

## Elevated Neutrophil-to-Lymphocyte Ratio following Stereotactic Body Radiation Therapy Predicts for Worse Outcomes in Patients with Localized Pancreatic Cancer Treated with Anti-PD-1 Antibody

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### Abstract

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## Abstract

**Objective:** The purpose of this study was to investigate the role of pre and post-stereotactic body radiation therapy (SBRT) neutrophil-to-lymphocyte ratio (NLR) in a cohort of patients with borderline resectable and locally advanced pancreatic adenocarcinoma (BRPC/LAPC) who was treated with multi-agent induction chemotherapy followed by anti-programmed cell death protein-1 (PD-1) antibody and SBRT.

**Methods:** Patients with BRPC/LAPC who were treated multi-agent induction chemotherapy followed by anti-PD-1 antibody and SBRT and had laboratory values available for review were included in the study. Median pre and post-SBRT laboratory values were compared with the Mann-Whitney U test. Univariate (UVA) and multivariable analyses (MVA) were performed to identify variables associated with clinical outcomes. Linear regression was performed to determine correlations between variables and laboratory values.

**Results:** A total of 68 patients were included in the study. The percent change between median pre and post-SBRT absolute lymphocyte count (ALC), absolute neutrophil count, and NLR were -44.0% ( $p < 0.001$ ), -10.0% ( $p = 0.190$ ), and +43.2% ( $p = 0.003$ ), respectively. Median overall survival (OS) after SBRT was 22.4 months, with 1-year, 2-year, and 3-year OS rates of 66.9%, 47.3%, and 28.2%, respectively. On UVA, pre-SBRT CA 19-9 (hazard ratio [HR]=1.00, 95% CI 1.00-1.00,  $p = 0.031$ ), post-SBRT ALC (HR=0.33, 95% CI 0.11-0.91,  $p = 0.031$ ), and post-SBRT NLR (HR=1.13, 95% CI 1.04-1.22,  $p = 0.009$ ) were associated with OS. On MVA, induction chemotherapy duration (HR=0.75, 95% CI 0.57-0.99,  $p = 0.048$ ) and post-SBRT NLR (HR=1.14, 95% CI 1.04-1.23,  $p = 0.002$ ) were significant predictors of OS. The optimal post-SBRT NLR threshold in predicting OS was 3.2. Patients with post-SBRT NLR > 3.2 had a median OS of 15.6 months versus 27.6 months in patients with post-SBRT NLR < 3.2 ( $p = 0.009$ ). On MVA linear regression, log10CTV had a significant negative correlation with post-SBRT ALC (regression coefficient: -0.314, 95% CI -0.626 to -0.003,  $p = 0.048$ ).

**Conclusion:** Elevated NLR after SBRT is primarily due to depletion of lymphocytes and associated with worse survival outcomes in BRPC/LAPC treated with anti-PD-1 antibody. Larger CTVs were associated with decreased post-SBRT lymphocyte count.