Author's response to reviews

Title: Design and Organization of the Dexamethasone, Light Anesthesia and Tight Glucose Control (DeLiT) Trial: A Factorial Trial Evaluating the Effects of Corticosteroids, Glucose Control, and Depth-of-Anesthesia on Perioperative Inflammation and Morbidity From Major Non-cardiac Surgery

Authors:

Basem Abdelmalak (abdelmb@ccf.org)
Ankit Maheshwari (mahesha@ccf.org)
Edward Mascha (maschae@ccf.org)
Sunita Srivastava (srivass@ccf.org)
Theodore Marks (markst1@ccf.org)
WH Wilson Tang (tangw@ccf.org)
Andrea Kurz (kurza@ccf.org)
Daniel I Sessler (sessled@ccf.org)

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Author's response to reviews: see over
Dear Dr. Alam,

We wish to thank you and the reviewer for your kind comments and constructive critique. Below is our point-by-point response to the reviewer’s comments.

For your comments:

1. Ethics

   Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/e/policy/b3.htm), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

   We have added the following statement (see page 9 under Ethics):

   “The protocol has been reviewed and approved by the Cleveland Clinic Institutional Review Board (IRB # 07-010)”

2. Competing interests
Please include a 'Competing interests' section between the Conclusions and Authors' contributions. If there are none to declare, please write 'The authors declare that they have no competing interests'.

**Financial disclosure:**

**BA:** Received research funding from Aspect Medical (currently Covidien), and Hutchinson Inc.

**AM, EM, AK, TM, SS, DS:** 'These authors declare that they have no competing interests

**WT:** Received Research Funding from Abbott Laboratories

**TS:** 'This contributor declares that she has no competing interests'.

3. Authors' contributions

Please include an Authors' contributions section before the Acknowledgements and Reference list.

**Authors Contributions:**

**Basem Abdelmalak, MD:** PI participated in study concept and design, study conduct, data analysis, manuscript writing.

**Ankit Maheshwari, MD:** study coordinator, participated in study conduct, patients' consenting, recruiting.

**Edward Mascha, PhD:** Senior Study Biostatistician: participated in study design, statistical analysis, plan, sample size calculations and, manuscript writing
Sunita Srivastava, MD: participated in the study design and conduct/recruiting and manuscript review

Theodore Marks, MD, Ph.D: participated in study conduct, manuscript review

W. H. Wilson Tang, MD: Co-investigator, participated in the biomarkers testing and analysis and manuscript review

Andrea Kurz, MD: participated in study design, manuscript review and editing

Daniel I. Sessler, MD: Senior investigator; participated in study concept and design, data analysis manuscript writing, corresponding author

All authors read and approved the final manuscript

4. Acknowledgements:

- The authors greatly appreciate the contributions of the Cleveland Clinic PACE clinic where patients were informed about the study and recruited for enrollment.
- Tanya Smith; participated in manuscript editing and submission.

Please list the source(s) of funding for the study, for each author, and for the manuscript preparation in the acknowledgements section. Authors must describe the role of the funding body, if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

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clinic where patients were informed about the study and recruited for enrollment.

This is an investigator-initiated trial,

- Aspect Medical provided financial support as well as equipment (BIS monitors)
- Cleveland Clinic Research project Committee provided financial support

For the reviewer:

We have added the following to explain our plans for evaluating the results of the glucose control intervention as per the reviewer’s request:

- We will use previously described methodologies to determine efficacy and safety of the insulin infusion protocols, including proportion of time spent within target range and number of hypoglycemic episodes (<40 mg·dL\(^{-1}\)).\(^{[39]}\), We will also measure time-weighted average (TWA) glucose and time taken to achieve desired level of glucose control. We will compare our results to other published findings in similar trials; the closest to our trial is that of Gandhi et al who investigated almost the same targets in their RCT in cardiac surgery patients, \(^{[32]}\).

- We have clarified our plans for the intention to treat analysis by stating so in the statistical analysis section per the reviewers’ request: “All analyses will be intent-to-treat”

References
