Author’s response to reviews

Title: FACTORS PREDICTING ONE-YEAR POST-SURGICAL MORTALITY AMONGST OLDER ASIAN PATIENTS UNDERGOING MODERATE TO MAJOR NON-CARDIAC SURGERY – A RETROSPECTIVE COHORT STUDY

Authors:

Lydia Liew (lydia_qn_liew@nuhs.edu.sg)
Wei Wei Teo (wei_wei_teo@nuhs.edu.sg)
Edwin Seet (seet.edwin.cp@ktph.com.sg)
Lyn Lean (lyn_li_lean@nuhs.edu.sg)
Ambika Paramasivan (ambika_paramasivan@nuhs.edu.sg)
Joanna Tan (joanna_tan@nuhs.edu.sg)
Irene Lim (irene_al_lim@nuhs.edu.sg)
Jiexun Wang (wang.jiexun@ktph.com.sg)
Lian Ti (anatilk@nus.edu.sg)

Version: 1 Date: 10 Jul 2019

Author’s response to reviews:

Dear Editor-in-Chief,

Thank you for taking the time to review our manuscript entitled “FACTORS PREDICTING ONE-YEAR POST-SURGICAL MORTALITY AMONGST OLDER ASIAN PATIENTS UNDERGOING MODERATE TO MAJOR NON CARDIAC SURGERY – A RETROSPECTIVE COHORT STUDY" (BSUR-D-19-00060).

We thank the reviewers for their valuable input regarding the following points. We have uploaded a cover letter comprising of the Kaplan Meier curves and detailing our replies to the reviewers, alongside the revised manuscript. Kindly see attached revised manuscript with the changes tracked and highlighted.

1. Reviewer 1 suggested the use of cox regression analysis as time was deemed as an important factor in the analysis.

Cox regression analysis is generally used to look for an outcome with respect to time, however, this was not our study’s primary aim. Rather, our study aimed to look at all variables that predicted mortality within one year. Using one-year mortality as a cut-off can then be used as a benchmark for
comparison with the few international studies done in Europe and the United States. These studies which used logistic regression showed one-year mortality in Caucasian populations to be 5-17% [Ref 1-5]. Future studies can be done to further compare and contrast our results with these studies.

In our study, Firth logistic regression was used over traditional logistic regression. This is because our outcome of mortality is considered a rare outcome (<10%). Traditional logistic regression could get infinite odds ratio estimates when there is complete separation or quasi-separation problem due to rare outcomes [Ref 6]. Firth’s logistic regression can handle this problem by using a penalized likelihood approach and reduces the bias in the estimates of coefficients in the model [Ref 7, 8].

2. Reviewer 1 suggests including Kaplan-Meier curves in the analysis.

Kaplan-Meier curves are traditionally used to look at comparisons of survival with respect to time, usually with a specific intervention or exposure to be studied. However, in our study, the aim was not to compare survival between two groups, but to look at factors affecting one-year mortality categorically. The only utility of Kaplan-Meier curves in our study would be to ensure that there is no marked ‘drop-off’ at any time point. As such, we have included the Kaplan-Meier curves (see Cover Letter) for the reviewer’s perusal, as requested, but not in our manuscript.

3. Both reviewers requested to know how death was determined.

Death was determined using electronic medical records that is linked to our national health registry. This registry includes information from all primary healthcare services and hospitals in Singapore. If the patient has deceased, this would be indicated on the record, including the date of death. Proof that a patient was alive was confirmed by searching for evidence of any subsequent healthcare visits, prescriptions, laboratory and radiological investigations within the time period. (This explanation has been added to our manuscript under Methods section paragraph 4).

4. Reviewer 1 requested to know the survival time and cause of death.

Survival time and time to death were not our primary objectives of the study. The primary objective was to look at the one-year perioperative mortality and its associated factors in an Asian surgical population after non-cardiac surgery. The survival times are reflected in the Kaplan Meier curves (see Cover Letter). We have not included this in our manuscript as it did not directly address our research question.

Data on the cause of death was not collected as per our research protocol. Furthermore, our dataset has been de-identified according to the Ethics Board regulations in Singapore. We are unable to collect this additional data field now as the cause of death was not the original objective of this study.

5. Reviewer 1 requested to have 5-year survival times incorporated in patients with cancer.

The study was carried out looking at patients undergoing surgery between January 2015 to July 2015. As five years have not elapsed at this point in time, we would not be able to obtain this data.
6. Reviewer 1 requested for an explanation why Asians have a different outcome in mortality compared to Caucasians.

Many studies have shown ethnicity to play a role in disease progression and severity. This is likely due to variations in genetics, lifestyle, culture and environment [Ref 9-11]. These differences may account for the difference in mortality. However, there is a paucity of studies done on one-year mortality in the Asian population. This study hopes to fill that gap, as well as compare and contrast our results to the few studies done among Caucasians [Ref 1-5].

7. Reviewer 2 suggested for tables 1 and 2 to be presented by mortality status.

The tables have been amended as suggested and is reflected in the manuscript (highlighted).

8. Reviewer 2 asked for clarifications with regards to variables included in the multivariable analysis, as well as why some variables were presented in Appendix 1 and not in Table 3.

Appendix 1 comprised of all the demographic, surgical and clinical variables included in the univariate analysis.

Variables that were found to be significant in the univariate analysis (p-value < 0.2) were included in the Firth logistic regression model for the multivariate analysis. These have been added into our manuscript, under the Methods section (highlighted). Significant variables (p-value of <0.05) in the multivariate analysis were then included in Table 3. Factors that were not statistically significant in the multivariate analysis were excluded in Table 3.

9. Reviewer 2 asked whether there was a marker of socioeconomic position such as education and income that could be included.

Data on socioeconomic position was not collected as it was unavailable. Our dataset has been de-identified according to the Ethics Board regulations, and we are unable to collect the data now.

Thank you for your kind consideration for publication in BMC Surgery. Please do not hesitate to inform us should there be further queries or clarifications. We would be most happy to amend and clarify.

We look forward to your favorable reply.

Sincerely,

Wei Wei TEO
Reference:


