Author's response to reviews

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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Version: 4 Date: 18 July 2012

Author's response to reviews: see over
Dear Editor,

We thank you for the reviews regarding our manuscript. Please find the point-by-point responses to the 3 reviewers. We hope our answers will suit your requirements. We thank the reviewers for giving us the opportunity to improve the quality of our manuscript.

Sincerely,
Dr Claire LAUNOIS

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
Version: 3 Date: 28 May 2012
Reviewer: Amanda Piper

Reviewer's report:
The purpose of this study was to evaluate the mMRC scale in the assessment of dyspnea in obese subjects and determine its relationship with lung function and functional capacity. As previously found and confirmed by this study, breathlessness is common in obese individuals although no specific tool has been developed to assess dyspnea in this specific population. The authors found significant correlations between the mMRC scale and BMI, some lung function parameters and six-minute walking distance, suggesting that this scale could be used as a tool in assessing dyspnea in daily living in obese individuals.

The premise for the study is clinically relevant, the manuscript is generally well-written, with conclusions in keeping with the study findings. However, there are a few issues that could be clarified.

Major revisions/questions
1. Were the patients studied consecutive referrals, and was the respiratory evaluation part of their routine assessment, or was there a specific reason that these individuals were referred for respiratory assessment?

R1: The patients studied were consecutive referrals. They came from the Department of Nutrition and were referred for a systematic respiratory evaluation. There was no specific reason that they were referred for a respiratory assessment. This point has been clarified in the revised manuscript (P5-line 2).

2. As highlighted by the authors, the most common abnormalities seen in obese individuals are a decrease in ERV and FRC and an increase in oxygen consumption. Other parameters such as TLC, MVV and inspiratory muscle performance although lower in obese individuals are usually still within the normal range (as stated in the references cited by the authors), unless the patient is morbidly++ obese. It would be better to shorten this section, addressing those lung function parameters that best characterize the abnormality seen obese subjects. This then frees up some word count to discuss point 3 below.

R2: We fully agree with the reviewer. This section has been shortened as required (P4-line 11).
3. Biological parameters (such as Hb, fasting glucose and CRP) were measured with only one significant association with mMRC found. However, there is no information either in the introduction or the discussion as to why these particular parameters were chosen and why some association with the mMRC might have been expected. This aspect of the hypothesis has not been made clear.

R3: Hemoglobin and NTproBNP were assessed as potentially confounding factors that could increase dyspnea related to anemia or cardiac insufficiency. Moreover, previous studies showed that type 2 diabetes, insulin resistance and metabolic syndrome are associated with reduced lung function in obesity (Lecube A, Type 2 diabetes impairs pulmonary function in morbidly obese women: a case-control study. Diabetologia, Lecube A, Insulin resistance is related to impaired lung function in morbidly obese women: a case-control study. Diabetes Metab. Res. Rev. 2010, Leone, Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. Am. J. Respir. Crit. Care Med. 2009). We then decided to analyze the association between triglyceride, total cholesterol, fasting glucose, Hba1c and the mMRC dyspnea scale. This point has been clarified in the new version in the background section (P4-line 14) and in the discussion (P10-line 20).

4. Males are more likely to demonstrate central/upper body obesity, and therefore the results could be influenced by the make up of participants in this study. However, I found it unclear what proportion of subjects were male versus female. In Table 2 it states 17 male/28 female, but in Table 5 there are 29 males and 16 females reported. This needs to be clarified. There may be gender differences in the perception of dyspnea, and this could be looked at in future studies.

R4: We apologize for the mistake in Table 5 regarding the M/F numbers. There are 17 male and 28 female. It has been corrected in the new manuscript in Table 5. We agree that gender differences could be involved in the perception of dyspnea, but the number of patients included in our study was too low to analyze this parameter. This point has been discussed in the revised manuscript in the discussion section (P11-line 1).

