The modified Medical Research Council scale misclassifies exertional breathlessness among people referred for exercise testing

David Gustafsson [1,2], Viktor Elmberg [1,2], Linus Schiöler [3], Dennis Jensen [4,5] and Magnus Ekström [1]

[1]Department of Respiratory Medicine, Allergology and Palliative Medicine, Institution for Clinical Sciences in Lund, Lund University, Lund, Sweden. [2]Department of Clinical Physiology, Blekinge Hospital, Karlskrona, Sweden. [3]Occupational and Environmental Medicine, School of Public Health and Community Medicine, Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. [4]Clinical Exercise and Respiratory Physiology Laboratory, Department of Kinesiology and Physical Education, Faculty of Education, McGill University, Montréal, QC, Canada. [5]Research Institute of the McGill University Health Centre, Translational Research in Respiratory Diseases Program and Respiratory Epidemiology and Clinical Research Unit, Montréal, QC, Canada.

Corresponding author: David Gustafsson (davidolofjohan@gmail.com)

Shareable abstract (@ERSpublications)
Among people referred for clinical exercise testing, a low mMRC scale rating (0–1) does not preclude the presence of abnormally high exertional breathlessness or impaired exercise capacity. https://bit.ly/3QuLmQI

Cite this article as: Gustafsson D, Elmberg V, Schiöler L, *et al*. The modified Medical Research Council scale misclassifies exertional breathlessness among people referred for exercise testing. *ERJ Open Res* 2023; 9: 00592-2023 [DOI: 10.1183/23120541.00592-2023].

Received: 14 Aug 2023
Accepted: 1 Nov 2023

Abstract

Background Exertional breathlessness is a major symptom in cardiorespiratory disease and is often assessed using the modified Medical Research Council (mMRC) questionnaire. The mMRC might underestimate exertional breathlessness in people with impaired exercise capacity who have reduced their physical activity to avoid the symptom. We aimed to evaluate the ability of mMRC to detect abnormally high exertional breathlessness or abnormally low exercise capacity during incremental cycle exercise testing (IET).

Methods A secondary analysis of data from a randomised controlled trial of outpatients aged 18 years or older referred for IET was carried out. Participants completed the mMRC before IET. Abnormally high exertional breathlessness was defined as a breathlessness (Borg 0–10) intensity response more than the upper limit of normal. Abnormally low exercise capacity was defined using published reference equations. The sensitivity, specificity, accuracy and discriminative ability of each mMRC rating to detect each outcomewas calculated.

Results 92 participants were included; the mean age was 59 years, 61% were male, and 64% and 15% had mMRC 1 and ⩾2, respectively. An mMRC ⩾2 had the highest accuracy (71%) to detect abnormally high exertional breathlessness, with a specificity of 93% but a sensitivity of only 28%, failing to identify 72% of people with abnormally high exertional breathlessness. The accuracy, specificity and sensitivity for abnormally low exercise capacity was 64%, 88% and 19%, respectively.

Conclusion Among people referred for clinical exercise testing, the mMRC dyspnoea scale misclassified exertional breathlessness and exercise capacity assessed using cycle IET, with substantial underdetection. A mMRC dyspnoea rating of 0–1 does not preclude the presence of abnormally high exertional breathlessness or abnormally low exercise capacity.

Introduction

Exertional breathlessness is a cardinal symptom in people with cardiorespiratory disease [1], and is linked to impaired physical capacity [2] and activity [3], which can lead to a downward spiral of deconditioning and further worsening of breathlessness [4]. High levels of exertional breathlessness in daily life are associated with impaired wellbeing [5], and an abnormally high risk of morbidity and mortality [4, 6].

Valid assessment of exertional breathlessness is important for clinical evaluation and management but is challenging [7]. In clinical practice and research, the individual is often asked to recall the level of breathlessness experienced during a time period using a questionnaire. The modified Medical Research Council (mMRC) breathlessness scale [8] is a widely used questionnaire to categorise the level of activity-related breathlessness and to determine eligibility for clinical trials [9]. The mMRC is also used by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) to assess symptom burden of COPD [10]. The mMRC reflects the level of exertion (such as walking uphill) at which breathlessness limits physical activity [8], but does not measure the symptom intensity *per se*, and may be influenced by other factors such as the person's cardiorespiratory fitness [11]. An important limitation of the mMRC is that it does not assess breathlessness in relation to a standardised level of exertion, and therefore might underestimate exertional breathlessness and impaired exercise capacity in people who have decreased their physical activity levels to avoid the symptom [12]. Misclassification of exertional breathlessness using the mMRC can also arise as some people find the questionnaire illogical or confusing to use [13].

