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Titel des Beitrags: Overexpression of TGF-beta1 in esophageal (Barrett's) adenocarcinoma is associated with advanced stage of disease and poor prognosis.

Abstract: Expression of TGF-beta1, a major member of the TGF-beta superfamily and important promoter of tumor growth, was investigated in a series of primary resected esophageal (Barrett's) adenocarcinomas to establish its potential clinical significance and prognostic relevance in this entity. A series of 123 primary resected adenocarcinomas of the distal esophagus, arising in association with Barrett's esophagus, and corresponding normal squamous epithelium (n = 12) and non-malignant Barrett's mucosa (n = 11), were investigated by means of quantitative RT-PCR for expression of TGF-beta1, using paraffin embedded tissue samples. Gene expression levels were correlated with clinical parameters and overall survival. TGF-beta1 mRNA was expressed in all tumors, but relative gene expression levels varied largely among different tumors. The relative gene expression was significantly higher in tumor tissue compared to squamous epithelium (P = 0.005) and Barrett's mucosa (P=0.002), expressing only low amounts of TGF-beta1. Relative overexpression of the TGF-beta1 gene was associated with advanced UICC stage (III/IV vs. I/II; P = 0.009), depth of tumor infiltration (pT3 vs. pT1/2; P< 0.001), nodal involvement (pN1 vs. pN0; P = 0.006), and lymphatic vessel invasion (L1 vs. L0; P = 0.011). On univariate survival
analysis, TGF-beta1 overexpression had a significant negative impact on survival (log rank test; \( P = 0.0255 \)). However, the prognostic impact was not independent from other strong predictors of survival (pT, pN) on multivariate survival analysis. Our data show that TGF-beta1 overexpression is associated with advanced stage of esophageal adenocarcinoma and implies a negative impact on survival. The TGF-beta pathway may be a potential target for molecular therapies of advanced tumors of this entity.