5. While this is only pilot work, adding the BDI and comparing it to the mMRC in the same population would have been interesting and is a limitation of the study, as pointed out by the authors. While the mMRC may be able to be used to classify obese individuals with more severe breathlessness with activity, it remains to be seen whether it is sensitive to changes with intervention in this population and requires further investigation. Finally, adding a measure of health related quality of life and determining the degree this was related to mMRC in this obese population is also something that could be considered. These points might be seen as limitations and areas for future investigation.

R5: We agree that adding the BDI and comparing it to the mMRC would have been of great interest. The association between quality of life and mMRC would also have been of great interest. These points are clear limitations to our study and would be interesting to assess in future studies. These point have been discussed in the new version in the discussion section (P11, line 3).
Minor essential
Abstract, Background, 4th sentence – change “evaluate the interest” to “evaluate the use of the mMRC scale”
Methods, 3rd sentence – “monoxide”
Background, 1st paragraph, 1st sentence – change “actual” to “significant”
2nd paragraph, 3rd sentence – “series’
5th sentence – “Although the mechanisms of dyspnea in obesity remain unclear, it is moderately correlated with lung function.”
Switch the 6th and 7th sentences, replacing “Of note” with “However”
3rd paragraph, 1st sentence – change “interest” with “use”, and the 6-minute walk test with walk distance.
Methods
Patients, 2nd sentence – “>18 years”.
3rd sentence – “pulmonary function testing”
Pulmonary function tests, 3rd sentence – “in a sitting position”
Results and discussion, Demographics, 2nd paragraph, 4th sentence – “regarding smoking status”
6th Sentence – “Severe obstructive sleep apnea syndrome”
Relationships between mMRC scale etc, 1st paragraph – “Of note,”
2nd paragraph, 2nd sentence – could you clarify what you meant by “as demonstrated for the nMRC scale”.
3rd sentence – “between the Borg score” is better
Page 9, 2nd paragraph, 2nd sentence – “Regarding the mMRC scale, two versions of this scale have been used…. Other scales have been also been used to assess dyspnea. The Baseline Dyspnea Scale… that these other scale are much more time consuming ….”
3rd paragraph, 1st sentence – delete “yet”
9th sentence – “the abdominal contents on diaphragm position’.
10th sentence – While the FEV1 may be slightly reduced in patients with severe obesity, the FEV1/VC ratio is preserved as seen in our study”.
12th sentence – “Two studies have shown”. Also in this sentence and elsewhere in the discussion, distinguish between the 6MWT (the actual test) and 6MWD (the result generated). In this sentence it should be 6MWD.
16th sentence – the information about the fasting glucose would be better included in the paragraph below (4th paragraph)
4th paragraph, 4th sentence – “Of note”
5th paragraph, last sentence – “mMRC scale might be of value in the assessment of dyspnea”.

R6: We thank the reviewer for these suggestions. We have made all the changes proposed in the new version.

Discretionary
1. It would be clearer for the reader if the normal values for the biological measures were added to Table 5 rather than being listed in the Methods section.

R7: We agree that including the normal values in Table 5 is clearer for the reader. We made this change in table 5.
2. Do the authors have any information regarding fat distribution (eg Waist circumferences or waist/hip ratios) as fat distribution may have affected abdominal loads and lung volumes, contributing to dyspnea?

**R8:** We agree that fat distribution is an important point to assess. These measures were not systematically recorded for this pilot study. This point should be assessed in future studies. We discuss this point as a limitation of our study in the discussion section (P11-line 8).

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being Published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:** I declare I have no competing interests
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

Version: 3 Date: 1 June 2012

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?

R1: As stated in the background section, dyspnea is a very frequent symptom in obesity which is very difficult to assess in clinical practice. The absence of a validated scale in obesity leads to difficulties to assess this symptom in clinical practice. The mMRC is a very simple widely used, and not time-consuming scale which can be easily used in clinical practice. However, it has never been assessed in the context of obesity.

This point was made clearer in the new version (P4-line 21).

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 HbAlc and activity-related dyspnea?

R2: Hemoglobin and NTproBNP were assessed as potentially confounding factors that could increase dyspnea related to anemia or cardiac insufficiency.

