**Author’s response to reviews**

**Title:** Clinicopathological variables influencing overall survival, recurrence and post-recurrence survival in resected stage I non-small-cell lung cancer

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**Author’s response to reviews:**

We thank the reviewers for the constructive criticisms again that have helped us to improve our manuscript. The point-by-point response to the comments is given below and the changes occur in the revised manuscript.

**Reviewer reports:**

Junaid Ahmed (Reviewer 1): 1. Well written article with good insights into recurrence patterns in non-small cell lung cancer. However, the quality of written English can be improved and a language correction tool should be used for the entire Manuscript.

Answer: Thanks a lot for the recognition from the reviewer. We have invited the native English speaker to edit for English language of grammar and word usage to make the manuscript more professionally.

2. The study would have carried more weight if long term follow-up results on patients with recurrence were evaluated for a period of more than 5 years wherever applicable.

Answer: We are in favor with the comments that recurrent patients with more than 5-year clinical follow-up will be of great significance. We found 43 recurrent patients with 5-year follow at least after the relapse and conducted the analysis. The results indicated that the 5-year PRS was 16.6%. Median PRS time for the recurrent patients was 25.5 months.
joaira bakkach (Reviewer 2): I reviewed the paper by Wang et al. The main objective of this work is to investigate the prognostic value of clinicopathologic factors and histologic subtypes in the overall survival, overall recurrence, and PRS in resected stage I non-small-cell lung cancer. The manuscript is well written and the data is convincing. However, there are some points listed as follows possibly needed to be further improved.

General remarks: Replace the terms by their abbreviations in the whole text: post-recurrence survival, lung adenocarcinoma, adenocarcinoma in situ, minimally invasive adenocarcinoma, overall survival...

Answer: We have replaced the terms by their abbreviations PRS, LUAD, AIS, MIA, OS in the whole manuscript such as post-recurrence survival, lung adenocarcinoma, adenocarcinoma in situ, minimally invasive adenocarcinoma, overall survival.

Abstract

Methods: "...The effecting..." please replace by "the effect"

Answer: We agree and have changed the term "effecting" into "effect"

Results: "...Taking the clinicopathological variables on PRS into consideration..." Taking the effect of clinicopathological variables on PRS into consideration...

Answer: We agree and have updated the related description. (Abstract section, line 5, page 2)

Background

"Reported locoregional recurrence rates elevated ...and range with various..." I propose:

Answer: The content “Reported locoregional recurrence rates were shown to elevate ...and to range with various” is more professional and we have updated the relevant information. (Background Section, line 6 & line 8, page 3)

"Appropriate surveillance strategies is ... to screen and identify the early detection of recurrent patients who have the high probability of mortality. " Please correct: Appropriate surveillance strategies are ... identify earlier and to screen recurrent patients who have the high probability of mortality

Answer: We have corrected the content. (Background Section, line 14 & line 15, page 3)
"…several studies have reported the role of the new classification on the prognostic value to predict mortality and recurrence mainly on LUAD or non-LUAD" I propose: …several studies have reported the prognostic value of the new classification to predict mortality and recurrence mainly in LUAD or non-LUAD

Answer: We have adopted the proposed description. (Background Section, line 26 & line 27, page 3).

"With regard to recurrence modalities" I think recurrence patterns is more adequate here

Answer: We regard the “recurrence patterns” as more adequate. (Background Section, line 29, page 3)

"We could explore and identify the risk factors on the overall survival…” please modify: could identify the risk factors and explore their effect on the OS…”

Answer: We agree and have modified the content. (Background Section, line 6, page 4)

Methods

"Exclusion criteria were that patients had received" Please modify: Exclusion criteria were patients who had received…

Answer: We agree and have modified the content. (Methods Section, line 20, page 4)

"The clinic follow-up" Please replace by: clinical follow-up

Answer: The clinical follow-up is more adequate. (Methods Section, line 7, page 5)

"if abnormal symptoms occurred to be noticed" I propose: if abnormal symptoms were noticed
Answer: We have adopted the description “if abnormal symptoms were noticed”. (Methods Section, line 10, page 5)

"… the prognostic value of clinicopathologic variables on the overall survival … " I propose: …the prognostic value of clinicopathologic variables in the OS…”

Answer: The related information has been updated. (Methods Section, line 24, page 5)

Results
The lung adenocarcinoma classification lacks the MIA (12) subtype. Please include this in the text.