Following the basic principles of psychophysics, exertional breathlessness should be measured in relation to the magnitude of symptom stimulus, *i.e.*, the level of exertion [14]. A gold standard method to assess exertional breathlessness is using an incremental cycle exercise test (IET) [7, 15, 16]. Reference equations for the breathlessness intensity response (on the Borg 0–10 category-ratio (CR10) scale [17]) during cycle IET were recently published [18]. Using these reference equations, abnormally high exertional breathlessness can be defined as a Borg CR10 intensity rating above the predicted upper limit of normal (ULN). The ULN corresponds to the 95th percentile of breathlessness intensity ratings in the healthy reference population for a given age, sex, height and power output (W) expressed as the percentage of the person's predicted maximum power output (%predW_{max}) [18]. The reference values enable evaluation of exertional breathlessness in a more standardised way during a standardised IET.

No study has previously evaluated the ability of the mMRC scale to identify people with abnormally high exertional breathlessness or abnormally low exercise capacity assessed using a standardised IET. This is important to investigate as mMRC might underestimate the presence of abnormally high exertional breathlessness as people reduce their activity level to avoid the symptom, and as mMRC is widely used in clinical care [19]. Standardised exercise testing could potentially be used to unmask this otherwise hidden breathlessness burden [12]. An improved understanding of the measuring of breathlessness could have implications for how patients' symptoms are assessed and managed across a wide range of conditions including cardiorespiratory diseases.

The aim of this study was to evaluate, among people referred for IET, the ability of the mMRC scale ratings to identify the presence of 1) abnormally high exertional breathlessness and 2) abnormally low exercise capacity on standardised cycle IET. We were particularly interested in evaluating the rate of symptom unmasking; that is, the rate of abnormally high exertional breathlessness on IET among people with little to no self-rated breathlessness in daily life (mMRC 0–1).

Methods

Design and population

This was a secondary analysis of data from a randomised controlled trial (RCT) of breathlessness during IET conducted at the Department of Clinical Physiology, Blekinge Hospital, Karlskrona, Sweden [20]. The trial included outpatients aged 18 years or older who were referred for cycle IET between March and December 2018. Reasons for referral were mostly suspected chronic coronary syndrome, as well as suspected exercise-induced arrythmias, occupational health screening and unexplained breathlessness [20]. The present analyses addressed *de novo* objectives independent of the original RCT that have not been presented previously.

Inclusion criteria for the present analysis were available self-reported data on the mMRC breathlessness scale before the IET and at least two Borg CR10 scale breathlessness intensity ratings at any time during the exercise part of the IET, including at peak exercise. In this analysis, only data from the start of the exercise phase to the symptom-limited peak of exercise were used. Breathlessness intensity ratings collected before and after IET were not included.

Ethical considerations

This study was approved by the ethics committee of Lund University in Sweden (Dnr: 2017/310). All participants provided informed written consent. The trial was registered with ClinicalTrials.gov (NCT03468205) before recruitment of the first participant. The study is reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [21].

Assessments

Before the IET, participants completed the mMRC breathlessness scale ("mark the alternatives that applies to your situation in the last two weeks"), and questionnaires about their smoking status (current, former, never) and presence of physician-diagnosed health conditions and medical procedures (including COPD; asthma; and cardiovascular disease (CVD), which was collectively defined in the present study as the participant having any one or combination of cardiovascular insult, myocardial infarction, angina, congestive heart failure, atrial fibrillation, prior invasive procedure against arterial stenosis, arterial aneurysm, bypass or balloon angioplasty of the coronary arteries).

A symptom-limited cycle IET was performed according to current Swedish guidelines [22]. The protocol was the same as that used in the cohort the normal range equations are based on. Initial work rate was usually 30 W for women and 50 W for men, although higher (up to 90 W) or lower values could be used depending on the participant's expected exercise capacity, as judged by the responsible staff. Incremental increases were also based on the expected exercise capacity, with the aim to obtain an IET duration of about 8 min. Increments of 10 $W \cdot min^{-1}$, 15 $W \cdot min^{-1}$ or 20 $W \cdot min^{-1}$ were used for all participants, with 10 $W \cdot min^{-1}$ increments used for older and frail participants and 20 $W \cdot min^{-1}$ increments used for younger and more fit participants, as judged by the staff. Every 2 min during IET and at peak exercise, participants rated the intensity of their perceived breathlessness using the Borg CR10 scale [17]. Participants were asked "How strong is your breathlessness now?" and rated their breathlessness from 0 "nothing at all" to 10 "extremely strong".

Statistical analyses

Abnormally high exertional breathlessness was defined as having a Borg CR10 scale breathlessness intensity rating more than the predicted ULN at any point during the exercise phase of the IET [23]. In addition, breathlessness was compared between participants by calculating each breathlessness rating's probability of normality, using the normative reference equations [23]. The probability of normality was defined as the probability of observing an equal or higher Borg CR10 scale breathlessness intensity rating among healthy people at a similar predicted maximal work capacity ($W\%pred_{max}$), according to Swedish reference ranges [24], with a lower probability reflecting more abnormal (severe) exertional breathlessness [23]. The lowest probability of normality (reflecting the most severe exertional breathlessness) during the IET was plotted against the mMRC ratings. Abnormally low exercise capacity was defined as a peak exercise capacity $<75\%predW_{max}$ according to Swedish reference ranges [24]. Characteristics were tabulated by the presence of abnormally high exertional breathlessness and abnormally low exercise capacity using mean±SD and median with range or interquartile range (IQR) for continuous variables with normal and skewed distribution, respectively.

Sensitivity, specificity, accuracy and discriminative ability (c-statistic) of each mMRC rating were calculated for detecting abnormally high exertional breathlessness and abnormally low exercise capacity, respectively. The c-statistic was analysed using receiver operating characteristic curves. Estimates were presented with 95% confidence intervals (CIs). Statistical significance was defined as two-sided $p<0.05$. Statistical analyses were conducted using the software packages STATA version 17.0 (StataCorp LP, College Station, TX, USA).

Results

Participants

A total of 92 participants were included with a mean±SD age of 59±13.5 years, 61% were male, 20 (22%) had an mMRC rating of 0, 59 (64%) had an mMRC rating of 1 and 13 (14%) had an mMRC rating of ⩾2 (table 1). The proportion of participants who had abnormally high exertional breathlessness during the IET was 35%. The proportion of participants who had abnormally low exercise capacity was also 35%. The proportion of participants who had both abnormally high exertional breathlessness and abnormally low exercise capacity was 22%. Compared to people whose exertional breathlessness was within the normal predicted range, people with abnormally high exertional breathlessness had significantly lower peak exercise capacity and were more likely to be current or former smokers and to have a comorbid cardiovascular and/or pulmonary disease (table 1).

mMRC to identify abnormally high exertional breathlessness

Although higher mMRC ratings were associated with abnormally high breathlessness during IET, people with mMRC 0–1 had variable breathlessness intensity ratings during IET, with some people having breathlessness intensity ratings well within normal predicted limits and some having abnormally high exertional breathlessness (figure 1).

