The activated stroma index is a novel and independent prognostic marker in pancreatic ductal adenocarcinoma.

Abstract:

BACKGROUND AND AIMS:
Pancreatic ductal adenocarcinoma (PDAC) is a highly desmoplastic tumor with an innate resistance to therapy. Pancreatic stellate cells (PSCs) produce this excessively desmoplastic microenvironment. The impact of PSC activity on PDAC behavior in vivo is analyzed. METHODS: 233 patients who underwent surgery for PDAC were evaluated by immunohistochemistry using antibodies against alpha-smooth muscle actin as a marker of PSC activity. Aniline was used to stain collagen deposition. The ratio of alpha-smooth muscle actin-stained area to collagen-stained area was defined as the activated stroma index (ASI). Survival analysis was performed using the Kaplan-Meier method. Prognostic factors were determined in a multivariable analysis using a Cox proportional hazards model. RESULTS: Four major patterns of collagen deposition were defined with regard to PSC activity. The combination of high stromal activity and low collagen deposition was associated with a worse prognosis, whereas the combination of high collagen deposition and low stromal activity indicated a better prognosis. Patients with the lowest ASI had the best median survival rate (25.7 mo). The highest ASI was found in patients with the worst median survival rate (16.1 mo; P = .007; lowest vs highest ASI: hazard ratio,
1.61; 95% confidence interval, 1.014-2.562). ASI was an independent prognostic marker in multivariable survival analysis comparable with the nodal status of cancer. CONCLUSIONS: The activated stroma index is a novel independent prognostic marker in PDAC in cases undergoing surgery. This finding highlights the impact of the microenvironment in cancer progression and on patient survival.