Author's response to reviews

Title: Anemia and hemoglobin serum levels are associated with exercise capacity and quality of life in chronic obstructive pulmonary disease

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Author's response to reviews: see over
We are indebted with Dr Boutou and Dr Silverberg for their suggestions which, we hope, allowed us to ameliorate the paper.

Reviewer: A. Boutou

In the introduction we emphasize that no study has been conducted in COPD on the relationship between anemia and muscle strength. Furthermore, in the same section, we underline that few works examined the relationship between hemoglobin, exercise capacity and HRQL, important clinical outcomes in chronic respiratory disease, potentially linked to anemia. These sentences constitute the premise to the aims of the study that we think are clearly reported.

Material and methods

1) The type of the study (retrospective) is now reported on page 7, line 102.

2) About 80% of COPD patients suffered of hypertension; among them 50% were treated with ACE inhibitor drugs, whereas no one used ARBs.

3) Patients with chronic obstructive pulmonary disease have often raised serum levels of C-reactive protein (CRP), as expression of systemic inflammation. The CRP levels may be of importance since systemic inflammation is associated with increased mortality and may also contribute to the extra pulmonary features associates with COPD, such as skeletal muscle dysfunction, osteoporosis and probably cardiovascular disease. For this reason the evaluation of CRP levels is systematically done in our outpatients.

4) The definition of polycythemia is now reported on page 8, line 130-132.

5) 6MWT is a simple test recommended for the evaluation of exercise capacity in COPD patients, and its measurement consents the calculation of the important composite index BODE. For these reason 6MWT is routinely executed in our patients. In our clinic, a simple individualized exercise program on stationary bike is offered to all COPD patients since GOLD guidelines recommend aerobic exercise as an important part of the treatments of this patients. Furthermore, peak VO₂ is a predictor of mortality. For these reason CPET is systematically performed in clinical stable COPD patients.

6) The time schedule of the data collection is now reported on page 7, line 121-124.

Results

1) In our study, CRP levels were higher in anemic than in non-anemic patients. Even though the difference was not significant (probably due to the high standard deviation of our data- this is now reported in the result section, page 10, line 180-181 ), our data are in agreement, rather than in contrast with the results reported by John et al (2005) and Boutou et al (2012). For this reason we have not added a sentence in the discussion section, but only a short comment in the result, as above mentioned.
2) The linear relationship between the hemoglobin, exercise capacity and HQRL was found in a range of hemoglobin values indicative of mild anemia or mild polycythemia. Therefore our results cannot be interpreted as indicative that severe polycythemia (as reported in the paper of Wedzicha, 1983) is related to a better exercise capacity or quality of life. A brief sentence underlining the fact that extrapolation out of the range of hemoglobin values considered in the analysis is not possible, has been added in the discussion (page 15, line 280-282).

Discussion

1) Unfortunately we have no AT data supporting the sentence.

2) We acknowledge that our data does not support the theory. Consequently, the sentence has been erased.

3) We acknowledge the Pindaric jump reported in lines 240-245 of the original version. As a consequence, we have substantially modified the paragraph (page 13, line 248-252 new version).

4) Line 278 has been erased.

Minor essential revisions

The type of the study, retrospective, is now reported in page 7, line 102

Typing errors have been corrected.
Reviewer: S. Silverberg

Typing errors have been corrected.

Line 186-188 (old version) has been modified (page 10, line 193 new version)

Line 195-197 has been corrected

"Do you have data...."
Patients with chronic renal failure were excluded from the study, as reported in the exclusion criteria in the methods section.

"We think a comment should be made......"
A comment about anemia correction in COPD has been added in the discussion (page 15, line 284-287)