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Positron Emission Tomography Parameters as Predictors of Pathologic Response and Nodal Clearance in Patients with Stage IIIA NSCLC Receiving Trimodality Therapy

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Abstract : Objective: Pathologic response following neoadjuvant chemoradiation (CRT) has been associated with improved overall survival (OS). Conflicting results have been reported regarding the pathologic predictive value of positron emission tomography (PET) response in patients with stage III lung cancer. The aim of this study was to evaluate the correlation between post-treatment PET response and pathologic response utilizing novel FDG-PET parameters. Methods: This retrospective study included patients with non-metastatic, stage IIIA (N2) NSCLC cancer treated with CRT followed by resection. All patients underwent PET prior to and after neoadjuvant CRT. Univariate analysis was utilized to assess correlations between PET response, nodal clearance, pCR, and near-complete pathologic response (defined as the microscopic residual disease or less). Maximal standard uptake value (SUV), standard uptake ratio (SUR) [normalized independently to the liver (SUR-L) and blood pool (SUR-BP)], metabolic tumor volume (MTV), and total lesion glycolysis (TLG) were measured pre- and post-chemoradiation. Results: A total of 44 patients were included for review. Median age was 61.9 years, and median follow-up was 2.6 years. Histologic subtypes included adenocarcinoma (72.2%) and squamous cell carcinoma (22.7%), and the majority of patients had the T2 disease (59.1%). The rate of pCR and near-complete pathologic response within the primary lesion was 28.9% and 44.4%, respectively. The average reduction in $SUVm_{ax}$ was 9.2 units (range -1.9-32.8), and the majority of patients demonstrated some degree of favorable treatment response. SUR-BP and SUR-L showed a mean reduction of 4.7 units (range -0.1-17.3) and 3.5 units (range –1.7-12.6), respectively. Variation in PET response was not significantly associated with histologic subtype, concurrent chemotherapy type, stage, or radiation dose. No significant correlation was found between pathologic response and absolute change in MTV or TLG. Reduction in $SUVm_{ax}$ and SUR were associated with increased rate of pathologic response ($p \leq 0.02$). This correlation was not impacted by normalization of SUR to liver versus mediastinal blood pool. A threshold of > 75% decrease in SUR-L correlated with near-complete response, with a sensitivity of 57.9% and specificity of 85.7%, as well as positive and negative predictive values of 78.6% and 69.2%, respectively (diagnostic odds ratio [DOR]: 5.6, p=0.02). A threshold of >50% decrease in SUR was also significantly associated pathologic response (DOR 12.9, p=0.2), but specificity was substantially lower when utilizing this threshold value. No significant association was found between nodal PET parameters and pathologic nodal clearance. Conclusions: Our results suggest that treatment response to neoadjuvant therapy as assessed on PET imaging can be a predictor of pathologic response when evaluated via SUV and SUR. SUR parameters were associated with higher diagnostic odds ratios, suggesting improved predictive utility compared to $SUVm_{ax}$. MTV and TLG did not prove to be significant predictors of pathologic response but may warrant further investigation in a larger cohort of patients.

Keywords : lung cancer, positron emission tomography (PET), standard uptake ratio (SUR), standard uptake value (SUV)
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