Peer Review File

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Reviewer A

This is a well-designed study, but I have a few comments as follows:

Comment 1: For the imaging findings used in the clinical characteristics, please provide a clear definition for each imaging parameter in the Materials and Methods section.

Reply 1: We thank the reviewer for this valuable comment. We have added precise definitions of the imaging findings (lobulated margin, spiculation, pleural indentation, and air bronchogram) to ensure clarity and reproducibility. These definitions are now included in the Materials and Methods section (see Page 3, line 111).

Changes in the text:

Definition of Imaging Findings

All imaging findings were evaluated by one radiologist with more than ten years of experience in thoracic imaging. The imaging parameters were defined as follows: lobulated margin was characterized by two or more outward convexities, resulting in a lobulated contour; spiculation was defined as fine linear strands radiating from the tumor margin into the surrounding lung parenchyma; pleural indentation was described as linear retraction of the adjacent pleura toward the tumor margin; air bronchogram was defined as air-filled bronchial structures visible within the lesion on CT images. All imaging features were assessed on lung window settings (window width, 1500 HU; window level, −600 HU).

Comment 2: Another limitation that may affect the generalizability of these models is that the study population consists of an Asian cohort with a high prevalence of EGFR mutations than other population. This should be mentioned in the Limitations section.

Reply 2: We appreciate the reviewer's insightful comment. We agree that the ethnic composition of the study cohort may affect the generalizability of the model. We have revised the Limitations section to acknowledge that our population consisted of an Asian cohort with a relatively high prevalence of EGFR mutations, which may limit model applicability to other populations, and we recommend validation in multiethnic cohorts in future research (see Page 20, line 532).

Changes in the text:

In addition, the study population consisted exclusively of an Asian cohort, which is known to have a higher prevalence of EGFR mutations compared with other populations. This ethnic homogeneity may limit the applicability of the model to more diverse patient populations, and future studies including multiethnic cohorts are warranted.

Reviewer B

This manuscript presents a very interesting and timely study that addresses an important topic with potential clinical relevance. The research question is well-motivated, and the overall findings contribute valuable insights to the field.

While the study holds promise and is worth publishing, the manuscript would benefit from further polishing in terms of clarity, consistency, and formatting.

The following comments are intended to help strengthen the presentation and improve the readability of the work:

Comment 1: Abbreviations such as SCC, RMR, LASSO, etc., are not clearly defined. These should be explicitly introduced and explained upon first use in the main text, not just in the abstract, to ensure clarity for all readers.

Reply 1: We thank the reviewer for this helpful comment. We have revised the abstract and main text to introduce and define all abbreviations at their first appearance (see Page 1, line 13, 22, Page 2, line 40, 44, 79, Page 4, line 150, Page 5, line 154, 156, 179, Page 10, line 289).

Comment 2: The manuscript contains frequent spelling mistakes and inconsistent spacing, such as unnecessary spaces before commas or missing spaces between words (e.g., "384 nodules(27,28)" should be "384 nodules (27,28)").

Reply 2: We appreciate the reviewer's careful reading and constructive suggestion. We have thoroughly proofread the entire manuscript, corrected all spelling errors, and standardized spacing throughout the text.

Comment 3: Inconsistent use of capitalization (e.g., "Univariate" vs "multivariate") should be corrected to maintain uniform style and professionalism.

Reply 3: We thank the reviewer for pointing out this issue. We have carefully revised the manuscript to ensure consistent capitalization throughout. Specifically, terms such as "univariate" and "multivariate" are now presented in lowercase for uniformity, except when appearing at the beginning of a sentence. We also standardized capitalization for other statistical terms and ensured consistency between the main text, figures, and tables (see Page 1, line 14, Page 9, line 259, 261, 266).

Changes in the text:

The results of the univariate and multivariate regression analysis for the clinical characteristics of the cohort for predicting EGFR mutation status and sites are presented in Table 2. In the univariate regression analysis, gender, spiculation, air bronchogram, tumor diameter, and nodule type were significantly associated with EGFR mutation status ($P < 0.05$). The multivariate regression analysis further revealed that gender and nodule type were independent predictors of EGFR mutation status ($P < 0.05$).
In the univariate regression analysis, age group, gender, spiculation, air bronchogram, and tumor diameter were significantly correlated with EGFR subtype mutation status ($P < 0.05$). The multivariate regression analysis identified age, gender, bronchial signs, and tumor diameter as independent predictors of EGFR subtype mutation status ($P < 0.05$).

Comment 4: There is inconsistent use of clinical terminology, such as "air bronchogram" vs "bronchial sign". Please clarify whether these terms refer to the same finding and use consistent terminology throughout the text.
Reply 4: We thank the reviewer for highlighting this important issue. We confirm that "air bronchogram" and "bronchial sign" refer to the same imaging finding in our study. To maintain consistency and align with standard radiologic terminology, we have replaced all instances of "bronchial sign" with "air bronchogram" throughout the manuscript. The definition of "air bronchogram" has also been clarified in the Materials and Methods section (see Page 9, line 269).
Changes in the text:
The multivariate regression analysis identified age, gender, air bronchogram, and tumor diameter as independent predictors of EGFR subtype mutation status ($P < 0.05$).

Comment 5: Lines 382–385 reference findings about EGFR mutations, age, and sex differences. It is unclear whether these are your own findings or cited from previous studies. If cited, please explicitly compare them to your study results to add clarity and relevance.
Reply 5: We have clarified that the results presented are from our own study, and we have compared them with findings from selected previous studies. This comparison highlights both the consistencies with prior research and the novel observations, such as the female predominance among patients with EGFR mutant (see Page 19, line 460).
Changes in the text:
Our findings indicate that EGFR mutations are more prevalent among female patients compared with those harboring wild-type EGFR, which is consistent with

prior studies (27,28). Furthermore, patients with exon 21 mutations tended to be older than those with exon 19 mutations, in line with previous reports (29). Notably, our study revealed a female predominance among patients with exon 21 mutations, a sex-related difference that was not observed in earlier studies (30).

Comment 6: At line 397, the phrase “previous studies” is used, but only one source is cited. Either provide additional references to support the claim or revise the wording appropriately.
Reply 6: We appreciate the reviewer’s suggestion. We have revised the sentence to attribute the finding to the specific cited study, thereby improving accuracy and clarity (see Page 19, line 470).
Changes in the text:
Ross A. Soo et al. reported that the incidence of EGFR mutations is notably higher in early-stage NSCLC patients compared to those with advanced-stage disease (31).