Moreover, previous studies showed that type 2 diabetes, insulin resistance and metabolic syndrome are associated with reduced lung function in obesity (Lecube A, Type 2 diabetes impairs pulmonary function in morbidly obese women: a case-control study. Diabetologia, Lecube A, Insulin resistance is related to impaired lung function in morbidly obese women: a case-control study. Diabetes Metab. Res. Rev. 2010, Leone, Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. Am. J. Respir. Crit. Care Med. 2009). We then decided to analyze the association between triglyceride, total cholesterol, fasting glucose, Hba1c and the mMRC dyspnea scale.

This point has been clarified in the new version in the background section (P4-line 14) and in the discussion (P10-line 20).
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.

Parshall et al. (http://ajrccm.atsjournals.org/content/suppl/2012/02/10/185.4.435.DC1/Feb_15_ATSdyspnea_recently reviewed the various scales used to assess dyspnea.

R3: We agree that other scales have been assessed in dyspnea in obesity. We discussed more precisely this point and added the references proposed by the reviewer in the Discussion section (P9, line 10).

As explained in the discussion section, the mMRC is a very simple not time consuming scale which is widely used in clinical practice. Our study suggests that the mMRC scale might be of interest to assess dyspnea in obesity.

# 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.

R4: We agree that this point was not clear in our manuscript. Using BDI, Collet et al. found that patients with a BMI > 49 kg/m² had more severe dyspnea than obese patients with a BMI ≤ 49 kg/m². This point has been clarified in the background section (P4, line 8).

# 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.
R5: We agree that we have not discussed all the possible mechanisms of activity-related dyspnea in obese subjects. However, and as required by an other reviewer, we shortened this section. We thank the reviewer for providing excellent references on this point. We have included these new references in the revised manuscript in the background section (P4-line 14).

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 comparisons 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).

R6: We agree that the absence of overweight or normal subjects to compare with is a limitation of our study. This limitation has been clearly stated in the new manuscript in the Discussion section (P11-line 1).

# 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.

R7: Sex has been used instead of gender in the new version.
Thirty-six percent of patients received statins, 31% oral hypoglycemics, 9% insulin, 29% beta blockers and 7% had a CPAP. We did not find any association between dyspnea and treatments.

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

R8: We used the ERS references for PFTs % predicted values. We provided the reference for the predicted equation used in the revised manuscript in the Method section (P6-line 3).

# 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.

R9: We agree that ABG can be considered as biological parameters, but we think that it is more logical to keep the ABG in the pulmonary function test section.
# Statistical analysis: What was the justification for separating groups into ‘dyspneic’ and ‘non-dyspneic’ according to an mMRC score of #1 and 0, respectively?

**R10:** As the patients were not addressed specifically for dyspnea, we have chosen to separate groups between non dyspneic and dyspneic patients.

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

**R11:** We agree that the number of patients is low and that it is a limitation of our pilot study. This point has been discussed in the discussion as a limitation (P10- line 31).

**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)?

**R12:** We think it is very difficult to compare our 6MWT results to published normative data. Of notes, Casanova et al. described significant variations between the different centers. To make real comparisons, we would need to have a group on non obese patients. The absence of a group without obesity in our study has been discussed as a limitation in the new version in the discussion section (P10- last line).

- **Relationships between the mMRC scale and clinical characteristics, PFTs and biological parameters**
  - 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.?

**R13:** We agree that this point was not clear. In the new version, we clearly specified in the results section that we analyzed the differences between groups.

Second, you have not reported in your Table 2 of subject characteristics your apnea/hypopnea index scores.

**R14:** The apnea/hypopnea index scores have been precised in the revised manuscript in Table 2.

- 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.

**R15:** We fully agree with the reviewer. Indeed, we referred to the results of our between-group comparisons and the word “correlation” has been used inappropriately. This point was corrected in the new version in the Results section.

…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.

**R16:** We performed an X-Y plots as suggested by the reviewer. However, we don’t think this plot add to the results presented. We made significant changes in the Figure 1, as suggested by an other reviewers. We think the new Figure 1 is easier to understand for the reader.

