Co-clinical assessment of tumor cellularity in pancreatic cancer

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Abstract

Pancreatic ductal adenocarcinoma (PDAC) is a fatal malignant disease. Pretherapeutic detection of relevant prognostic marker would greatly facilitate patient care. Given recently reported protective role of tumor stroma, non-invasive detection of tumor composition is relevant for personalized approaches. In this proof-of-concept study we aimed to evaluate and image tumor cellularity as a prognostic marker in PDAC.

We stratified PDAC developed in genetically engineered mouse models (GEMM) and patients that underwent curative resection based on tumor cellularity in three subgroups: low, medium and high. We applied diffusion weighted- (DW-) MRI and thereof derived apparent diffusion coefficient (ADC) for their detection and correlated ADC with the overall survival of patients.

Histopathological analysis showed an inverse relationship of tumor cellularity and stroma content in both murine and human PDAC. Patients exhibiting low tumor cellularity revealed a significantly prolonged mean survival time (PDAC\text{low} = 21.93 versus PDAC\text{med} = 12.7 months, Log rank, p<0.0004, Hazard ratio 2.23). Multivariate analysis using Cox regression method confirmed this observation (p = 0.049, HR = 1.69). Tumor cellularity showed a strong negative correlation with the ADC in murine (r=-0.84, CI=-0.90 – -0.75) and human (r=-0.66, CI=-0.84 – -0.36) PDAC. Examination of the lowest ADC value, found in pre-operative DW-MRI revealed prolonged survival for PDAC patients with high values (ADC\text{high} = 41.7 months; ADC\text{low} = 14.77 months, Log rank, P=0.040).

In conclusion, this study identifies high tumor cellularity as a negative prognostic factor in PDAC and supports ADC parameter as a candidate marker for the non-invasive stratification of PDAC.