Reviewer's report

Title: Interest of the modified Medical Research Council scale for the assessment of dyspnea in daily living in obesity: a pilot study

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Reviewer: Dennis Jensen

Reviewer's report:

The purpose of the present study was to examine whether the modified MRC (mMRC) dyspnea scale can be used to assess activity-related dyspnea in obese subjects. To this end, the authors examined the correlative relationships between mMRC scale measures of activity-related dyspnea and performance on the 6 minute walk test as well as various lung function and biological parameters in 45 obese subjects with a mean BMI of 43 kg/m2. Based on their observations, the authors concluded that the mMRC scale might be a useful and pragmatic tool to assess chronic activity-related dyspnea in this group of subjects.

MAJOR & MINOR COMMENTS...

Background:

# The rationale for the study was poorly developed – why is it important (clinically, physiologically, etc.) to validate a scale to assess dyspnea in daily living in obesity subjects? Will such validation aid in their clinical management? You provide no rationale as to why the correlation between the various biological parameters and mMRC dyspnea scale measures were examined? For example, is there evidence to support a mechanistic link between HbA1c and activity-related dyspnea?

o Why did you choose the mMRC when several previous studies have reported on the possible utility and responsiveness of the BDI, OCD and CRQ in obesity? For example, Ofir et al. (Journal of Applied Physiology, 102, 2217-2226, 2007) and Collet et al. (Int. J. Obesity, 31, 700-706, 2007) have already provided some evidence that the Baseline Dyspnea Index (BDI) may be a good tool to evaluate the severity of activity-related dyspnea in obesity. Ofir et al., (2007) also provided some evidence to support the utility of the Oxygen Cost Diagram (OCD) to evaluate activity-related dyspnea in obesity. Finally, El-Gamal et al., (Chest 128, 3870-3874, 2005) previously demonstrated the responsiveness of the Chronic Respiratory Disease Questionnaire (CRQ) to surgically induced weight loss by gastroplasty in morbidly obese subjects.

o Parshall et al.,(http://ajrccm.atsjournals.org/content/suppl/2012/02/10/185.4.435.DC1/Feb_15_ATSdyspnea_statement.pdf) recently reviewed the various scales used to assess dyspnea.

# Paragraph 2, 3rd sentence: “..., Collet et al. found that a BMI > 49 kg/m2 was associated with more severe dyspnea.” More severe dyspnea than who/what –
less obese and/or normal weight subjects? You should also mention that the BDI was used by Collet et al. to evaluate activity-related dyspnea.

# Paragraph 2, 5th sentence: You point out that the mechanisms of dyspnea in obesity remain unclear, but you don’t allude to the possible contributory factors, including increased metabolic and, by extension, ventilatory demands of exercise, particularly weight bearing exercise. There are several recently published articles (both original and review) on the topic of dyspnea and obesity in both health and disease that you have not referenced (see examples below). These articles may help you allude (briefly) to the possible mechanisms of activity-related dyspnea in obese subjects.


# You may also want to consider the recent work of Sava et al., (BMC Pulmonary Medicine, 10:55, 2010) in your background/rationale as well as in your discussion.

Methods:

# A limitation of the current study is failure to include age and sex matched groups of overweight and normal weight subjects for comparison purposes. Inclusion of various BMI groups would have allowed you to make mMRC comparisions between BMI categories rather than to compare BMI and physical characteristics between groups arbitrarily defined as ‘dyspneic’ and ‘non-dyspneic’ according to the mMRC (see below).

# Clinical characteristics and mMRC scale: use “sex” rather than “gender” throughout text. You mention in this section that information on “treatments” were systematically recorded; however, you did not report in your results the number of subjects receiving pharmacological (e.g., statins) or non-pharmacological (e.g., CPAP) treatments for the various co-morbidities (e.g., diabetes, dyslipidemia, sleep apnea, etc.) present in your study population.

# Pulmonary function tests: Results were expressed as a % of predicted values – what predicted equations did you use? Provide the relevant references.

- It could be argued that arterial blood gases should be included in the biological parameters section rather than the pulmonary function tests section of the methods.

# Statistical analysis: What was the justification for separating groups into ‘dyspneic’ and ‘non-dyspneic’ according to an mMRC score of #1 and 0, respectively?

- The number of subjects included in this study (n=45) is relatively small considering the cross-sectional and correlative study design.
Results:

# Dyspnea assessment by the mMRC scale and 6MWT

- How does the mean distance of 420 meters covered during the 6MWT compare to published normative data (e.g., Casanova et al., Eur. Respir. J. 37, 150-156, 2011)?

