

Role of Foxp3-positive tumor-infiltrating lymphocytes in the histologic features and clinical outcomes of hepatocellular carcinoma.

Mathai AM, Kapadia MJ, Alexander J, Kernochan LE, Swanson PE, Yeh MM.

Source

Department of Pathology, University of Washington, Seattle, WA 98195, USA.

Abstract

The role of Foxp3-positive regulatory T cells (Foxp3 Tregs) in suppression of antitumoral immune response is well documented in patients with cancer. However, it is not known whether Foxp3 Tregs are associated with specific clinicopathologic characteristics of hepatocellular carcinoma (HCC). The aims of the present study were: (1) to investigate the relationship between Foxp3 Tregs and histologic differentiation, Edmondson-Steiner (ES) nuclear grade, vascular invasion, and pathologic stage of HCC in patients undergoing surgery for their disease; and (2) to evaluate any Foxp3 Treg-defined difference in the risk for tumor recurrence or death. The study sample included 131 histologic sections of HCC. The number of tumor-infiltrating CD3, CD8, and Foxp3 lymphocytes was assessed by immunohistochemistry. An increased Foxp3:CD3 ratio was associated with more poorly differentiated HCC ($P=0.0016$) and higher ES nuclear grade ($P=0.0407$). An increased Foxp3:CD8 ratio was also associated with poorer differentiation ($P=0.0044$), higher ES nuclear grade ($P=0.0179$), recurrence ($P=0.0183$), decreased overall survival (hazard ratio=1.153; 95% confidence interval, 1.019-1.304; $P=0.0235$), and decreased disease-free survival (hazard ratio=1.138; 95% confidence interval, 1.016-1.273; $P=0.0249$). Tumor size and type of surgery (surgical resection) were associated with decreased disease-free survival on univariate analysis but not on multivariate analysis. In conclusion, a higher concentration of tumor-infiltrating Foxp3 Tregs in HCC is associated with higher grade and poorly differentiated tumors and signifies an unfavorable prognosis.