Co-clinical Assessment of Tumor Cellularity in Pancreatic Cancer.

Purpose: Tumor heterogeneity is a hallmark of pancreatic ductal adenocarcinoma (PDAC). It determines tumor biology including tumor cellularity (i.e., amount of neoplastic cells and arrangement into clusters), which is related to the proliferative capacity and differentiation and the degree of desmoplasia among others. Given the close relation of tumor differentiation with differences in progression and therapy response or, e.g., the recently reported protective role of tumor stroma, we aimed at the noninvasive detection of PDAC groups, relevant for future personalized approaches. We hypothesized that histologic differences in PDAC tissue composition are detectable by the noninvasive diffusion weighted- (DW-) MRI-derived apparent diffusion coefficient (ADC) parameter. Experimental design: PDAC cellularity was quantified histologically and correlated with the ADC parameter and survival in genetically engineered mouse models and human patients. Results: Histologic analysis showed an inverse relationship of tumor cellularity and stroma content. Low tumor cellularity correlated with a significantly prolonged mean survival time (PDAC(low) = 21.93 months vs.
PDAC(med) = 12.7 months; log-rank P < 0.001; HR = 2.23; CI, 1.41-3.53). Multivariate analysis using the Cox regression method confirmed tumor cellularity as an independent prognostic marker (P = 0.034; HR = 1.73; CI, 1.04-2.89). Tumor cellularity showed a strong negative correlation with the ADC parameter in murine (r = -0.84; CI, -0.90- -0.75) and human (r = -0.79; CI, -0.90 to -0.56) PDAC and high preoperative ADC values correlated with prolonged survival (ADC(high) = 41.7 months; ADC(low) = 14.77 months; log rank, P = 0.040) in PDAC patients. Conclusions: This study identifies high tumor cellularity as a negative prognostic factor in PDAC and supports the ADC parameter for the noninvasive identification of PDAC groups. Clin Cancer Res; 23(6); 1461-70. ©2016 AACR.