

## **Diagnosis of Iron Overload**

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Patients with hereditary defects in the regulation of iron balance or who require repeated blood transfusions for the treatment of conditions such as thalassaemia major, sickle cell disease, and myelodysplastic syndromes are at risk of iron overload. Circulating excess iron causes serum transferrin saturation, circulating non-transferrin bound iron in the plasma, promotes the generation of free hydroxyl radicals and the deposition of insoluble iron complexes, causing tissue damage and end-organ toxicity, including cardiac failure, liver cirrhosis/fibrosis/cancer, diabetes, infertility, and growth failure. To avoid these clinical sequelae, patients at risk of iron overload must be regularly monitored.

A variety of methods are available for the assessment of iron overload, including established tests such as transferrin saturation (%), serum ferritin levels, and liver biopsy, as well as newer methods utilizing magnetic resonance imaging (MRI) and biomagnetic liver susceptometry (SQUID). Each of these methods is associated with advantages and disadvantages. Regardless of the methodology chosen, however, the management of iron overload should not be based on a single test alone.

Normal values for transferrin saturation are between 16% and 30%, with values >40% indicating iron overload. Serum ferritin, an inexpensive, noninvasive procedure, is considered the basic parameter of iron overload, and maintenance of serum ferritin <2500 µg/L significantly correlates with cardiac disease-free survival. However, since serum ferritin values can fluctuate in response to several factors, including inflammation, abnormal liver function, and metabolic deficiencies, serial measurements are required for accurate assessment. Liver iron concentration (LIC) accurately reflects total body iron stores and, like serum ferritin, has a positive correlation with morbidity and mortality. Although it does not provide an indication of heart iron concentration, LIC >15 mg/g dry weight is associated with cardiac disease and early death. As a direct method of measuring LIC, liver biopsy is a quantitative, sensitive, specific tool that also provides information on liver histology, pathology, and non-heme storage iron. On the other hand, it is a painful invasive procedure that can be associated with serious complications and is limited by the possibility of sampling errors. LIC can also be assessed non-invasively through a variety of MRI techniques or through SQUID, which measures the paramagnetic properties of liver iron. Although the latter may prove practical in the future, at present there are only 4 machines in operation

worldwide. MRI offers the advantage of assessing iron throughout the liver and allows for parallel assessment of the pathological status of the heart and liver. R2 MRI is an approved and standardized means of measuring LIC. Although T2\* MRI is the emerging new standard for assessing heart iron, this methodology has not yet been standardized and validated.

Both serum ferritin and LIC have demonstrated prognostic value in managing individual patients. Although T2\* MRI cardiac iron has been linked to left ventricular ejection fraction, the prognostic significance of this test has not yet been established. Nevertheless, cardiac risk as reflected in heart iron should be assessed by T2\* MRI at least once. Although a positive T2\* result should be used as a basis for treatment, a negative result should not exclude the possibility of total body iron overload.

### **Suggested Readings**

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