Quantification of iron deposition in chronic liver disease

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Introduction: Although hepatic iron deposition is commonly observed in patients with chronic liver disease (CLD), to our knowledge no studies have systematically assessed iron deposition in CLD using a quantitative MR method. MRI techniques for the quantification of iron deposition in the liver have been described (1). Further, a multi-echo gradient echo MR sequence which measures the T2* value of liver has been previously validated as a means to estimate the amount of iron in the liver (2). It has been proposed that increasing iron deposition in the liver may be a marker for advanced CLD, and it may be an independent risk factor for the development of hepatocellular carcinoma (HCC) (3-5). This study utilized a breath-hold multi-echo gradient echo sequence as a means to measure quantitatively hepatic iron deposition in patients with CLD compared with controls (patients without known CLD imaged for another indication).

Methods: This HIPPA compliant, retrospective study included 78 consecutive patients. From these, 2 patients were excluded based on a history of sickle cell disease, as this was likely to result in abnormal liver iron deposition. The remaining 76 patients (46 male, 30 female, mean age 57 years) included 33 patients with clinical evidence of CLD and 43 patients with no known liver disease. All were evaluated on a single MR unit at 1.5T (Avanto, Siemens Medical Solutions). The MR protocol included a multi-echo GRE sequence (TR 169, TE 4.8-28.7 (5 echoes), slice thickness 10mm, FOV 400x 400, 15 slices, acquisition time 44 seconds). Standard post-processing software available on the Siemens Syngo workstation allowed for an automated calculation of T2* for each image. Measurements were then obtained of 6 standardized locations within the liver (the 4 liver lobes at the level of the portal bifurcation, the liver dome, and inferior tip of the liver) with all measurements located at least 1 cm from the liver capsule. Mean T2* value and standard deviation were recorded.

Results: Among the 76 patients, there was a significant difference between the mean T2* of patients with CLD (16.2 ms +/- 2.1) and controls (28.3 ms +/- 2.6) ($p<0.001$). The range of mean T2* values for CLD patients was 9.6 ms – 33.1 ms and 21.3 ms – 41.4 ms for controls. As no absolute T2* value has been yet established to define significant levels of iron deposition, an analysis was performed using arbitrary cut-of values. In this population, no control patients had a T2* value below 21 ms, while 20 CLD patients (61%) did. At a cut-off value of 23 ms, 24 CLD patients (73%) would be considered to have iron deposition but only 3 of the control patients (7%). Please see Table 1. 5 patients (15%) with CLD had a mean T2* value of 12 ms or less. Among the etiologies for CLD, hepatitis C was the most common with 24 patients. 2 patients had positive genetic markers for hemochromatosis but both also had hepatitis C. When these patients were excluded, the mean T2* value of the remaining 31 patients (16.6 ms +/- 2.2) was still significantly different than the control patients ($p<0.001$).

Table 1: Percent with T2* value less than cut-off value

T2* value (ms)	CLD	Control
21	61%	0%
22	67%	5%
23	73%	7%
24	76%	12%

Conclusion: In this patient population, there was quantitatively significantly greater liver iron deposition among those with CLD than those without as indicated by a lower mean T2* value of the liver parenchyma. This was true even when patients with potential hemochromatosis were excluded. Further, 61% of CLD patients had a mean T2* value less than the lowest T2* value among the control population.

Discussion: This study indicates that abnormal iron deposition is common in CLD. Given that reports have suggested that iron deposition may be both an indicator of the severity of ongoing chronic liver disease and may be a prognostic factor in the development of HCC, a quantitative MR method has potential utility in identifying both the presence and severity of iron deposition in individual patients. This MR method may also potentially provide a means to non-invasively monitor treatments for chronic liver disease or attempts to reduce iron stores, although further studies are needed. Future studies in liver iron imaging should also seek to better define a lower limit for the T2* value of liver parenchyma in normal patients so as to better define what constitutes significant levels of iron deposition.

References:
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