https://doi.org/10.1183/23120541.00592-2023

TABLE 1 Characteristics of participants

	All participants	With abnormally high exertional breathlessness during IET	With normal exertional breathlessness during IET	With abnormally low exercise capacity	With normal exercise capacity
Participants n	92	32	60	32	60
Age years	59.0±13.5	60.4±13.3	58.3±13.7	57.9±16.4	59.9±11.7
Male	56 (61)	17 (53)	39 (65)	18 (56)	38 (63)
Smoking status					
Current smoker	14 (15)	7 (22)	7 (12)	6 (19)	8 (13)
Former smoker	39 (42)	13 (41)	26 (43)	11 (34)	28 (47)
Never-smoker	38 (41)	12 (38)	26 (43)	15 (47)	23 (38)
COPD	1 (1)	1 (3)	0	1 (3)	0
Asthma	10 (11)	5 (16)	5 (8)	4 (12)	6 (10)
Hypertension	40 (43)	19 (59)	21 (35)	15 (47)	25 (42)
Cardiovascular disease	17 (18)	10 (31)	7 (12)	9 (28)	8 (13)
mMRC breathlessness rating					
0	20 (22)	3 (9)	17 (28)	3 (9)	17 (28)
1	59 (64)	20 (62)	39 (65)	23 (72)	36 (60)
2	11 (12)	7 (22)	4 (7)	5 (16)	6 (10)
3	1 (1)	1 (3)	0	1 (3)	0
4	1 (1)	1 (3)	0	0	1 (2)
Referred for IET as part of occupational screening	12 (13)	1 (3)	11 (18)	1 (3)	11 (18)
Peak power output W	158.9±56.5	126.4±46.3	176.3±54.0	121.4±46.2	178.9±51.3
Peak power output % pred	80.8±16.4	69.3±15.7	87.0±13.2	63.0±9.6	90.3±10.2
Abnormally low exercise capacity[#]	32 (35)	20 (62)	12 (20)	32 (100)	0
Abnormally high exertional breathlessness during IET	32 (35)	32 (100)	0	20 (62)	12 (20)

Data are presented as mean±SD or n (%). IET: incremental exercise test; mMRC: modified Medical Research Council scale. [#]: <75% pred.

