

Update on Imaging: Detection of Iron in Liver and Heart

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Accurate assessment of iron concentrations in the liver and heart is central to determining appropriate chelation therapy and preventing/reducing the morbidity and mortality associated with excess iron stores. Liver iron concentration (LIC) is the best measure of total body iron stores and is used to guide decisions about initiating chelation therapy, increasing/decreasing chelation dose, and/or changing the mode of chelation delivery. LIC is a strong predictor of long-term prognosis. Studies have shown that 93% of patients with initial LIC <7 mg Fe/g dry weight (dw) are free of cardiac disease 13 years later, whereas only 71% of those with initial LIC 7 to 15 mg Fe/g dw and a mere 50% of those with initial LIC >15 mg Fe/g dw are cardiac disease-free after 13 years. Changes in heart iron stores generally lag behind changes in liver iron. Cardiac MRI measures of heart iron increase the sensitivity and specificity for predicting cardiac failure within 12 months. In a large study in thalassaemia major patients, 83% of those who developed arrhythmia had a cardiac T2* of <20 ms, whereas, 98% of those who developed heart failure had a T2* score of <10 ms.

There are a variety of methods for monitoring body iron stores, including serum ferritin, LIC by biopsy, and noninvasive methods, such as biomagnetic liver susceptometry (SQUID), and magnetic resonance imaging (MRI). Although serum ferritin measures are useful in monitoring trends in patient transfusional iron loading, intra-patient variability in measurements makes this method unsuitable for providing information on the degree of patient iron loading. Biopsy also has limitations as a means of monitoring LIC, including complications such as death, bile leak, bleeding, and pain, and the heterogeneity of iron concentrations in the liver can result in wide variability in concentration depending on the tissue sectioned.

As a result, noninvasive methods of tissue iron measurements are now the preferred means. In MRI, iron concentration is determined by the rate of decay of the magnetic signal from the tissue. This rate is different for different tissues and is highly influenced by the presence of iron. Depending on the data acquisition technique used, the rate of signal decay is known as R2 or R2*, whereas the time of decay is known as T2 or T2*. Relaxometry measurement of R2 is the most common method for measuring liver iron concentration, and T2* is the most

common method for assessing cardiac iron. MRI data acquisition is relatively simple for the liver, but requires extra hardware and software on the scanner for acquisition of cardiac data. In contrast, MRI data analysis is relatively easy for the heart, but more problematic for the liver due to a high error risk as a result of low signal to noise ratios. Staff training needs also differ for MRI data acquisition and analysis in the liver and heart. Whereas no face-to-face training is needed for MRI data acquisition for the liver, data acquisition for the heart may require technicians to undergo training with an expert. Technicians analyzing MRI heart data analysis should also receive training from experts, and quality assurance measures should be implemented or data outsourced to a quality assured core lab in analyzing MRI liver data.

Finally, in patients on regular blood transfusion, liver iron should be measured annually and heart iron should be measured annually after 20 units have been transfused. Liver iron should be measured at diagnosis in those with hereditary haemochromatosis if the patient is >40 years of age and serum ferritin >1000 ng/mL. In patients with thalassaemia intermedia, both heart and liver iron should be measured annually after age 10. If the baseline cardiac T2* is normal, subsequent cardiac T2* should be done no more frequently than 3 to 5 years, unless there are problems in controlling liver iron.