Author’s response to reviews

Title: Ventilatory efficiency testing as prognostic value in patients with pulmonary hypertension

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Author’s response to reviews:

Dear Prof. Kowalczuk,

thank you very much for the opportunity to revise our manuscript according the excellent reviewer’s comments. All changes were highlighted with red text.

The authors would be pleased, when the manuscript fulfilled the journal’s criterions and could be published in the revised version in your journal.

Sincerely, yours

Martin Schwaiblmair

Enclosed:
Point-by-point response to the reviewer’s comments

Point-by-point response to the reviewer’s comments:

Reviewer 1:

According to the very constructive recommendations we make the following changes:
Ad 1) We have changed the word “ventilatory drive” in ventilatory response – see page 2, paragraph 1

Ad 2) Blood gas analysis was performed in arterialized capillary blood from the ear lobe without supplemental oxygen - see page 6, paragraph 4

Ad 3 and 4) According the reviewers recommendation, we have removed the value of mean physiological dead space from the main document and from the tables.

Ad 5) It is correct that it is problematically to cite cut-off values from a heart failure cohort. Therefore we have removed this part and we have only used the cut-off value of peak O2 uptake (< 10.4 ml O2/kg/minI) from the study of Wensel et al. (see reference list: number 2) according the guidelines for the diagnosis and treatment of pulmonary hypertension (see reference list: number 23). To our knowledge, a generally accepted cut-off value of Ve/VCO2 did not existed in patients with PAH.

Ad 6)

a. It is correct that we used for peak VO2 the recommended cut-off value of 10.4 according the European guidelines to make it possible for the reader to compare different CPET values. In default of failed generally accepted cut-off value of Ve/VCO2, we searched a comparable value in the heart failure cohort, but - according to the reviewers recommendation – it is certainly incorrect. It is therefore correct that the Ve/VCO2 value of 55 is only the “optimal” cut-off value for our study population and we have emphasized this limitation in the manuscript – see page 11, paragraph 1

b. According to the recommendation, we performed a uni- and multivariate Cox analysis – see page 8, paragraph 4, page 10, paragraph 4 and table 3.

c. It goes without saying that we have calculate the optimal value for prediction by receiver operating curves – see page 8, paragraph 4

Ad 7) The aim of our study was not to compare haemodynamics with CPET parameters. Once more, we have specified this point in the introduction section – see page 4, paragraph 5.

In no way, we intend to doubt the prognostically relevant RHC parameters (see Cox proportional hazard analysis). For example, we did not determine the cut-off values of right atrial pressure or cardiac output. Nevertheless, our two study groups (of survivors and of non-survivors) did not show significant haemodynamic differences at the beginning of the study, but – of course – a cut-off value of RAP > 15 mmHg of a CI < 2.0 L/min/m2 would be differentiate our study groups, too.

Reviewer 2

According to the excellent recommendations, we make the following changes:
Ad 1) It is correct that we did not examine the relationship between haemodynamics and CPET. Therefore we have specified the study aim in the introduction - see page 4, paragraph 5.

Ad 2) We have introduced the inclusion period and the patients were included consecutively – see page 6, paragraph 1.

Ad 3) We have deleted this section.

Ad 4) According the recommendation, we performed Cox-model analyses and we have changed some sentences in the abstract and result section – see page 8, paragraph 4, page 10, paragraph 4 and table 3.

Ad 5) We omitted the calculations of positive and negative predictive values.

Ad 6) According to the reviewers recommendation, we introduced a table with the main characteristics of the overall group, and, in the same table, baseline characteristics of patients with PAH and with CTEPH – see table 1.

Ad 7) We have specified the cause of mortality in each group of patients – see page 9, paragraph 1.

Ad 8) We have introduced a abbreviation list after the abstract section and we have tried to eliminate the inconsistent abbreviations – see page 2.

Ad 9) Of course, it is correct that we did not supported this statement in our study and therefore we omitted this addition.

Editorial Office Comments

Ad 1) We included a “Competing interests” section between the Conclusions and Authors’ contributions – see page…..

Ad 2) Once again, the manuscript was checked by a native-English speaker with scientific expertise.

Ad 3) We hope that our revised manuscript conforms to the journal style.