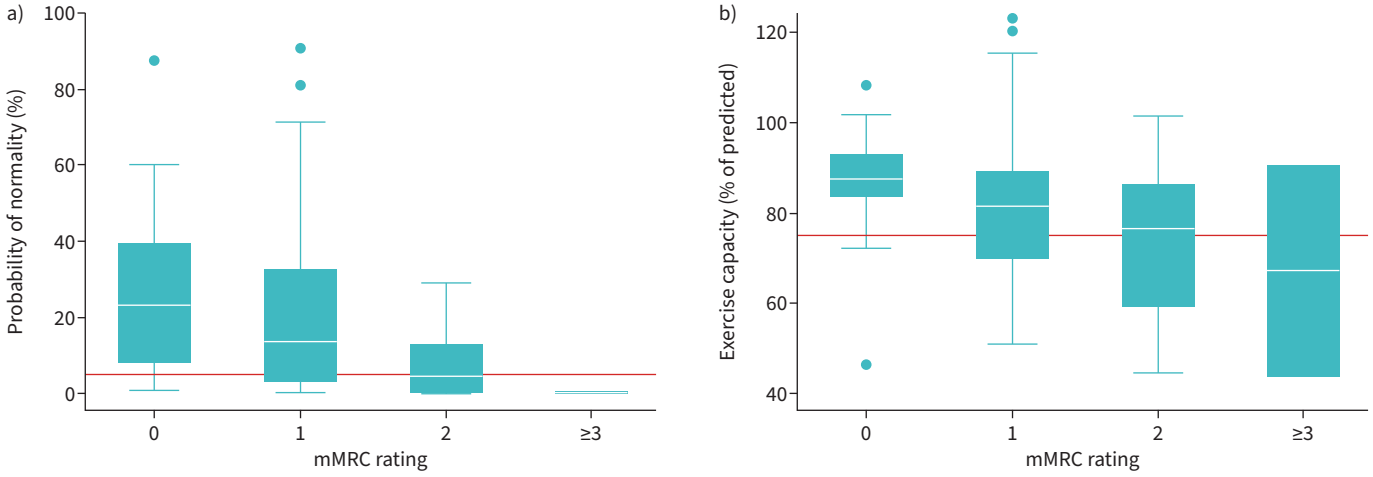

FIGURE 1 a) Low modified Medical Research Council (mMRC) ratings tends to have a higher probability of normality. Relationship between self-rated breathlessness before the test on the mMRC scale and the severity of exertional breathlessness during incremental cycle exercise testing (IET). The severity of exertional breathlessness during IET was expressed as the probability of normality (y-axis), which is the predicted probability of having an equal or higher breathlessness (Borg CR10) rating among healthy people calculated using normative reference equations [24]. A low probability reflects more abnormally high (severe) breathlessness. For each participant, the lowest probability of normality (the most abnormal breathlessness during the IET) was analysed. The red line denotes the upper limit of normal breathlessness according to the reference equations (*i.e.* only 5% have an equal or higher breathlessness rating/the probability of normal is 5% or lower). The plot shows that participants with low mMRC ratings tend to have more normal breathlessness rating during IET, but with a high level of intra-individual variation. For instance, among the participants with an mMRC rating of 1, the lower quartile is below the 5% line, meaning that >25% of those participants experience abnormally high breathlessness at some point during cycle IET. b) Participants with high mMRC ratings tend to have lower exercise capacity. Exercise capacity is described as a percentage of the predicted value according to the normal range interval. Reference line denotes the lower limit of normal (75% of predicted exercise capacity). The higher the mMRC score, the lower the exercise capacity is. The plot shows there is a connection between mMRC rating and exercise capacity, but among those with an mMRC rating of ⩾3, >25% have normal exercise capacity whereas >25% of those with an mMRC rating of 1 have abnormally low exercise capacity.

Abnormally high exertional breathlessness was present in 69% of people with mMRC ⩾2 *versus* 29% of people with mMRC 0–1 (p=0.024) (table 2). For identifying abnormally high exertional breathlessness during the IET, mMRC ⩾1 had an accuracy of 50%, specificity of 91% and sensitivity of 28%; and mMRC ⩾2 had an accuracy of 71%, specificity of 93% and sensitivity of 28%. The cut-off with the greatest discriminative ability was mMRC ⩾2, with a c-statistic of 0.67 (figure 2).

mMRC to identify abnormally low exercise capacity

Although higher mMRC ratings were associated with lower exercise capacity, a considerable proportion of people with higher mMRC ratings had normal exercise capacity, or vice versa (figure 1).

TABLE 2 Ability of mMRC to detect the presence of abnormally high exertional breathlessness and abnormally low exercise capacity identified using symptom-limited incremental cycle exercise testing (IET)

mMRC cut-off rating	Prevalence, n (%)	Sensitivity % (95% CI)	Specificity % (95% CI)	Accuracy %	C-statistic (95% CI)
Abnormally high exertional breathlessness[#]					
⩾1	72 (78)	91 (75–98)	28 (18–41)	50	0.59 (0.52–0.67)
⩾2	13 (14)	28 (14–46)	93 (84–98)	71	0.67 (0.57–0.76)
Abnormally low exercise capacity[¶]					
⩾1	72 (78)	91 (75–98)	28 (18–41)	50	0.59 (0.52–0.67)
⩾2	13 (14)	19 (7–36)	88 (77–95)	64	0.61 (0.51–0.71)

The discriminative ability of mMRC cut-offs to identify the presence of abnormally high exertional breathlessness during a cycle IET. C-statistics were calculated using receiver operating characteristic analysis. mMRC: modified Medical Research Council breathlessness scale; c-statistic: concordance statistic. [#]: Borg CR-10 above the limit of normal; [¶]: <75% pred.

