Background

The standard of care for locally advanced, unresectable NSCLC includes chemoradiation (CRT) followed by consolidative immunotherapy (IO). Pneumonitis is a well-known complication of radiation therapy (RT) and has been increasingly reported in association with IO. Although rare, pneumonitis can cause severe morbidity and possibly death in extreme cases. Differentiating RT and IO-induced pneumonitis (RTP vs IOP) is crucial for both acute management and future considerations of individualized treatment. However, the clinical and radiological features of RTP and IOP are often indistinguishable. Texture-based computed tomography (CT) radiomics has previously been used to distinguish benign and malignant nodules on lung CT. In this study, we explore if such radiomic features can distinguish between RTP and IOP.

Methods

Eligible subjects were those with locally advanced, unresectable NSCLC who underwent CRT followed by consolidative IO and subsequently developed pneumonitis. Cases were identified through a retrospective chart review of electronic medical records and independently verified by three oncologists using features such as extent of lung involvement, inflammatory changes within and/or outside the field of RT, the temporal relationship to IO, and overall response to glucocorticoids or biologic agents. Inflammatory lesions were manually annotated using Slicer 3D. Patients were divided randomly into two sets (training and validation) with the constraint that there were equal numbers of RTP and IOP in the training set. A multivariable logistic regression (MLR) model trained with top discriminating radiomic texture features extracted from post-treatment pneumonitis CT images was used to distinguish RTP versus IOP and the classifier performance was assessed by the area under the receiver operating characteristic curve (AUC).

Results

108 patients were eligible for radiomic analysis: RTP n=61; IOP n=47. The training set comprised 55 patients and 53 patients. The top 7 radiomic texture features in conjunction with a MLR classifier yielded an AUC of 0.87 (95% CI, 0.77 – 0.96) on the training set and corresponding AUC of 0.81 (95% CI, 0.7 – 0.92) on the validation set (Table 1).

Conclusions

Pneumonitis is a severe complication of both RT and IO that must be taken into consideration when evaluating future risks of IO-based therapies. The distinction between RTP and IOP remains challenging based on CT findings alone. Radiomic texture features analysis of post-treatment CT images can potentially differentiate RTP from IOP in patients with locally advanced, unresectable NSCLC who received RT followed by consolidative durvalumab. Additional multi-site independent validation of these quantitative image-based biomarkers is ongoing.

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Ethics Approval

The study conformed to Health Insurance Portability and Accountability Act (HIPAA) guidelines and was approved by the Institutional Review Board (IRB) at Cleveland Clinic Foundation (IRB 19-559). IRB waived the requirements for patient informed consent due to the retrospective and non-interventional nature of this study.

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