Susceptibility weighted MRI for assessment of ferritin content in liver and spleen in people at high risk for type 2 diabetes and detection of changes after phlebotomy

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Introduction

There is evidence, that iron overload is related with type 2 diabetes mellitus (T2DM) [1,2]. Hemochromatosis is the disease resulting from significant iron overload, affecting mainly liver and spleen as 80-90% of the total body iron is stored in these organs. Iron overload is diagnosed by blood tests, determining transferrin saturation and serum ferritin. Preferred treatment for reducing iron stores in patients with hemochromatosis is phlebotomy [3]. Susceptibility weighted MRI (T2*) offers a non-invasive tool for estimation of ferritin content in liver and spleen [4]. Aims of this study were twofold: 1. to see whether there is a correlation between serum ferritin, T2* and insulin sensitivity in a high-risk population for type 2 diabetes, and 2. to test whether phlebotomy in patients with high serum ferritin content leads to a reduction to the lower reference level and whether these changes can be visualized by SW-MRI.

Material and Methods

1. Seventy volunteers at increased risk for type 2 diabetes (37 females, 33 males) were recruited in the framework of the TULIP-study (TUebinger Lifestyle Intervention Program) due to increased risk for type 2 diabetes. Inclusion criteria were obesity (body mass index BMI > 27 kg/m²), and/or impaired glucose tolerance, and/or family history of diabetes, and/or gestational diabetes. Serum ferritin as well as insulin sensitivity (IS) were determined in the early morning. IS was estimated from an oral glucose tolerance test (oGTT) by the Matsuda-index.
2. 10 patients with high serum ferritin levels (serum ferritin > 50µg/dl) were recruited for phlebotomy (3 times 800 ml each, filtering of erythrocytes, serum is given back) at the local blood bank of the University Hospital. MR examinations were performed in the early morning after overnight fasting on a 1.5 T whole body imager (Magnetom Sonata, Siemens Medical Solutions, Germany). Gradient-echo (GRE) images were acquired from 5 axial slices, including liver and spleen, applying following sequence parameters: TR = 248 ms, TE = 2,4 – 46,4 ms in steps of 4 ms (12 echoes), slice thickness 5 mm, matrix: 108 x 192, field of view: 285 x 380 mm. Postprocessing was performed applying the syngo software of the scanner, creating T2*-maps from the 12 recorded images. Circular regions of interest were drawn in liver and spleen, as shown in Figure 1.

Results

Figure 1 shows exemplary parameter images from (a) a female volunteer with low serum ferritin (0.8 µg/dl) and (b) a male patient with high serum ferritin (55.4 µg/dl). Differences become clearly obvious in liver and spleen, where the female volunteer is characterized by brighter signal and therefore higher T2*-values compared to the patient. Data of serum ferritin concentration and T2* from SW-MRI were log-transformed to reach normal distribution. Linear correlation resulted in r = -0.70 between serum ferritin and T2* in liver and r = -0.78 between serum ferritin and T2* in spleen (see Figure 3). Neither serum ferritin, nor T2* from liver and spleen showed significant correlation with IS in our cohort. Patients undergoing phlebotomy showed reduction of the serum ferritin concentration to the lower reference level and all patients had clearly increased T2* in liver and – particularly – in spleen. Figure 2 shows exemplary images of a patient before (a) and after (b) phlebotomy with a very bright signal in spleen – equivalent to an increased T2*. Serum ferritin dropped from 61.3 µg/dl to 5.9 µg/dl in this patient. IS was slightly improved after phlebotomy.

Discussion

SW-MRI allows a valid estimation of ferritin concentrations in liver and spleen with high negative correlations to serum ferritin concentration. Diabetes is common in people with untreated hemochromatosis because high amounts of iron destroy the pancreatic cells responsible for making insulin. Phlebotomy leads to a depletion of serum ferritin to the normal range, thus preventing development of hemachromatosis. These changes can be visualized by SW-MRI.

References

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Acknowledgements

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Fig. 1

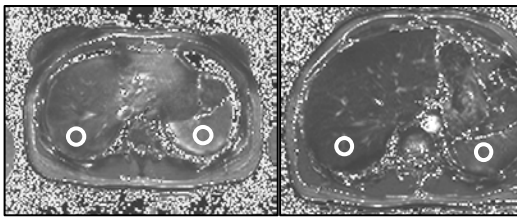

Figure 1: Parameter images of a female volunteer (a) with normal ferritin concentration and a male patient (b) with high serum ferritin. ROI's for evaluation are indicated.

Fig. 2

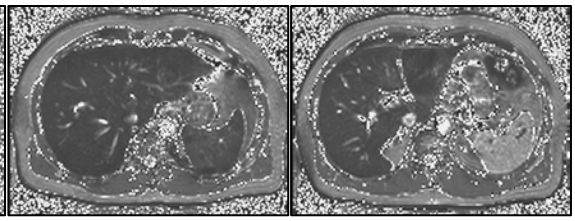

Figure 2: Parameter images of a male patient before (a) and after (b) phlebotomy.

Fig. 3

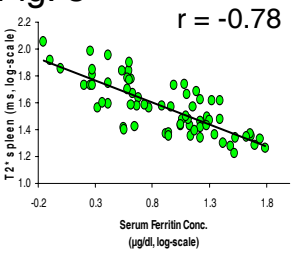

Figure 3: Correlation between Serum ferritin and T2 in spleen (data are log-transformed)*