Author's response to reviews

Title: Smoking and timing of cessation on postoperative pulmonary complications after curative-intent lung cancer surgery

Authors:

Sebastian Lugg (luggs@bham.ac.uk;Sebastian.Lugg@nhs.net)
Theofano Tikka (theofano.tikka@gmail.com)
Paula Agostini (paulaagostini@aol.com)
Amy Kerr (amy.kerr@heartofengland.nhs.uk)
Kerry Adams (kerry.adams@heartofengland.nhs.uk)
Maninder Kalkat (maninder.kalkat@heartofengland.nhs.uk)
Richard Steyn (richard.steyn@heartofengland.nhs.uk)
Pala Rajesh (pala.rajesh@heartofengland.nhs.uk)
Ehab Bishay (ehab.bishay@heartofengland.nhs.uk)
David Thickett (d.thickett@bham.ac.uk)
Babu Naidu (b.naidu@bham.ac.uk;alice.wareham@aspire-scientific.com)

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Author's response to reviews:

Dear Vipin Zamvar

RE: JCTS-D-16-00335

Please find our reply to the reviewer’s comments for our manuscript, 'Smoking and timing of cessation on postoperative pulmonary after curative-intent lung cancer surgery', Lugg ST et al.; which has been considered in the Journal of Cardiothoracic Surgery for publication following revision. We very much thank the reviewer for their time taken, and have addressed each point in turn with reference to amended manuscript. We have also submitted a marked copy with track changes as well as the amended manuscript.

Reviewer 1
Authors assessed the clinical implication of smoking status to predicting postoperative pulmonary complication (PPC) and long term survival resulting in that the ex-smokers there was a trend for a lower frequency of PPC and intensive care unit (ITU) admission but there was no difference between the <6 weeks or >/= 6 weeks ex-smoking groups prior to surgery and there was no significant difference in long-term survival found between the groups of differing smoking status.

The results are very interesting but there is room for improvement in this article.

Main point: What is the primary end-point? Since the study is prospective, one primary end-point should be selected. I consider the primary end point is ‘occurrence of PPC’ and the secondary end point is ‘long term survival’, the context of which should be cleared.

Response to main point: We thank the reviewer for their comment, and have therefore made clear that the primary endpoint is ‘incidence of PPC’ and secondary endpoints include both ‘short-term outcomes (hospital length of stay, intensive therapy care unit admission, 30-day hospital readmission rate) and long-term survival’.

Amended in manuscript: We have therefore amended the manuscript accordingly to make this clear within the abstract, introduction (line 89-95) and results section (line 210-217). We have also added subheadings in the methodology and results.

Major point 1: Evaluation of optimal duration of smoking cessation. Authors revealed that the cut-off point of 6 weeks smoking cessation can’t predict occurrence of PPC. As occurrence of PPC is dichotomous ROC curve analysis is available, which will provide proper cut off duration of smoking cessation. It is strongly recommended.

Response to major point 1: We would not be possible to calculate this as data has been collected as a categorical variable (<6 weeks; >/= 6 weeks), as this was thought to be an important time point from the literature. We have added this to the studies limitations in the discussion section.

Amended in manuscript discussion, limitations (line 359-362): ‘Smoking cessation data was collected as a categorical variable, and therefore additional statistical analysis using ROC curve analysis could not be performed to further inform on a cut-off for the duration of smoking cessation needed to reduce PPC incidence’.

Major point 2: Long term survival according to smoking status. The method used in this investigation is uncommon. Propensity score matched analysis is recommended.

Response to major point 2: Survival analysis using COX proportional Hazard modelling was used to analyse long time survival which is the standard approach to perform survival analysis using multivariate modelling. Propensity score matching prior to survival analysis was discussed with the study statistician prior to analysis of data but it was not considered appropriate for our dataset. Propensity score matching can be used to adjust for bias present between two groups in terms of treatments received or when there is rarity of events prior to performing logistic
regression type analysis. We looked at late deaths, which was not a rare event in our study. We are also not looking specifically in comparing deaths between two different treatments, which could potentially have associated bias, requiring propensity score matching of cases. There was no selection bias in the variables including in our model. On this occasion, attempting to perform propensity matching can increase hidden bias due to dormant unobserved confounders as described by Pearl (2009).

Reference:


Minor points 1: Grade of COPD. Severity of COPD varies, thus the grade of COPD needs to be informed.

Response to minor point 1: We agree with the reviewer with regards to this point, and have amended table 1 to include this data; there was no significant difference of the severity of COPD between groups (p=0.358).

Amended in methods (line 131-132): ‘COPD severity staged according to percentage predicted FEV1.

Amended in results (line 205-206): ‘there was no significant difference of the severity of COPD between groups’.

Minor point 2: TNM classification – Ver. 8 classification has applied in 2017. Version of TNM classification is needed

Response to minor point 2: Ver. 7 of TMN classification has been used, the methodology has been amended to reflect this.

Amended in methods (line 126-127): ‘All patients included in the study had a confirmed pathologically staged diagnosis of NSCLC (TNM 7th edition).’

Final comments from authors: We hope following these major amendments that this journal will be suitable for publication in the Journal of Cardiothoracic Surgery.

Yours sincerely,

Mr Babu Naidu
Honorary Consultant Thoracic Surgeon,
Department of Thoracic Surgery,
Heart of England NHS Foundation Trust,
Bordesley Green East,
Birmingham, B9 5SS
United Kingdom
Email: b.naidu@bham.ac.uk