…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 mMRCan/d 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 andmMRC? 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.

**R17:** We thank the reviewer for this question. We analyzed this point and we found no statistically different change in Borg scale ratings of dyspnea from rest to the end of the 6MWT between the two groups \((p=0.39)\). This result has been presented in the Results section (P8-last sentence).

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 CRO 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).

R18: We agree with the reviewer that the results of these studies have to be discussed. These studies have been discussed in the new Discussion section (P9-line 11).

# 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.

R19: We agree that the word correlation has been inappropriately used. This point has been changed in the new discussion.

# 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.

R20: This point has been discussed in the R2 response (see R2). This point has been clarified in the new version in the background section (P4-line 14) and in the discussion (P10-line 20).

# 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?

R21: We agree that the term useful is more appropriate. This point has been modified in the revised manuscript (P).

# 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.
R22: We agree that the 6MWT does not provide a standardization of the exercise stimulus. Exercise testing on cycloergometer or shuttle walking test would allow to standardize exercise stimulus. This point is a limitation to our study. We discussed this point in the revised manuscript in the Discussion section (P10-line11).

# 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.

R23: This point has been corrected in the new version. The term correlation has been avoided, and the term association has been used.
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
Version: 3 Date: 29 May 2012
Reviewer: Antonia Koutsoukou

Reviewer's report:
In this report, Launois et al studied a cohort of 45 obese subjects. In these subjects they recorded dyspnea in daily living as assessed by the mMRC scale along with exertional dyspnea after six minute walk test (6MWT) assessed by the Borg scale, pulmonary function tests (PFTs) and biological parameters. They found that the majority of the obese subjects exhibited dyspnea in daily living (mMRC>1 was found in 38 subjects), and that Group mMRC>1 individuals had higher BMI and smaller FEV1%pred, distance covered in 6MWT, and serum hemoglobin levels than those in Group mMRC=0.

There are some major concerns regarding the methodology and interpretation of this study.

General concerns
The main problem of the study is that the results, as they are currently presented, are not supported by the analysis used.

Table 5 presents comparisons of the two groups of subjects (Group mMRC=0 and Group mMRC>1) based on the study of different parameters, not including relationships and associations as it is repeatedly mentioned in the Results and Discussion sections.

R1: We agree that Table 5 provides comparisons between groups and not correlations. This point has been modified in the new version in the Result and the Discussion section (P8,P9 and P10).

Figure 1 is rather confusing. Please provide information about what is presented in this figure due to lack of clarity regarding
a) which statistical test was used,

R2: We precised in the legend of the new Figure 1 that the Wilcoxon test was used.

b) whether the significant differences presented in the figure represent comparisons between the two mMRC groups (as it is described in the text and shown in Table5) or between the three groups presented in Figure 1,

R3: We agree the Figure 1 was not clear regarding which group was compared. We provide a new Figure 1 showing results for the two groups: MmRC=0 and mMRC ≥1, as analyzed in our study. We present in the text data regarding an association between Borg after 6MWT and a mMRC ≥ 2.

c) if the authors applied Chi-square test to assess relationships of a categorical variable (mMRC groups) with non-categorical variables (BMI or ERV).
We performed a comparison between 2 groups (MMRC=0 vc mMRC ≥1). In the new Figure 1, this point was made clearer.

Specific comments
Title: The title does not actually define the content of the manuscript

We agree that the term interest was not appropriate. We modified the title of the manuscript as suggested.

Aim: The aim of the study is not clearly stated. If the aim were to evaluate mMRC scale as a tool for assessing dyspnea sensation in daily living, comparison of this scale with other scores of dyspnea recorded would be appropriate. If the aim were to study the predictive role of mMRC scale in exercise capacity in this cohort of obese subjects a different protocol should had been followed.

The aim of the study was to evaluate mMRC scale as a tool for assessing dyspnea sensation in daily living. We agree that it would be interresting to compare the mMRC scale with another scales.

We discussed this point in the discussion (P11-line 3)

Statistical analysis: Given the small number of subjects studied, the authors (correctly) used Wilcoxon test (a non parametric statistical test) to compare related samples. However, they used Pearson’s correlation coefficient (a parametric test) to test possible correlations between different variables! Please explain

We agree that this point was not clear. We used Wilcoxon test for the averages comparisons because the groups were small (less than 30 patient: 38 patients vs 7 patients). We used Pearson’s correlation when the tests were applied to all patients (>30 patients).

Discussion: Given the questionable analysis of the data, the interpretation of the findings is rather arbitrary.
In addition, possible explanations for the study results are not provided, the findings are not in context with results of similar studies and the clinical relevance of the findings is not stated.

In the new version, the results obtained in previous studies have been much more discussed (P 9-line 11). Moreover, as suggested by the reviewers, we made significant changes to Figure 1.

Conclusions: The conclusions are not sufficiently supported by the findings

We would like to emphazise that our study is a pilot study and we fully agree that this study has limitations. These limitations have been discussed much more extensively in the discussion section.
We think that our study suggests that the mMRC scale might be an useful and easy-to-use tool to assess dyspnea in daily living in obese subjects. As discussed in the discussion, further studies are needed to confirm these results (P11-line11)
Additional comments
Results, page 7, 3rd paragraph and Table 5: Please provide the comparison of the Borg scale data between the two groups.

R 10: The comparison of the Borg scale between the two groups are presented in Table 5.

How many of the subjects with abnormal PFTs exhibited dyspnea in daily living?

R 11: There were an obstructive ventilatory disorder defined by a FEV1/VC < 0.7 in 5/38 (13%) of patients, a restrictive ventilatory disorder defined by a TLC < 80% in 5/32 (16%) of patients and a decrease in alveolar diffusion defined by DLCO < 70% in 9/32 (28%) of patients. The number of patients with abnormal PFTs is low, and makes it difficult to analyze associations between obstructive or restrictive limitation and dyspnea in our study.

This point has been clarified in the new version (P8, first sentence).

In which mMRC group did the subjects who developed desaturation during the 6MWT belong?

R 12: The number of patients which developed desaturation during the 6MWT is low and we think that it is difficult to draw any conclusion based on a small number of patients.

(Five patients were in the dyspneic group and two patients were in the group without dyspnea. The patient who had a SpO2 after 6MWT < 90% was in the dyspneic group.)

What is the rationale of measuring biological parameters (Cholesterol, CRP etc) in an investigation aimed to study “the interest of mMRC scale for the assessment of dyspnea”?

R 13: Hemoglobin and NTproBNP were assessed as potentially confounding factors that could increase dyspnea related to anemia or cardiac insufficiency. Moreover, previous studies showed that type 2 diabetes, insulin resistance and metabolic syndrome are associated with reduced lung function in obesity (Lecube A, Type 2 diabetes impairs pulmonary function in morbidly obese women: a case-control study. Diabetologia, Lecube A, Insulin resistance is related to impaired lung function in morbidly obese women: a case-control study. Diabetes Metab. Res. Rev. 2010, Leone, Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. Am. J. Respir. Crit. Care Med. 2009). We then decided to analyze the association between triglyceride, total cholesterol, fasting glucose, Hba1c and the mMRC dyspnea scale.

This point has been clarified in the new version in the background section (P4-line 14) and in the discussion (P10-line 20).

Page 10, lines 5-8 “….demonstrates some correlations between the 6MWT and dyspnea..” Please be more precise. Was the distance covered in 6MWT correlated with any dyspnea scale?
R 14: The word “correlation” has been used inappropriately. We find a difference statistically significant between the “dyspneic group” and the “non dyspneic group” as regards the distance covered in 6MWT (p < 0.01).

Table 3, first line, mMRC scale (0-4): Something is missing in the parenthesis. Please correct.

R 15: We made the change regarding the mMRC scale, including the range of the scale (0-4).
The change has been made in Table 3.