Answer: We have added the related information in the results section. (Results Section, line10, page 6)

"… (21.7%) had developed the recurrence…” please modify: had developed recurrence

Answer: We have deleted the term “the”. (Results Section, line22, page 6)

"The 5-year overall recurrence for all stage I patients were about 20.2%." This sentence is mentioned twice. Please delete one.

Answer: We have deleted the same sentence.

Authors stated that 230 patients had distant recurrence. Moreover, it was mentioned that the most commonly involved organs for distant recurrence were the lung (n=193), brain (n= 82), bone (n=85) and liver (n= 30). The total here is 390 cases and not 230 patients.

Answer: Some patients have developed more than one recurrent site such as having both brain and liver metastasis.

Other treatments details are presented in Table 2. Please insert this sentence to avoid any confusion.

Answer: We have added the related information in the results section. (Results Section, line7, page 7)

"We further the explored risk factors" please correct : We further explored risk factors

Answer: We have corrected the content as “We further explored risk factors ”. (Results Section, line9, page 7)

"Taking the clinicopathological variables on PRS into the account"

Answer: We have updated the related information. (Results Section, line10, page 7)

Discussion
"To our knowledge, this present study is the first to comprehensively explore the clinicopathologic factors on oval survival…" To our knowledge, this present study is the first to comprehensively explore the influence of clinicopathologic factors on OS…

Answer: We agree and have adopted the content. (Discussion Section, line24 & line25, page 7)

"The prognostic value of the new IASLC/ATS/ERS classification system on …" please modify: … classification system in…

Answer: The term “classification system in” has been updated. (Discussion Section, line28, page 7)

"…who experienced the operation…” I suggest: …who underwent the surgery…

Answer: We have changed "…who experienced the operation…” into “who underwent the surgery”. (Discussion Section, line2, page 8)

"…possibility of recurrence similar to the reported results…” please modify:…similarly to …. 

Answer: We have adopted the term “similarly”. (Discussion Section, line12, page 8)

"…we could find it was within the first two years after the curative-intent surgical section that the most recurrences or disease progression appeared…” please modify: we found that most recurrences or disease progression appeared within the first two years after the curative-intent surgical section…

Answer: The modified description has been adopted in the updated manuscript. (Discussion Section, line14 & line15, page 8)

"… is still to be warranted to investigated and validated in case of excessive medical treatment or delayed the illness due to insufficient diagnosis” please modify: still warrants to be investigated and validated in case of excessive or delayed medical treatment

Answer: We agree and modified the related content. (Discussion Section, line17 & line18, page 8)

"… which needed more medical care for the postoperative clinical contact…” which highlights the need for more medical care for the postoperative clinical contact
Answer: We have replaced the term “needed” by the term “highlights the need” (Discussion Section, line20, page 8)

"….the most effective treatment modalities … studies have reported the incidence …" please modify: …the most effective treatment modality… studies have reported an incidence

Answer: We agree and updated the information. (Discussion Section, line24, page 8)

"We examined the clinicopathological variables on overall survival and overall recurrence in stage I NSCLC and identified a number of risk factors ….were significantly associated with worse overall survival" Please modify: We examined the impact of clinicopathological variables on OS and overall recurrence and identified a number of risk factors that were significantly associated with worse OS including the older age….

Answer: We have adopted the related description “We examined the impact of clinicopathological variables on OS and overall recurrence and identified a number of risk factors that were significantly associated with worse OS including the older age…” (Discussion Section, line28 & 29, page 8)

"Shimada et al demonstrated that liver metastasis…”please insert the reference for this statement
Answer: We have inserted the reference for this statement in the discussion section. (Discussion Section, line11, page 9)

"…facilitated the quality of life and survival benefit…”
Answer: We have updated the related information (Discussion Section, line24 & 25, page 9)

"…, the present study had three limitations. First, the retrospective nature of the current study had its limitation to assess …" I propose: the present study had some limitations. First, the retrospective nature hinders us to assess…

Answer: We agree and adopted the recommend description “the present study had some limitations. First, the retrospective nature hinders us to assess…” (Discussion Section, line1, page 10)

Conclusion

Authors repeat here the same conclusion of the abstract. Please reformulate the context and add some perspectives of your study.
Answer: We are in favor with the comments. We have reformulated the context and add some perspectives of the present study. In conclusion, the clinicopathological variables have significant prognostic and predictive value for the OS, overall recurrence, and PRS, which will likely affect the clinical decision making in the near future. This study also provides new insight to help clinicians to identify high-risk patients, make personalized postoperative follow-up strategies and conduct the appropriate post-recurrence therapies. (Conclusion Section, line11-15, page 10)