Cardiac Iron Deposition

Claudia M. Hillenbrand, Ph.D.
Division of Translational Imaging Research, Department of Radiological Sciences
St. Jude Children's Research Hospital, Memphis, Tennessee, USA

Heart failure from myocardial iron deposition is a severe complication for patients with hematological disorders who have increased body iron burden because of repeated blood transfusions. Myocardial iron deposition leads to progressive heart dysfunction and remains the leading cause of death in patients with beta thalassemia major[1,2] despite considerable improvements in diagnosis and iron chelation therapy[3]. Cardiac siderosis can also be found in other transfusion-dependent anemias such as Diamond–Blackfan[4], myelodysplasia[4], and sickle cell anemia[5], and in patients with homozygous hereditary hemochromatosis[6,7].

Progressive heart damage from iron overload can cause left ventricular systolic and diastolic dysfunction; left ventricular systolic dysfunction (decreased ejection fraction) is usually a late finding of heart disease from iron accumulation[5]. Increased cardiac iron content impacts the contractility of cardiomyocytes and can also lead to myocarditis, pericarditis, and arrhythmias[8,9]. The severity of cardiac dysfunction depends on the amount of iron deposited in the myocardium[10] and the overall body iron burden. It was found that hepatic iron content (HIC) persistently >15 mg Fe/g of dry weight liver is associated with cardiac morbidity[11], but also that there is no statistical association between cardiac and liver iron levels[10].

Prospective data confirm that iron cardiomyopathy is reversible, if appropriate chelation is initiated[4]. However, patients are often asymptomatic for a long time which prevents early diagnosis and therapy. The prognosis of patients with established heart damage is poor, with rapid detorioration and death, despite intensive chelation therapy.

It is therefore imperative to quantitatively monitor cardiac iron deposition in these patients to be able to apply intensified iron-chelation in time and to guide the therapy. Cardiac biopsy is not suitable for routine monitoring because it is invasive, therefore risky, and is prone to sampling errors[12-14]. Non-invasive MRI tests have emerged in the past decade to reliably identify patients with subclinical cardiac iron deposition and to assess their risk of developing cardiac dysfunction[10]. Myocardial iron overload can be quantitatively assessed by T2- or T2* weighted imaging as T2 decreases in the presence of iron. Because of the initial lack of fast quantitative T2 techniques suitable for cardiac imaging, multi-gradient echo based T2* methods have been developed first and established in iron overload cardiomyopathy[10,15]. Risk stratification is based on the T2* value measured in the interventricular septum[9]: it has been found that a shortening of myocardial T2* to <20ms (implying increased myocardial iron) is associated with an increased chance of decreased left ventricular function[10]. Chances of decreased left ventricular ejection fraction are 10% in the T2* =10-20ms range, 18% for T2*=8-10ms, 38% for T2*=6ms, and 70% for T2*=4ms[9,16].

In this presentation we will review the following topics related to cardiac iron overload: (a) the mechanisms of cardiac iron storage (e.g., [4,9,17]), (b) the clinical relevance of quantitative assessment of myocardial iron overload (e.g., [4,9,18-22]), (c) suitable MR imaging strategies and

analysis methods for quantitative assessment of myocardial iron overload (e.g., [10,23,24]) as well as indirect measures such as serum ferritin (e.g., [2,19]), and (d) patterns of myocardial iron storage (e.g., [13,25,26]).

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