MRI-serum based score accurately identifies liver transplant patients without rejection avoiding need for liver biopsy: a multisite European study

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Background and Aims: Liver function and histological assessment for fibrosis, inflammation and T-cell mediated rejection are essential elements of post-liver transplant monitoring. However, liver biopsy carries a risk of complications which are preferably avoided in low-risk patients. Multiparametric MRI (mpMRI) is a reliable non-invasive diagnostic method which quantifies liver disease activity (including fibroinflammation (cT1), liver fat content (PDFF) and liver iron) and has shown prognostic utility in chronic liver disease management. Our aim was to determine whether using mpMRI in combination with standard serum biochemistry (serum) tests could noninvasively identify low-risk post-liver transplant patients who are eligible to avoid invasive liver biopsies.

Methods: RADIcAL2, a multicentre prospective study, included 131 adult and paediatric (children and adolescent) patients with previous liver transplant from the Netherlands, Portugal and UK. Biopsies were centrally read by two expert pathologists. T-cell mediated rejection (rejection) was assessed using BANFF global assessment (BANFF-GA). Diagnostic accuracy to discriminate no rejection vs. indeterminate or T-cell mediated liver transplant rejection was performed using area under the receiver operating characteristic curve (AUC).

Results: In the RADIcAL2 cohort, 38% of patients had no rejection, while 62% had either indeterminate (21%) or T-cell mediated rejection (41%). There was a wide range of inter-observer variability ($0 \leq$ Cohen's Kappa < 0.85) across all histology scores with moderate agreement between pathologists (Kappa <0.58) for BANFF-GA. A combination of mpMRI cT1 and liver fat with standard serum tests had AUC 0.7 (NPV:

0.8) to identify those without rejection (either indeterminate or T-cell mediated rejection). In the 18% of RADIcAL2 participants where therapy changed, cT1 (841ms vs. 789ms; p=0.006), and GGT (284 vs. 125; p=0.013) were significantly higher compared to those who did not get a change in therapy.

Conclusion: A combination of mpMRI cT1 and liver fat with standard serum tests accurately identified patients without indeterminate or T-cell mediated rejection who could avoid liver biopsy. mpMRI used alongside serum markers has utility to support noninvasive patient management in both adult and paediatric post-transplant populations.