



ASO Author Reflections: Colorectal Cancers with Extramural Vascular Invasion Are Associated with a Low Immune Microenvironment

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PAST

Extramural vascular invasion (EMVI) is a well-established poor prognostic factor in colorectal cancer. Patients with EMVI-positive stage II colon cancer have been shown to have significantly worse survival than patients with EMVI-negative stage III disease.¹ This study aims to elucidate the immune microenvironment of EMVI-positive tumors.

PRESENT

This study² investigated the clinicopathological records of 1018 chemo-naïve patients across TNM stages I–IV who underwent surgical resection at the authors' institution. Immunohistochemistry was performed on the tissue microarrays of the resected specimens for immunological markers. There were 340 EMVI-positive and 678 EMVI-negative chemo-naïve samples. There was a generalized low expression of CD8, LAG-3, FOXP3, PU.1, and PD-L1 immune cells and β_2 -microglobulin on tumor cells in EMVI-positive tumors compared with EMVI-negative tumors ($p \leq 0.001$) on univariate analysis. On multivariate analysis, PU.1 (odds ratio 0.8, 0.7–0.9) and low PDL1 (odds ratio 1.6, 1.1–2.3) independently predicted EMVI among all biomarkers examined.

FUTURE

This study demonstrated that EMVI-positive tumors were associated with a low immune state, which could be responsible for their worse prognosis. Tumor-associated macrophages, as indicated by PU.1 and PD-L1, seem to play the most crucial role in predicting EMVI. The seemingly paradoxical down expression of immunoregulatory cells such as FOXP3, LAG-3, and PD-L1 in EMVI-positive tumors could challenge the conventional understanding of immunoregulatory cells in colorectal cancer and warrants in-depth exploration. Future studies should also attempt to understand the mechanisms of the spread of tumor cells in extramural blood vessels via epithelial-to-mesenchymal signatures.

DECLARATIONS

DISCLOSURES The authors have no disclosures to report.

REFERENCES

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