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Dear Editor,

Thank you for the reviewer comments regarding our *invited* manuscript titled, "Preoperative Nuclear Stress Testing in the Very Old Patient Population" (MS# 52604) written by Amgad N. Makaryus MD, John N. Makaryus MD and Joseph Diamond MD. We have revised the manuscript according to the suggestions (please see the outline of revisions below). We believe that this revision has improved this manuscript substantially, and hope that it will be received in a favorable manner.

All authors listed on the manuscript have contributed sufficiently to the project to be included as authors, and have read and approved the manuscript. This work has not been previously published, and is not currently under review elsewhere. There are no conflicts of interest with regard to this paper to any of the authors. Please address any correspondence to me at the address below. Should you need to contact me by telephone, my work telephone number is 516-296-4983. My fax number is 516-572-3172.

**LIST OF REVISIONS AND RESPONSES in bold/italic (highlighted in yellow in paper):**

- Reviewer ID 02549231:** -Relationship between type of surgery, NST and adverse events; ***We thank the reviewer for the comments. We did not specifically correlate type of surgery with outcomes as each of these surgeries have their own risk profile which is known and additionally, we mention this limitation of referral bias on page 12 as it is not unreasonable to surmise that many patients who had abnormal NST might have had their surgeries cancelled due to their assumed high risk. This introduced referral bias has the potential for decreasing the correlation between abnormal studies and unfavorable surgical outcomes. It is also assumed that certain surgical techniques may have been modified as a result of the findings on NST.***  
-"prognostic utility of both methods": but treadmill method only two cases; ***In this elderly patient population, due to comorbidities and less mobility, most of these patients cannot tolerate an exercise test and this is reflected in our data.***  
-Zafrin study on 83 year old patients: compare and discuss differences with present study; ***The Zafrin study is discussed on pages 10 and 11 compared to present study.***  
-is there a group of 85 year old pts not undergoing NST (control group) ? ***We did not have a control group of 85-year old patients not undergoing NST in our retrospective analysis.***
- Reviewer ID 02948419:** Authors reported good written and well-balanced research paper that is depicted nuclear stress testing in elderly patients. The study is quite well designed, while sample size is small. Authors reported MACEs in patients' population after nuclear stress testing and found that SSS  $\geq 9$  predicted the development of MACE in the immediate

peri-/post-operative period in elderly patients  $\geq 85$  years undergoing moderate to high-risk surgery. The findings of the study are clinically important and they deserve to be published.

***We thank the reviewer for the comments.***

1. Study design. Please, report flow chart with clear criteria of inclusion / non-inclusion ***A Flow Chart labelled figure 1 (page 21) has been added as recommended. Prior figure is now labelled figure 2.***
  2. Result. Please, report demographics, risks, other performances for patients with  $SSS > 9$  and  $< 9$  ***Demographics for the study population are reported in table 1 (pg. 17) including prior history, medications, and surgical procedures. Further breakdown relating to adverse events in patients with  $SSS > 9$  or  $< 9$  is given in table 4 (pg. 20).***
  3. Please, explain whether patients with HF were enrolled in the study or HF was determined as MACE only. Additionally, explain why  $HF < 45\%$  and  $> 45\%$  were determined. ***HF was determined as MACE only and we apologize for the incorrect number of 45%, we actually used 40% for the cutoff of heart failure. This has been corrected throughout the paper.***
  4. Please, re-consider Cox proportional regression as adjusted model to CV risk factors and give discussion further. Compare some predictive models with C-statistic. ***We employed logistic regression to examine the multivariate effects of nuclear stress test results and presence of cardiac risk factors prior to admission on intraoperative cardiac events (one or more, none). A Cox proportional hazards regression analysis was used to examine the multivariate effects of nuclear stress test results, presence of cardiac risk factors prior to admission and intraoperative cardiac events on time until first post-operative cardiac event. This discussion is included on page 6.***
3. **Reviewer ID 00503286:** The paper "Preoperative Nuclear Stress Testing in the Very Old Patient Population" should be published in journal after the minor correction with the editor. A graphical presentation were welcome! ***We thank the reviewer for the complementary comments!***

Many thanks in advance for your consideration.

Sincerely,



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