Prediction of Tumor PD-L1 Expression in Resectable Non-Small Cell Lung Cancer by Machine Learning Models Based on Clinical and Radiological Features: Performance Comparison with Preoperative Biopsy

Objective: CheckMate816 demonstrated improved recurrence-free survival with neoadjuvant immunotherapy for non-small cell lung cancer (NSCLC) and a greater response with tumor program cell death ligand 1 (PD-L1) expression levels of >1%. In clinical practice, however, PD-L1 expression can be indeterminable despite biopsy. We investigated if PD-L1 expression can be predicted by machine learning using clinical information and imaging features.

Methods: We included 117 patients with c-stage I/II (ver. 8) NSCLC who underwent radical resection (no preoperative treatment) at our institution. A total of 3951 radiomic features were extracted by defining the tumor (within tumor contour), tumor rim (contour±3 mm) and tumor exterior (contour+10 mm) on preoperative contrast computed tomography. After feature selection by Boruta algorithm, prediction models of tumor PD-L1 expression (22C3:>1%, <1%) of resected specimens were constructed using Random Forest: radiomics, clinical (gender, smoking, tumor size), and combined models. Their performance was evaluated by 5-fold cross-validation, and area under the curve (AUC)s were compared using Delong test. Next, study groups were categorized as patients without biopsy (training set), and those with biopsy (test set). Predictive ability of biopsy for PD-L1 expression in the resected tumor was compared to that of each prediction model.

Results: Of 117 patients (66±10 years old, 48% male, and c-stage I/II 87%/13%), 33 (28.2%) had PD-L1>1%. The PD-L1>1% group had significantly more males, smokers, and larger tumor diameter than the PD-L1<1% group. Mean AUC of PD-L1>1% for the validation set in radiomics, clinical, and combined models were 0.80, 0.80, and 0.83 (p=0.32 vs. clinical model), respectively. The diagnosis of malignancy was made in 22/38 (58%) patients with attempted biopsies, and PD-L1 was measurable in 19/38 (50%) patients. Diagnostic accuracies of PD-L1>1% from 19 determinable biopsies and 38 all attempted biopsies were 68.4% and 34.2%, respectively. These were outperformed by machine learning: 71%, 71%, and 74% for radiomics, clinical, and combined models, respectively.

Conclusions: Our machine learning model predicted tumor PD-L1 positivity in resectable NSCLC with AUC of 0.83. Incremental effect of radiomic features on clinical features was limited. Machine learning could be an adjunctive tool in estimating PD-L1 expression prior to neoadjuvant treatment, particularly when PD-L1 is indeterminable with biopsy.

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