Author's response to reviews

Title: Nitrous Oxide Does Not Increase the Risk of Cancer Recurrence after Colorectal Surgery: A Randomized, Blinded Study

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Author's response to reviews:


Sabina Alam PhD
Assistant Editor
BMC-series journals

RE: MS: 1614674353227923
Nitrous Oxide Does Not Increase the Risk of Cancer Recurrence after Colorectal Surgery: A Randomized, Blinded Study

Dear Sabina Alam

Thank you for reviewing our manuscript. Please find enclosed a revision of our manuscript. We used the issues, concerns, and other suggestions made by the reviewers to guide our revision of the current manuscript.

Furthermore, in our response to the reviewers, we respond to each reviewer’s concerns on a point-by-point basis and indicate how the manuscript was changed.

We look forward to your further comment.

Thank you again for your kind consideration.

Sincerely,
Daniel Sessler, MD
DS@OR.org

Reviewer’s report

Rev. 1: Philip Peyton

General comments:

P7: Fig. 1 needs a caption: we have added the phrase “Trial Profile” and referenced the original trial in the manuscript Fleischmann E, Lenhardt R, Kurz A, Herbst F, Fulesdi B, Greif R, Sessler DI, Akca O: Nitrous oxide and risk of surgical wound infection: a randomised trial. Lancet 2005, 366(9491):1101-1107.

The word recividism: has been changed to locoregional recurrence

P9: Para 2: we have changed the text to read as follows: A multivariable-Cox-proportional-hazards-regression model including all baseline variables independently significant at P<0.25 (that is, significant at P<0.25 in the presence of other covariables) in the model, was fit in order to better balance the treatment groups and to increase precision in the estimation of the effect of type of gas on survival. Any factor showing some univariable relationship with type of gas administered (as determined by univariable tests with a significance criterion of P<0.40) was considered in building the model

P10: Para 2, please consider these comments submitted by Jarrod Dalton, author: The reported incidences of mortality are likely lower than the true incidences in our patient population since many patients were censored to follow-up before death. Furthermore, direct comparison of these proportion estimates without covariable adjustment leaves open the possibility of confounding attributable to those covariables. Thus, a multivariable survival analysis of mortality rate (which instead of a estimation of the proportion in each group who died is rather an estimate of the ratio of instantaneous risk of death at any given time point postoperatively) is appropriate to 1) adjust for covariables and 2) adequately address the incompleteness in the data caused by censoring of subjects postoperatively.

P10: please change Fig 2 instead of Fig 1 We have made this change.

Rev. 2: Peter Kranke

General comments:

Major Compulsory Revisions
1. Page 9, 2nd paragraph, 3rd sentence: Please consider the following comment by Jarrod Dalton, Author: On point #1, I agree with the reviewer. The title should be changed to “Nitrous Oxide May Not Increase the Risk of Cancer Recurrence after Colorectal Surgery: A Follow-up of a Randomized Controlled Trial.” Based on this, the title of the manuscript has been changed to “Nitrous Oxide May Not Increase the Risk of Cancer Recurrence after Colorectal Surgery: A Follow-up of a Randomized Controlled Trial.”

2. Page 14, 3rd paragraph: Please consider the follow comment by Daniel I Sessler, MD, author: Although we list misdiagnosis as a potential limitation, it seems quite unlikely that many patients with a death-certificate listing colon cancer as the cause of death actually died of anything else. We thus doubt that a sensitivity analysis for this particular issue will add much value.

Minor essential Revisions

1. Page 24: please change Figuer 2 to Figure 2: We have changed the spelling to Figure.

2. pages 26 and 27 as opposed to page 28 and 29: It appears that the figures were created in the pdf twice. The revision will include the figures only once.

Discretionary Revisions

1. Page 13: attenuate the sentence usually the best hope for cure: Based on this, we have changed the sentence to read: Cancer surgery, sometimes the best hope for cure, is nearly always associated with minimal residual disease [1], and competence of host defense, especially natural killer cell function, appears to be a critical determinant of whether residual disease develops into clinical recurrence [4, 18].

General:

competing interests: please add between the conclusions and authors contribution: The authors declare the have no competing interests. This section has been added.

Authors contribution: please add to the paper before the Acknowledgements: Based on this comment, the following contributions have been added.

EF designed the study, collected data, and drafted the manuscript.
CM collected the data and helped to write the manuscript.
KS collected the data.
JD performed the statistical analysis.

TG and FH participated in the design of the study and helped to interpret the results.

AK and DS participated in the design of the study, interpreted the data and drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgements: Please add before ref. Based on this comment, a list of acknowledgements has been added directly before the references.