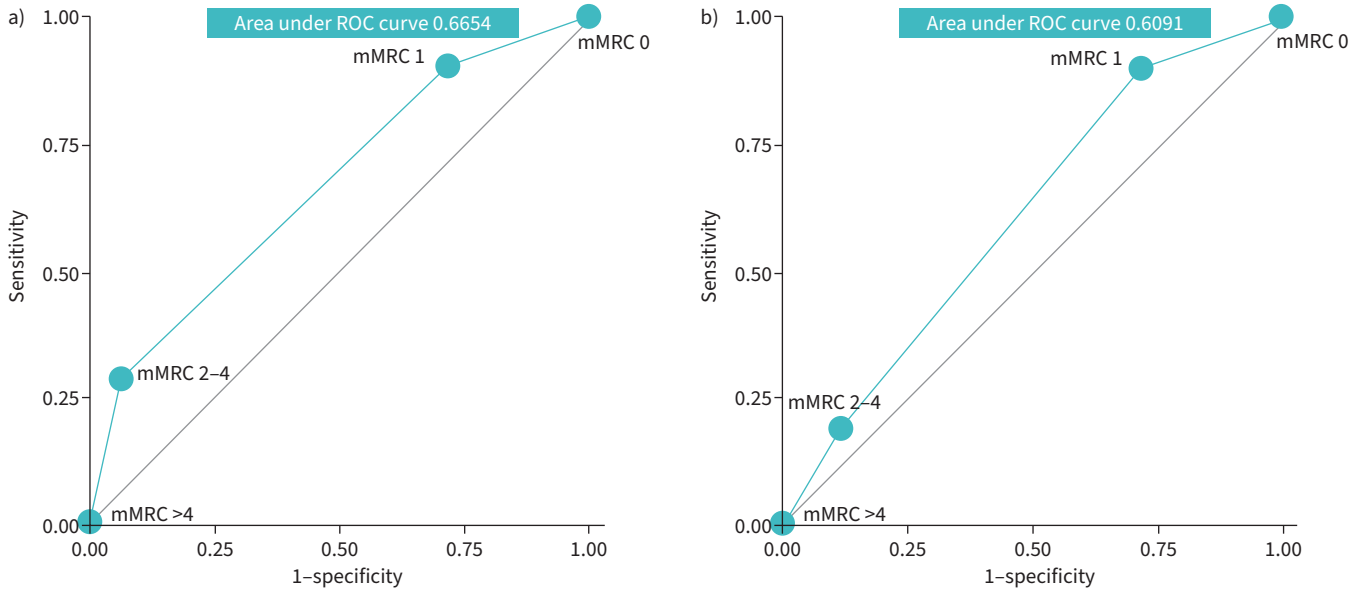

FIGURE 2 Discriminative ability of the modified Medical Research Council (mMRC) breathlessness ratings to predict the presence of a) abnormal breathlessness and b) reduced exercise capacity during a subsequent incremental cycle exercise test. ROC: receiver operating characteristics.

Abnormally low exercise capacity was present in 46% of people with mMRC ⩾2 *versus* 33% of people with mMRC 0–1 (p=0.14). For identifying abnormally low exercise capacity during the IET, mMRC ⩾1 had an accuracy of 50%, specificity of 28% and sensitivity of 91%; and mMRC ⩾2 had an accuracy of 64%, specificity of 88% and sensitivity of 19%. The cut-off with the greatest discriminative ability was mMRC ⩾2, with a c-statistic of 0.61 (figure 2).

Unmasking of abnormal exertional breathlessness and exercise capacity

Among participants with mMRC 0 (n=20), three (15%) had abnormally high exertional breathlessness. Among the 59 participants with mMRC 1, 20 (34%) had abnormally high exertional breathlessness. Altogether, among the 79 participants with mMRC 0–1, 29% had abnormally high exertional breathlessness. The prevalence of abnormally low exercise capacity was 15% for participants with mMRC 0, 39% with mMRC 1 and 33% with mMRC 0–1 (table 1).

Discussion

Main findings and importance

The main findings are that: 1) the mMRC breathlessness scale misclassifies abnormally high exertional breathlessness on IET among people referred for clinical exercise testing; and 2) IET can unmask abnormally high exertional breathlessness among individuals that present clinically with little to no self-reported burden of breathlessness (mMRC 0–1). We also found that although an mMRC rating of ⩾2 was the most accurate cut-off point for identifying abnormally high exertional breathlessness or abnormally low exercise capacity, this cut-off had a sensitivity of only 28% and 19%, meaning that 72% and 81% of people who had abnormally high exertional breathlessness and abnormally low exercise capacity on IET were "false negative" using mMRC, respectively. Thus, an mMRC rating of 0–1 does not preclude the presence of abnormally high exertional breathlessness or abnormally low exercise capacity, both of which can be unmasked using a standardised cycle IET.

This is the first study to assess the sensitivity and specificity of the mMRC scale for identifying people with abnormally high exertional breathlessness, evaluated using reference equations during cycle IET [23]. Even if this study was conducted in a relatively unselected sample of people referred for IET in clinical care, and does not pertain to any specific disease group such as COPD, the current findings raise concerns regarding the use of mMRC to classify the respiratory symptom burden in clinical guidelines and care, such as in COPD [19] and heart failure (where an adapted version of the mMRC is used [25], the New York Heart Association (NYHA) scale [26]). The mMRC is also widely used in epidemiological studies [27] and for selecting people to participate in clinical trials on breathlessness [28]. The low sensitivity of mMRC for identifying people with abnormally high exertional breathlessness (and/or

abnormally low exercise capacity) may contribute to delayed or insufficient identification and management of exertional breathlessness (and/or exercise intolerance) and the underlying condition(s) – which warrants further investigation.

