

## Peer Review File

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### Reviewer A

**Comment 1:** The authors demonstrated that poor differentiation and micropapillary + solid component  $\geq 5\%$  were independent risk factors for postoperative recurrence along with other factors and used these factors to establish a nomogram. However, poor differentiation and the presence of micropapillary/solid components generally overlap. Authors should explain how tumor differentiation were evaluated. Did they evaluate it with predominant histologic pattern, or a combination of predominant histologic subtypes and the extent of high-grade components (IASLC new grading system)?

**Reply 1:** Thank you very much for your professional comment. The results of tumor differentiation (highly differentiated, moderately differentiated and poorly differentiated) were recorded in the medical record system. Tumor differentiation was defined according to the 2015 WHO classification of lung adenocarcinoma. Grade 1: Well differentiated adenocarcinoma=lepidic predominant; Grade 2: Moderately differentiated adenocarcinoma=acinar or papillary predominant; Grade 3: Poorly differentiated adenocarcinoma=solid or micropapillary predominant.

**Changes in the text:** We have modified our text as advised (see Page 7, line 110 -114)

**Comment 2:** The authors described “adhesive type” as one of the histologic subtypes. It is assumed to mean the same as “lepidic”, but the term is not common. They should describe it according to the WHO and IASLC definitions.

**Reply2:** Thank you for your constructive suggestion. We have changed the “adhesive type” to “lepidic type”.

**Changes in the text:** we have modified our text as advised (see Page 7, line 107)

**Comment 3:** Similarly, nerve invasion as histologic evaluation is uncommon. In fact, positive cases should be rare (only 1.4%). I would recommend that authors not use

uncommon and rare histologic evaluations.

**Reply3:** Thank you very much for reading our manuscript so carefully. We are sorry to make you confused about the nerve invasion. Maybe it's better to use “perineural invasion” instead of “nerve invasion”. Previous studies have found that perineural invasion has an impact on postoperative recurrence and metastasis, so we included perineural invasion in the analysis.

**Changes in the text:** we have modified our text as advised (see Page 6, line 85;Page7, line 104;Page 10, line 184 -185;Page 11, line 196)

**Comment 4:** Authors used IHC to examine EGFR and ALK gene status. However, the method is not common for EGFR testing, and the positivity does not mean positive for EGFR mutation. Therefore, they cannot discuss the relationship between EGFR mutation status and prognosis using their study method. The results of other molecular testing should be used.

**Reply4:** Thank you very much for your professional comment. After our repeated confirmation, the status and types of EGFR mutation were assessed using the ARMS (amplification refractory mutation system). The human EGFR gene mutation fluorescence PCR (Polymerase Chain Reaction) Diagnostic Kit was used to identify the most common EGFR mutations. Besides, we used FISH (Fluorescence In Situ Hybridization) to examine the status of the ALK gene.

**Changes in the text:** we have modified our text as advised (see Page 4, line 114-119)

**Comment 5:** Authors performed risk grouping based on the nomogram model. They mentioned the cutoff was 0.797, but it's unclear what this number means. In Figure 6, they seem to have defined nomogram score >155.3 as high-risk. They should elaborate more on the grouping method.

**Reply5:** Thank you very much for your professional comment. We use the “surv\_cutpoint” function in the “survminer” R package to get the cutoff value according to the nomogram score for each patient in the internal cohort, and the cutoff value was 155.3. Besides, the overall 5-year RFS ratio corresponding to the cutoff value is 0.797. Based on the cutoff value, we divided the cohort of patients into two groups: a low-risk group and a high-risk group.

**Changes in the text:** We have modified our text as advised (see Page 13, line 240-244)

## **Reviewer B**

Line 47: “Nomograms have **been** proven **a** useful **tool**” (passive voice; singular no “s”)

Line 49: please first define “TNM” (abbreviations have to be defined in both the Abstract and the Main Text.)

Line 50: “most **published** articles **have** provided verification that a single factor affects ~~affected~~ the” (simple present tense would be fine for general facts or beliefs description)

Line 66, 67: “+” => “and” (formal writing)

Line 72: please check if “EGFR”, “ALK” can be defined first, please define them here

Line 89: ‘6’ => ‘six’ (better to spell out number <10 for formal writing; please check across the whole paper)

Line 124: “is defined” => “was defined” (please standardize as either in simple present tense or in simple past tense across the whole Method part; Line 125 is in past tense while some other similar usages are in present tense; simple past tense is better; please review this issue in the whole Method part)

Line 125: please first define “RFS” (abbreviations have to be defined in both the Abstract and the Main Text.)

Line 130, 131-132: ‘are expressed’ => ‘were expressed’ (simple past tense for Method and Result presentation)

Line 133: “are” => “were” (simple past tense for Method and Result presentation)

Line 135: “Chi-squared”

Line 180: “analysis” => “analyses” (plural)

Line 238: please first define “NCCN” (abbreviations have to be defined in both the Abstract and the Main Text.)

Line 256: “showed” => “show” (simple tense would be fine for general facts or

beliefs description)

Line 257, 258: “correlates”; “is associated” (simple present tense would be fine for general facts or beliefs description)

Line 269: “play” => “plays” (for the subject “LVI”)

Line 304: “which was” => “which is” (simple present tense would be fine for general facts or beliefs description)

Line 314: no need to have “However”, please consider delete

**Reply:** Thank you very much for the professional comments. We have revised the issues according to your comments and suggestions.