Impact of peritumoral and intratumoral budding in esophageal adenocarcinomas.

Tumor budding has prognostic significance in many carcinomas and is defined as the presence of detached isolated single cells or small cell clusters up to 5 cells at the invasion front (peritumoral budding [PTB]) or within the tumor (intratumoral budding [ITB]). For esophageal adenocarcinomas (EACs), there are currently only few data about the impact of this morphological feature. We investigated tumor budding in a large collective of 200 primarily resected EACs. Pancytokeratin staining was demonstrated to be superior to hematoxylin and eosin staining for the detection of buds with substantial to excellent interobserver agreement and used for subsequent analysis. PTB and ITB were scored across 10 high-power fields (HPFs). The median count of tumor buds was 130/10 HPFs for PTB (range, 2-593) and 80/10 HPFs for ITB (range, 1-656). PTB and ITB correlated significantly with each other ($r = 0.9; P < .001$). High PTB and ITB rates were seen in more advanced tumor categories ($P < .001$ each); tumors with lymph node metastases ($P < .001/P = .002$); and lymphatic, vascular, and perineural invasion and higher tumor grading ($P < .001$ each). Survival analysis showed an association with worse survival for high-grade ITB ($P = .029$) but not PTB ($P = .385$). However, in multivariate analysis, lymph node and resection
status, but not ITB, were independent prognostic parameters. In conclusion, PTB and ITB can be observed in EAC to various degrees. High-grade budding is associated with aggressive tumor phenotype. Assessment of tumor budding, especially ITB, may provide additional prognostic information about tumor behavior and may be useful in specific cases for risk stratification of EAC patients.

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