJ Open Respir Res.* 2016;1(1):1–7.
 29. Yorke J, Swigris J, Russell AM, Moosavi SH, Ng Man Kwong G, Longshaw M, et al. Dyspnea-12 is a valid and reliable measure of breathlessness in patients with interstitial lung disease. *Chest.* 2011;139(1):159–64.
 30. Beaumont M, Couturaud F, Jego F, Pichon R, Le Ber C, Péran L, et al. Validation of the French version of the London chest activity of daily living scale and the dyspnea-12 questionnaire. *Int J COPD.* 2018;13.
 31. DELACOUR H, SERVONNET A, PERROT A, VIGEZZI J, RAMIREZ J. La courbe ROC (receiver operating characteristic): principes et principales applications en biologie clinique. *Ann Biol Clin.* 2005;63(2):145–54.
 32. Copay AG, Subach BR, Glassman SD, Polly DW, Schuler TC. Understanding the minimum clinically important difference: a review of concepts and methods. *Spine J.* 2007;7(5):541–6.
 33. Sedaghat AR. Understanding the Minimal Clinically Important Difference (MCID) of Patient-Reported Outcome Measures. *Otolaryngol - Head Neck Surg (United States).* 2019;161(4):551–60.
 34. Jones PW, Beeh KM, Chapman KR, Decramer M, Mahler DA, Wedzicha JA. Minimal clinically important differences in pharmacological trials. *Am J Respir Crit Care Med.* 2014;189(3):250–5.
 35. Johnson MJ, Yorke J, Hansen-Flaschen J, Lansing R, Ekström M, Similowski T, et al. Towards an expert consensus to delineate a clinical syndrome of chronic breathlessness. *Eur Respir J.* 2017;49(5).
 36. Müllerová H, Lu C, Li H, Tabberer M. Prevalence and burden of breathlessness in patients with chronic obstructive pulmonary disease managed in primary care. *PLoS One.* 2014 Jan;9(1):e85540.
 37. Sergysels R. Question 3-1 . L 'évaluation fonctionnelle de repos. *Rev Mal Respir.* 2005;22:20–3.
 38. Kroenke K, Arrington ME, Mangelsdorff a D. The prevalence of symptoms in medical outpatients and the adequacy of therapy. *Arch Intern Med.*

- 1990;150:1685–9.
39. Ekström M, Elmberg V, Lindow T. Breathlessness measurement should be standardised for the level of exertion. *Eur Respir J.* 2018;16(9–10):342–4.
 40. Holland AE, Spruit M a., Troosters T, Puhan M a., Pepin V, Saey D, et al. An official European Respiratory Society/American Thoracic Society Technical Standard: field walking tests in chronic respiratory disease. *Eur Respir J.* 2014 Oct 30;1–19.
 41. Puente-Maestu L, Palange P, Casaburi R, Laveneziana P, Maltais F, Neder JA, et al. Use of exercise testing in the evaluation of interventional efficacy: an official ERS statement. *Eur Respir J.* 2016;429–60.
 42. Borel B, Wilkinson-Maitland CA, Hamilton A, Bourbeau J, Perrault H, Jensen D, et al. Three-minute constant rate step test for detecting exertional dyspnea relief after bronchodilation in COPD. *Int J COPD.* 2016;11(1):2991–3000.
 43. Sava F, Perrault H, Brouillard C, Darauay C, Hamilton A, Bourbeau J, et al. Detecting improvements in dyspnea in COPD using a three-minute constant rate shuttle walking protocol. *COPD J Chronic Obstr Pulm Dis.* 2012;9(4):395–400.
 44. Meek PM, Banzett R, Parshall MB, Gracely RH, Schwartzstein RM, Lansing R. Reliability and Validity of the Multidimensional Dyspnea Profile (Mdp). *Chest.* 2012;141(6):1546–53.
 45. Williams MT, Johnn D, Frith P. Comparison of the Dyspnoea-12 and Multidimensional Dyspnoea Profile in people with COPD. *Eur Respir J.* 2017;49(3).
 46. Al-Gamal E, Yorke J. Perceived breathlessness and psychological distress among patients with chronic obstructive pulmonary disease and their spouses. *Nurs Heal Sci.* 2014;16(1):103–11.

