Background Immune checkpoint inhibitors (ICIs) provide enhanced survival benefits for lung cancer patients but can cause potentially fatal adverse events such as checkpoint inhibitor-related pneumonitis (CIP).

Methods This retrospective, case-control study enrolled 666 lung cancer patients receiving ICIs. Patients exhibiting The CIPs were divided into mild (grades 1–2) and severe (grades ≥3). Logistic regression identified risk factors for all grade and severe CIP, and a risk score for severe CIP was constructed. The model was validated in a separate patient cohort of 187 patients.

Results In the evaluation cohort, 95 patients developed CIP, of which 37 were severe cases Multivariate analysis revealed age ≥65 years (OR=1.95), current smoking (OR=3.00), chronic obstructive pulmonary disease (COPD, OR=2.49), squamous cell carcinoma (SCC, OR=1.67), prior thoracic radiotherapy (OR=3.12), and extrathoracic radiotherapy during ICI (OR=2.80) were independently associated with CIP events. Five factors, emphysema (OR=2.87), interstitial lung disease (ILD, OR=4.76), pleural effusion (OR=3.00), history of radiotherapy during ICI (OR=4.30), and single agent immunotherapy (OR=2.44) were independently associated with severe CIP and were incorporated into a risk-score model (score ranging 0–17). The area under the model receiver operating characteristic curve for the model was 0.769 in the evaluation cohort and 0.749 in the validation cohort (figure 1).

Conclusions Advanced age, current smoking, COPD, SCC, previous thoracic radiotherapy and extrathoracic radiotherapy during ICI treatment were independent risk factors for CIP incidence. The risk of severe CIP was observed to be independently associated with emphysema, ILD, pleural effusion, radiotherapy during ICI, and immunotherapy alone. The model has a promising predictive capacity for severe pneumonitis.

Ethics Approval This study was approved by the local Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (No.2021-38).