Strengths and limitations

Strengths of the present study are the inclusion of a relatively unselected sample of people undergoing clinical cycle IET, who provided standardised self-ratings of breathlessness in daily life using the mMRC and during the IET using the Borg CR10 scale as part of a clinical trial. Breathlessness intensity and peak power output responses were evaluated using published normative reference equations for the present IET protocol in a large Swedish database [23, 24]. Limitations include that this was a single-centre study with few participants with mMRC ratings of 3 or 4, and only one person with COPD.

Implications

For the clinician, the present findings suggest that: 1) the mMRC breathlessness scale is likely to misclassify the presence of abnormally high exertional breathlessness and/or abnormally low exercise capacity in patients – with a sensitivity of just 28% for detecting abnormally high exertional breathlessness and 19% for detecting abnormally low exercise capacity among people referred for clinical cycle IET; and 2) a standardised cycle IET can uncover "hidden" exertional breathlessness and/or exercise intolerance in a substantial number of patients. However, given obvious differences in cost, time, equipment, resources and feasibility of people completing the mMRC breathlessness scale compared with a cycle IET, and given its high specificity, the mMRC could be useful as a first step to identify people with a rating $\geqslant$2, who are likely to have abnormally high exertional breathlessness and/or abnormally low exercise capacity, which is also in accordance with international clinical guidelines [29]. But importantly, a low mMRC breathlessness rating of 0–1 does not preclude the presence of abnormal "hidden" exertional breathlessness and/or exercise intolerance, and a wider clinical evaluation including standardised exercise testing should be considered in people suspected of having abnormally high exertional breathlessness and/or abnormally low exercise capacity.

An important next research step is to evaluate the potential misclassification of using mMRC, compared with IET, in clinical populations, such as people with COPD, where mMRC is part of the GOLD management recommendations [19], and in people with heart failure where management is guided by the NYHA scale, which is an adapted version of the mMRC breathlessness scale [30]. Regarding the use of the normal range intervals and IET, it would be valuable to validate their use in the evaluation of treatment results, for instance through intra-individual comparisons before and after exercise intervention used in cardiopulmonary rehabilitation.

Conclusion

Among people referred for clinical exercise testing, mMRC breathlessness ratings misclassified the presence of abnormally high exertional breathlessness and abnormally low exercise capacity assessed using a standardised cycle IET, with low sensitivity and frequent false negative results for people with mMRC 0–1.

Provenance: Submitted article, peer reviewed.

This study is registered at www.clinicaltrials.gov with identifier number NCT03468205. Upon reasonable request and after ethical approval, the study data can be obtained by contacting Susanne Lundgren, head of the clinical physiology department, Blekingesjukhuset, Karlskrona, Sweden.

Conflict of interest: None declared.

Support statement: This study was supported by Vetenskapsrådet grant 2019-02081. Funding information for this article has been deposited with the Crossref Funder Registry.

Ethics statement: This study was approved by the ethics committee of Lund University in Sweden (Dnr: 2017/310). All participants provided informed written consent. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

References

1 Parshall MB, Schwartzstein RM, Adams L, *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: 435–452.

2 Punekar YS, Riley JH, Lloyd E, *et al.* Systematic review of the association between exercise tests and patient-reported outcomes in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 2487–2506.

