Peer Review File
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Reviewer A

Regarding the response to major comment 1, I am surprised that PPCs include pneumothorax, pleural effusion, atelectasis, and pneumonia. Suppose they think pneumothorax and pleural effusion are the complications of lung surgery. In that case, they should define when pneumothorax and pleural effusion are considered complications because it occurs in more or less all surgical patients.
Besides, regarding minor comment 3, I asked the authors "All citations number with brackets are put after period, like ". (1)". However, citation number with brackets should be put BEFORE period, like "(1).".
However, they only change Line 601. I think authors should change all the citation site.
Reply: We further clarified the definition of PPCs. (see page 10, line 177-178).
We have already made a correction as advised. All citations number with brackets are put before period. (see page 6-21).

Reviewer B

Comment 1: Regarding postoperative complications, the definition of pneumothorax is unclear. I think pneumothorax means air leak. It is usually easier for the reader to understand if pneumothorax is changed to air leak.

Reply 1: We have already made a correction as advised. (see page 10, line177; page19, line369-370; table1)

Comment 2: The study shows that 413 patients (70.2%) had postoperative air leak complications. This result seems too high. Usually, the postoperative air leaks that are clinically problematic are prolonged air leaks of 5 to 7 days or longer.
How many days or longer do the authors consider an air leak to be a postoperative complication?
Reply 2: In our study, air leak was defined as prolonged air leakage over 5 days. (see Page 10, line 177-178). In terms of the high incidence of air leakage, we considered that the possible reason was that in the imaging examination on the 5th day after surgery in our hospital, even a small amount of gas in the pleural cavity would be cautiously considered as air leakage by the radiologist based on chest x-ray. This could be the cause of the systematic bias.

Comment 3: Postoperative pleural effusions also occurred in 195 cases (33.2%), again a very high complication rate.
Postoperative pleural effusions are a very natural occurrence in the postoperative course.

The authors consider postoperative pleural effusion a complication, but is it a postoperative effusion associated with a clinical problem? Asymptomatic pleural effusions that do not require drainage should not be included as a complication.
Please supplement the rationale for including pleural effusions as a complication.
Reply 3: We chose pleural effusions as a complication according to the previous literature. (see reference 11). We reviewed the data and retained cases of pleural effusion requiring drainage as advised. We further clarified the definition of pleural effusions. (see page 10, line 177-178; table 1).

Comment 4: The whole picture of postoperative complications needs to be sorted out once again by clinically problematic criteria.
Then, it is necessary to reanalyze the relationship between the complications and predictive parameters.
Again, the percentage of postoperative air leaks and postoperative pleural effusions included in complications is very high, and the criteria that made these postoperative complications should be reviewed (duration of drainage, need for drainage, use of diuretics, etc.).
Reply 4: We reviewed the data and further clarified the definition of air leak and pleural effusions as advised. (see page 10, line 177-178; table 1). Although the number of cases of pleural effusion decreased according to the new definition, the corresponding cases with complications did not change because there was a significant overlap between the pleural effusion cases and the air leakage cases. Therefore, our previous statistical results were not affected. Furthermore, we mainly discussed the relationship between perioperative anesthetic factors and overall complications in this study, and did not explore the association of predictors and any specific complications in depth. However, the results suggested that perioperative anesthetic factors might have influence on the complications of patients to some extent. We will further explore the predictors of specific complications in future studies as well.

Comment 5: Tables
Initial letters are not consistent between upper and lower case. Also, some letters are out of alignment. Please review all tables.
Reply 5: We have already made a correction as advised. (see table 1, 3)

Comment 6: In the text, univariate and univariable are mixed as methods of analysis. I believe univariable is the analysis used in this paper. Please correct the analysis method in the text to be accurate (Kaplan-Meier univariate → Kaplan-Meier univariable).
Reply 6: We have already made a correction as advised. (see page10, line 182,186; page 11, line187,191; page 12, line 214; page 13, line 231,249)

Comment 7: The author states that opioids cause immunosuppression, which in turn is a risk factor for pneumonia. Immunosuppression is also a risk factor for cancer progression. The authors discuss the possible opposing effects of opioids on cancer suppression and immunosuppression (cancer progression), respectively.

Ultimately, can the authors offer a theoretical and valid interpretation of these conflicting effects of opioids on OS and RFS?
Reply 7: According to previous research, opioids have dual the effect of on tumors. For example, morphine may reduce natural killer cell activity and T-lymphocyte proliferation as well as cytokine secretion, and eventually promote tumor growth and metastasis, which reflects immunosuppressive effects. On the other hand, morphine was shown to inhibit the migration of tumor-infiltrating leukocytes and suppress angiogenesis associated with tumor growth. Therefore, the effects of opioids probably varied according to cancer subtype, because the different expression of opioid receptors in lung cancer cells would be a crucial factor for opioid effects on oncologic outcomes. (see page16-18, line307-349).

Comment 8:
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Please correct the “but” as it is followed by two times.
Reply 8: We have already made a correction as advised. (see page 8, line132).