Table 1: baseline characteristics of patients

Population (n)	60
Sex-ratio M/F (%)	67 / 33
Age (years)	64.4±8.2
COPD Stage III / IV (%)	32 / 68
BMI	25.4±6.2
FEV1 (%pred)	28.6±8.1
RV (%pred)	200.6±72.6
TLC (%pred)	115.2±34
RV/TLC (%)	164.4±35.3
IC (liter)	1.9±0.6
6MWD (%pred)	45±13.2
STST1 (n of movements)	13.9±6.5
Quadriceps peak torque(%pred)	61.6±20.4
PImax (cmH20)	57.1±19
BODE index	6.5±1.2
D-12	23.9±8.9
SGRQ	66±11.9
LCADL	38±13.9
HAD-A	11.4±4.3
HAD-D	9.1±4.4
CAT	24.6±5.8
MMRC	3.0 [3 – 4]

Values are expressed as mean ± SD or median [Q1-Q3].

BMI: body mass index; CAT: COPD Assessment Test; D-12: dyspnea-12 questionnaire; FEV1: forced expiratory volume in 1 s; HAD-A: Hospital Anxiety and Depression scale, item anxiety; HAD-D: Hospital Anxiety and Depression scale, item Depression; IC: Inspiratory Capacity; LCADL: London Chest Activity of Daily Living

scale; MMRC: Modified Medical Research Council dyspnea scale; % pred: % predicted; P_{lmax}: maximal inspiratory pressure; RV: residual volume; SGRQ: St George's Respiratory Questionnaire; 6MWD: 6-minute walking distance; STST1: 1-minute Sit to stand test; TLC: total lung capacity; VC: vital capacity;

Table 2: Evolution of evaluation criteria during the pulmonary rehabilitation program

	Before PRP	After PRP	P value
6MWD (m)	290,3±97,4	326,3±104,2	0,0001
STST1 (n of repetitions)	13,9±6,5	16,9±6,7	<0,0001
Quadriceps strength (N.m)	76,23±35,8	84,11±38,8	<0,0001
PI _{max} (cmH ₂ O)	57,1±19	65±18,9	<0,0001
BODE index	6,5±1,2	5,6±1,5	<0,0001
D-12 (Total score)	23,9±8,9	17,6±9,4	<0,0001
D-12 (Sensory domain)	15,2±5,1	11,6±5,6	<0,0001
D-12 (Emotional domain)	8,6±5	6±4,9	<0,0001
SGRQ	66±11,9	54,7±15,2	<0,0001
LCADL	38±13,9	31,6±11,6	<0,0001
HAD-A	11,4±4,3	9,2±4,2	0,0011
HAD-D	9,1±4,4	7,1±4,5	0,0013
CAT	24,6±5,8	18,1±6,6	<0,0001
MMRC	3,1±0,7	2,2±1,1	<0,0001

Values are expressed as mean ± SD.

BMI: body mass index; CAT: COPD Assessment Test; D-12: dyspnea-12 questionnaire; HAD-A: Hospital Anxiety and Depression scale, item anxiety; HAD-D: Hospital Anxiety and Depression scale, item Depression; LCADL: London Chest Activity of Daily Living scale; MMRC: Modified Medical Research Council dyspnea scale; PI_{max}: maximal inspiratory pressure; SGRQ: St George's Respiratory Questionnaire; 6MWD: 6-minute walking distance; STST1: 1-minute Sit to stand test.

Table 3: correlations between Dyspnea-12 and the anchors (Pearson r)

anchors	Correlation with D-12	p-value
SGRQ	0.33	0.011
LCADL	0.40	0.002
CAT	0.35	0.006
6MWD	- 0.33	0.01
mMRC	0.41	< 0.001

CAT: COPD Assessment Test; D-12: Dyspnea-12 questionnaire; mMRC: modified Medical Research Council dyspnea scale; LCADL: London Chest Activity of Daily Living scale; SGRQ: St George's Respiratory Questionnaire; 6MWD: 6-minute walking distance

Table 4: Anchor-based and distribution-based estimates of the MID for D-12

Method	MID calculation	MID D-12
SD	$0.5 \times \text{SD}$	- 4.45
SEM	$\text{SD} \times \sqrt{1 - (\text{test} - \text{retest})}$	- 2.67
Anchor	With SGRQ	- 6

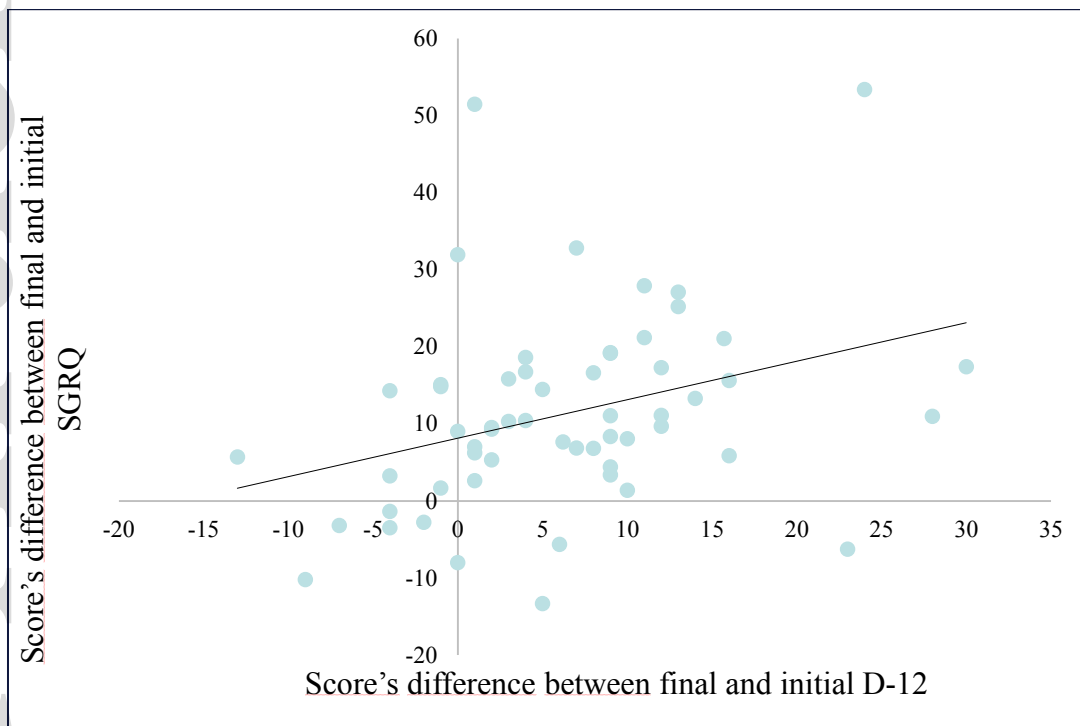
SD: Standard Deviation; SEM: Standard Error of the Measure; SGRQ: St George's Respiratory Questionnaire

Figure legends:

Figure 1: association between change in D-12 and change in SGRQ during Pulmonary rehabilitation.

Figure 2: Receiver operator characteristic (ROC) curve using a change in D-12 score of -6 to best predict achievement of minimum clinically important improvement in SGRQ.

Figure 1: association between change in D-12 and change in SGRQ during Pulmonary rehabilitation



D-12: Dyspnea-12 questionnaire; SGRQ: St George's Respiratory Questionnaire

Figure 2: Receiver operator characteristic (ROC) curve using a change in D-12 score of -6 to best predict achievement of minimum clinically important improvement in SGRQ