3 Kochovska S, Currow D, Chang S, *et al.* Persisting breathlessness and activities reduced or ceased: a population study in older men. *BMJ Open Respir Res* 2022; 9: e001168.
4 Sassi-Dambron DE, Eakin EG, Ries AL, *et al.* Treatment of dyspnea in COPD. A controlled clinical trial of dyspnea management strategies. *Chest* 1995; 107: 724–729.
5 Currow DC, Dal Grande E, Ferreira D, *et al.* Chronic breathlessness associated with poorer physical and mental health-related quality of life (SF-12) across all adult age groups. *Thorax* 2017; 72: 1151–1153.
6 Ramon MA, Ter Riet G, Carsin AE, *et al.* The dyspnoea-inactivity vicious circle in COPD: development and external validation of a conceptual model. *Eur Respir J* 2018; 52: 1800079.
7 Lewthwaite H, Jensen D, Ekstrom M. How to assess breathlessness in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2021; 16: 1581–1598.
8 Elliott-Button HL, Johnson MJ, Nwulu U, *et al.* Identification and assessment of breathlessness in clinical practice: a systematic review and narrative synthesis. *J Pain Symptom Manage* 2020; 59: 724–733.e19.
9 Ekström M, Ferreira D, Chang S, *et al.* Effect of regular, low-dose, extended-release morphine on chronic breathlessness in chronic obstructive pulmonary disease: the BEAMS randomized clinical trial. *JAMA* 2022; 328: 2022–2032.
10 Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD, 2023. Date last accessed: 26 December 2022. Date last updated: November 2022. https://goldcopd.org/
11 Hajiro T, Nishimura K, Tsukino M, *et al.* Analysis of clinical methods used to evaluate dyspnea in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998; 158: 1185–1189.
12 Soumagne T, Laveneziana P, Veil-Picard M, *et al.* Asymptomatic subjects with airway obstruction have significant impairment at exercise. *Thorax* 2016; 71: 804–811.
13 Yorke J, Khan N, Garrow A, *et al.* Evaluation of the individual activity descriptors of the mMRC breathlessness scale: a mixed method study. *Int J Chron Obstruct Pulmon Dis* 2022; 17: 2289–2299.
14 Ekstrom M, Elmberg V, Lindow T, *et al.* Breathlessness measurement should be standardised for the level of exertion. *Eur Respir J* 2018; 51: 1800486.
15 Bonini M, Fiorenzano G. Exertional dyspnoea in interstitial lung diseases: the clinical utility of cardiopulmonary exercise testing. *Eur Respir Rev* 2017; 26: 160099.
16 Stickland MK, Neder JA, Guenette JA, *et al.* Using cardiopulmonary exercise testing to understand dyspnea and exercise intolerance in respiratory disease. *Chest* 2022; 161: 1505–1516.
17 Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982; 14: 377–381.
18 Elmberg V, Schioler L, Lindow T, *et al.* Reference equations for breathlessness during incremental cycle exercise testing. *ERJ Open Res* 2023; 9: 00566-2022.
19 Bereza BG, Troelsgaard Nielsen A, Valgardsson S, *et al.* Patient preferences in severe COPD and asthma: a comprehensive literature review. *Int J Chron Obstruct Pulmon Dis* 2015; 10: 739–744.
20 Elmberg V, Ekstrom M. Effect of the trajectory of exertional breathlessness on symptom recall and anticipation: a randomized controlled trial. *PLoS One* 2020; 15: e0238937.
21 von Elm E, Altman DG, Egger M, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014; 12: 1495–1499.
22 Jorfeldt L, Pahlm O. Kliniska Arbetsprov: Metoder för Diagnos och Prognos. Lund, Studentlitteratur, 2013.
23 Elmberg V, Schiöler L, Lindow T, *et al*. Reference equations for breathlessness during incremental cycle exercise testing. *ERJ Open Res* 2023; 9: 00566-2022.
24 Brudin L, Jorfeldt L, Pahlm O. Comparison of two commonly used reference materials for exercise bicycle tests with a Swedish clinical database of patients with normal outcome. *Clin Physiol Funct Imaging* 2014; 34: 297–307.
25 Ahmadi Z, Igelstrom H, Sandberg J, *et al.* Agreement of the modified Medical Research Council and New York Heart Association scales for assessing the impact of self-rated breathlessness in cardiopulmonary disease. *ERJ Open Res* 2022; 8: 00460-2021.
26 Booth S. Improving research methodology in breathlessness: a meeting convened by the MRC clinical trials unit and the Cicely Saunders Foundation. *Palliat Med* 2006; 20: 219–220.
27 Olsson M, Currow DC, Johnson MJ, *et al.* Prevalence and severity of differing dimensions of breathlessness among elderly males in the population. *ERJ Open Res* 2022; 8: 00553.
28 Lammi MR, Baughman RP, Birring SS, *et al.* Outcome measures for clinical trials in interstitial lung diseases. *Curr Respir Med Rev* 2015; 11: 163–174.
29 Venkatesan P. GOLD COPD report: 2023 update. *Lancet Respir Med* 2023; 11: 18.
30 McDonagh TA, Metra M, Adamo M, *et al.* 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2021; 42: 3599–3726.