Periductal iron-corrected T_1 is a predictor of adverse outcomes in large-duct primary sclerosing cholangitis

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Background: Concentric periductal fibrosis, commonly referred to as “onion skin” fibrosis, is a histological hallmark of primary sclerosing cholangitis (PSC). Our aim was to evaluate whether a periductal fibroinflammatory disease, characterized using MRI, is predictive of adverse clinical events.

Methods: Standardised 3D MRCP and axial liver T1 and T2* maps were acquired on patients with a known diagnosis of large-duct PSC patients and healthy volunteers (HV). A 3D parametric biliary tree model was aligned to the axial liver corrected T1 (cT1) maps are each voxel over multiple slices in the liver using quantitative MRCP (MRCP+) and LiverMultiScan respectively. Periductal cT1 (Pd-cT1) was quantified over fixed radial distances surrounding the bile ducts at regions of interest (ROIs) with radius 1.5mm to 9.5mm from the bile duct: ROI-1: 1.5–3.5mm, ROI-2: 3.5–5.5mm, ROI-3: 5.5–7.5mm and ROI-4: 7.5–9.5mm. A cT1 of >800ms was considered elevated and indicative of the presence of fibroinflammatory disease activity. Liver stiffness (LSM) >9.6kPa and Amsterdam-Oxford model score >2 were considered as advanced fibrosis. Outcome data were collected by review of the medical record. The hazard ratio (HR) for prognostic performance of Pd-cT1 to predict adverse events was investigated using the cox proportional hazard model.

Results: Seventy-two participants with PSC (median age 44 years; 65% male) and 20 HV (median age 35 years; 65% male) were recruited. In PSC, mean Pd-cT1 in ROIs 1 and 2 was higher than ROIs 3–4 ($p<0.05$) at baseline and follow-up indicating elevated fibroinflammatory disease activity around the ducts. There were no differences between ROIs in HV. Participants with advanced fibrosis had higher Pd-cT1 than those without (baseline: $p<0.01$; follow-up: $p<0.02$). There were 42 adverse events including cholangitis (N=10), development of new dominant stricture (DS) (N=8), ascites (N=7), gallbladder cancer (N=1), death (N=3) and the need for ERCP (N=13). Elevated Pd-cT1 at ROI-4 had HR: 4.42 for predicting adverse events including cholangitis, gallbladder cancer and death.

Conclusion: Elevated periductal cT1 in the ring of tissue 7.5–9.5mm around the bile ducts may represent a macroscopic finding that correlates to the histologic “onion skin” fibrosis

and is predictive of adverse clinical outcomes in patients with large duct PSC. Our findings demonstrate how quantitative MRI techniques can be used to assess features of disease that were previously seen only at histology.

Figure: Co-registration of two quantitative MRI techniques for periductal cT1 quantification in a 33-year old woman with large-duct PSC. (a) Four segmented liver axial cT1 maps from LiverMultiScan analysis acquired at different levels with prominent blood vessels excluded and liver parenchyma colour-coded to liver cT1 values. (b) 3D biliary tree model derived from MRCP+ analysis, colour-coded according to duct diameter size and orientation in geometric space depicted in the top right corner. (c) Co-registration of both images using MRI acquisition coordinates for the purpose of periductal cT1 quantification.