Malignant degeneration of Barrett's esophagus: the role of the Ki-67 proliferation fraction, expression of E-cadherin and p53.

Abstract:
Barrett's columnar epithelium with dysplasia is the most important risk factor for adenocarcinoma of the distal esophagus. The molecular mechanisms responsible for progression of columnar metaplasia to dysplasia and invasive carcinoma are mostly unknown. We investigated expression of the tumor suppressor gene p53, E-cadherin expression and cell proliferation in the metaplasia-dysplasia-carcinoma sequence of esophageal adenocarcinoma. In 24 patients with R0-resected adenocarcinomas of the distal esophagus we evaluated the expression of E-cadherin (antibody HECD-1), mutated p53 (antibody DO1) and cell proliferation (antibody MiB1) by immunohistochemistry in sections of adenocarcinoma, columnar metaplasia, with and without dysplasia, and in squamous epithelium of the esophagus. No p53 immunoreactivity was seen in sections of normal squamous epithelium or columnar metaplasia. Fifty per cent of invasive adenocarcinomas stained positive for mutated p53. The p53 expression correlated with the T-category (P = 0.048) and the N-category (P = 0.024). There was a significant decrease in the expression of E-cadherin from columnar metaplasia to dysplasia and to esophageal adenocarcinoma (P< 0.0001). Expression of E-cadherin in columnar metaplasia without dysplasia was similar to that seen in normal squamous epithelium of the esophagus.
esophagus. The Ki-67 proliferation fraction increased significantly from normal squamous epithelium to columnar metaplasia to dysplasia and to invasive carcinoma (P< 0.001), with a marked expansion of the proliferative component. There was no correlation between cell proliferation, E-cadherin expression and the tumor stage. In contrast to the alterations in the p53 expression, a decreased E-cadherin expression and the expansion of the proliferative component represent an early phenomenon in the malignant degeneration of Barrett's esophagus. This might aid in the early detection of esophageal adenocarcinoma.