Reviewer’s report

Title: A double blind randomized placebo control crossover trial on the effect of dietary nitrate supplementation on exercise tolerance in stable moderate chronic obstructive pulmonary disease

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Reviewer: Corey Tomczak

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Lines 84-95: I appreciate the authors’ intent of laying out and rationalizing their hypothesis. In doing so, however, their research hypothesis is lost – that is, this section would benefit from simplification. For example, “hypothesized/hypothesis” is stated 3 times – which is the actual research hypothesis (this can be lost on the reader too easily)? Please simplify this section for reader clarity without losing the important background information being presented.

Line 95: please clarify primary endpoint. Are you really talking about walk test distance or time to fatigue?

This study reports human ethical approval and patient consent.

Statistical analyses are appropriate. Data reporting can be enhanced with adding t-value and d.f. – though this is unlikely the convention of the journal.

The study design is justified and well executed.

Lines 114-115: I’d suggest removing funding source listed in lines 114-115 and place at end of manuscript following typical convention. I see it on line 57.

Line 217: Please indicate how many patients were screened during the enrollment period and add this to the associated enrolment figure detailing how many patients were identified and reasons for not including them (declined participation etc…).

I would suggest a diagram/flow chart of testing days/visits to make the methods clearer for the reader.

Line 223: 4 patients were deemed “too fit”. This is not listed as exclusion criteria in the manuscript. Please rectify/better justify this. For example, at what point was it decided to exclude these patients relative to data analysis? My point being that the reader needs to be confident that there were some a priori decision making rules in place for these patients’ exclusion.

Line 224: continuing with my note directly above I would suggest there is some confusion regarding the line 224 “measurement of the ESWT is limited to …15ml/kg/min…” 1) What is meant/the point of this statement? 2) Is not the VO2max value of 14.9 ml/kg/min reported in Table 1 approximate to the rationale
of 15 ml/kg/min being too fit? As it reads, it is not intuitive for the reader what is the thinking of the authors’ along this line of rationale.

Line 178: please provide rationale/reference for the washout period.

A majority of the results is dedicated to blood pressure and heart rate metrics (3 tables). I think better rationale about these outcomes is needed in the introduction. Currently there is minimal to none about these outcomes, though they occupy much of the readers attention in the data reporting.

Figure 2 legend: I’d suggest reiterating the boxplot boundaries for the reader.

Each Figure Legend seems to have a header and then description. I’m not sure if that’s convention for the journal. I’d suggest merging these 2 descriptors to 1 succinct legend description.

Figures 2 and 3: use the same axis labels between the 2 figures and arrange data in same order (Fig 2 BR then PL; Fig 3 PL then BR). Units needed on Y –axis on Fig 3.

Lines 51-53: I’d suggest reporting a conclusion linked to the data findings, not the future directions.

“Major Addition” Needing Attention:
I believe the discussion section would strongly benefit from discourse related to potential physiology that may explain the study’s negative finding. Why was there no “functional” effect of dietary nitrate on exercise performance? An elegantly crafted section along this line would benefit future research. Specifically, the introduction highlights the favorable NO effect of dietary NO3- --- this suggests the authors’ expected a potential reversal in adverse exercise blood flow to be an important/primary modulating factor for exercise limitation in COPD. This notion would benefit from stronger rationale for this underlying physiological rationale for NO3- supplementation and, consequently, a measured discussion addressing the lack of exercise benefit in this light (that of exercise vascular benefit in COPD – and if the authors’ believe this was/wasn’t the case, or if this can even be supported by the data).

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
I have no competing interests. I answer "no" to all the questions noted above.