# Relationships between the mMRC scale and clinical characteristics, PFTs and biological parameters

- Paragraph 1: “Of notes, there was no correlation between the mMRC scale and age, gender, smoking history, arterial blood gases, metabolic parameters and the apnea/hypopnea index.” First, how do you correlate mMRC scale ratings with gender? In other words, I don’t understand the analyses you performed that allowed you to draw the conclusion that these parameters had no influence on mMRC scores? Does “there was no correlation” mean that there were no between group differences (i.e., dyspneic vs. non-dyspneic) in these parameters; that is, dyspneic and non-dyspneic groups were matched for age, gender, smoking history, etc.? Second, you have not reported in your Table 2 of subject characteristics your apnea/hypopnea index scores.

- Paragraph 2: I’m confused by the following sentence: “The Borg score after 6MWT was correlated with a higher BMI (r=0.44, p<0.005) and lower FEV1 (r=-0.33, p<0.05), as demonstrated for the mMRC scale.” What do you mean by “…as demonstrated for the mMRC scale”? Are you referring to the results of your between-group comparisons here? If yes, then the word “correlation” is being used inappropriately.

- In my opinion, the most important correlative inter-relationships to examine in your study are those between Borg dyspnea ratings after the 6MWT, BMI and mMRC. You report a positive correlation between Borg scores after the 6MWT and BMI but you do not report the correlation coefficient of the relationship between (i) mMRC and dyspnea after the 6MWT or (ii) BMI and mMRC. Demonstration of statistically significant inter-relationships of these parameters provides some validation for the use of the mMRC in the assessment of dyspnea in obesity. In each case, the authors should include a figure the X-Y plots showing the relationships between these parameters? These figures would help the reader to identify the strength of the relationship and the scatter of the data around the line of best fit.

- Was the change in Borg scale ratings of dyspnea from rest to the end of the 6MWT different between “dyspneic” and ‘non-dyspneic’ groups? Did the change in Borg scale ratings from rest to the end of the 6MWT correlate with mMRC and/or BMI? By looking at the change, you account (at least in part) for variations in resting Borg dyspnea intensity ratings, which may vary depending on BMI and mMRC? For example, perhaps there’s no difference in the exercise-induced change in Borg scale dyspnea intensity ratings between ‘dyspneic’ and ‘non-dyspneic’ subgroups when potential differences in baseline Borg scale ratings are accounted for.
Discussion:

# Page 9, Paragraph 2: This seems like a relevant place to discuss the results of previously published studies by Collet et al., Ofir et al., and El-Gamal et al. who have provided some evidence to support the use of the BDI, OCD and CRQ to evaluate dyspnea in obesity. In fact, the study by El-Gamal is ideally designed to evaluate the utility and responsiveness of an assessment tool in obesity as they did measurements before and after gastroplasty-induced weight loss within the same subjects (rather than using a cross-sectional and/or correlative approach).

# Page 9, Paragraph 3: You should omit the word “compelling” from the following sentence: “Our study provides compelling evidence for the use of the mMRC scale in the assessment of dyspnea in daily living in obese subjects.” Furthermore, the sentence “Firstly, our results demonstrate some correlations between the mMRC scale and the Borg scale after 6MWT which assesses exertional dyspnea” is very misleading since you did not observe correlations (but rather between-group differences) between these parameters. Again, in my opinion, the word “correlation” is inappropriately used in this context.

# Page 10, Paragraph 2: Again, the authors provide no clear rationale for examining the relationship between mMRC and biological parameters. It would be nice to see inclusion of some physiological rationale to support these examinations.

# Page 10, Paragraph 3, last sentence: “Despite these limitations, this pilot study suggests that the mMRC scale might be interesting for the assessment…” I find the use of the word “interesting” in this sentence, in the manuscript title and in several parts of the manuscript to be quite awkward. By “interesting” do you mean useful?

# A limitation of the present study is the lack of standardization of the exercise stimulus used to provoke activity-related dyspnea (i.e., the 6MWT). Furthermore, there were no measures of cardio-metabolic, ventilatory and/or breathing pattern responses to explain between group differences in mMRC and/or Borg scores after the 6MWT. The data are difficult to interpret since both the distance walked during the 6MWT as well as the Borg scale ratings of dyspnea intensity after the 6MWT appeared to vary as a function of BMI and/or mMRC score. For example, your mMRC=0 group walked ~125 m farther in 6 minutes and had a BMI that was, on average, 8 kg/m2 lower than the mMRC #1 group. Standardization of the exercise stimulus is very important in any psycho-physiological study and would have helped to interpret your study results.

# Page 11, Conclusions: Again, you did not report a correlation between mMRC and Borg scores after the 6MWT – the terminology needs to be adjusted accordingly.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'