Radiología. 2017;59(6):487–495

RADIOLOGÍA

www.elsevier.es/rx

UPDATE IN RADIOLOGY

Diagnosis and quantification of the iron overload through magnetic resonance☆

J.M. Alústiza Echeverría*, M.C. Barrera Portillo, A. Guisasola Iñiguiz, A. Ugarte Muño

Servicio de Radiología, Hospital Universitario Donostia, San Sebastián, Spain

Received 8 November 2016; accepted 13 July 2017
Available online 9 November 2017

KEYWORDS
Hemochromatosis;
Iron overload;
Magnetic resonance imaging

Abstract There are different magnetic resonance techniques and models to quantify liver iron concentration. T2 relaxometry methods evaluate the iron concentration in the myocardium, and they are able to discriminate all the levels of iron overload in the liver. Signal intensity ratio methods saturate with high levels of liver overload and cannot assess iron concentration in the myocardium but they are more accessible and are very standardized. This article reviews, in different clinical scenarios, when magnetic resonance must be used to assess iron overload in the liver and myocardium and analyzes the current challenges to optimize the application of the technique and to be it included in the clinical guidelines.

PALABRAS CLAVE
Hemocromatosis;
Sobrecarga férrica;
Resonancia magnética

Diagnóstico y cuantificación de la sobrecarga férrica mediante resonancia magnética

Resumen Existen diferentes técnicas y modelos de resonancia magnética (RM) para cuantificar la concentración de hierro en el hígado. Los métodos de relaxometría T2, además de evaluar la concentración de hierro en el miocardio pueden discriminar todos los niveles de sobrecarga férrica en el hígado. Los métodos de ratio de intensidad de señal saturan con los altos niveles de sobrecarga en el hígado y no pueden evaluar la concentración de hierro en el miocardio. Sin embargo, son más accesibles y están muy estandarizados. En este artículo se revisan las diferentes técnicas de RM para evaluar la concentración de hierro en el hígado y en el miocardio, sus indicaciones en diferentes escenarios clínicos y los retos actuales para lograr su optimización y su inclusión en las guías clínicas.

☆ Please cite this article as: Alústiza Echeverría JM, Barrera Portillo MC, Guisasola Iñiguiz A, Ugarte Muño A. Diagnóstico y cuantificación de la sobrecarga férrica mediante resonancia magnética. Radiología. 2017;59:487–495.
* Corresponding author.
E-mail address: jmalustiza@osatek.net (J.M. Alústiza Echeverría).

Introduction

Iron is a key element of many chemical reactions. To avoid the toxicity from its free form it should be bound to a certain protein, and since the organism cannot cleanse the excess of iron, the balance between stores and the losses is very important. An excessive amount of iron will eventually cause iron overloads.[1]

Iron overloads can be due to different causes. Type 1 hereditary hemochromatosis (HH), bound to the HFE gene, is the most prevalent conditions of all and starts with an increased abdominal absorption of iron. The conditions with an increased destruction of red blood cells are called secondary hemochromatosis or hemosiderosis. Included in the category of secondary hemochromatosis, we find those due to hepatopathies that, due to an unknown mechanism, also cause iron overloads.[1]

In its maintained excess form, the iron stores in its toxic form in different organs (liver, heart, thyroid, gonads, hypophysis, skin, pancreas) to later determine cell death and fibrosis. The most serious complications are hepatic cirrhosis and heart failure.[1,2]

In the HH, the treatment prior to the irreversibility of lesions through phlebotomy procedures is highly effective.[2] Patients with iron overloads and anemia, as it is the case with many hemosiderosis, cannot be phlebotomized and iron chelators are used. Recently, new chelating drugs have hit the market, and they are highly effective when taken orally, which has dramatically changed our management of these patients.

The first step toward diagnosis is measuring the transferrin saturation index (TSI) and the blood ferritin levels. Both are high in presence of iron overloads.[3] When on suspicion of HH, and once the elevation of both parameters has been confirmed, a genetic study of C282Y and H63D mutations of the HFE gene is conducted in order to rule out the most common form of HH.[4,5]

The standard method for the direct assessment of iron deposits in the organism is measuring the liver iron concentration (LIC), since 70 per cent of iron stores itself in the liver.[6] The LIC is >36 μmol Fe/g in normal concentrations. In primary and secondary hemochromatosis, the LIC is usually >80 μmol Fe/g, except in overloads secondary to hepatopathies.[2,5,7] The measurement of the LIC is, therefore, the standard method to diagnose hemochromatosis.

Typically, measuring the LIC requires the biopsy of the liver, and quantifications using the spectrophotometry of part of the biopsized material. The biopsy of the liver is an invasive procedure with high result variability due to sample errors. All this justifies the interest for having a non-invasive technique for measuring the LIC.

Today, due to its availability and results, the resonance magnetic imaging (RMI) is considered the most interesting non-invasive modality for the quantification of the LIC.[6]

In this paper we will review the different MRI modalities available for the assessment of iron concentrations in the liver and the myocardium, their indications in different clinical scenarios, and the actual challenges we face in order to optimize and include them in the clinical guidelines.

Hepatic magnetic resonance imagine

The MRI detects iron overloads due to the paramagnetic effect of iron that translates into shortened T2 relaxation times, and a reduced signal that is proportional to the LIC. This direct correlation between the liver signal in the MRI and the LIC has been confirmed by numerous works.[7–12]

There are two (2) different modalities for the quantification of LICs using MRIs:

- Measurement of relaxation times or relaxometry.
- Measurement of signal intensity ratios (SIR).

Measurement of relaxation times or relaxometry

Theoretically speaking, the best most direct method[8] for measuring LICs is measuring the T relaxation time in order to quantify its shortening. The T2 value is defined as the time required for transverse magnetization to reach 37 per cent of its original magnitude. Its measurement requires multiple echoes that will eventually allow us to draw the exponential decay curve of the signal in the most precise way possible (Fig. 1). When gradient echo-sequences are used with respect to the relaxation time measured, this is called T2*.

Various papers published have quantified LICs using T2 relaxometry studies or T2*, with a high correlation when compared to the quantification of the LIC in the liver biopsy.[9–12] Different studies have obtained mathematical formulas to make reliable transformations of T2 values or T2* into the LIC measured in standard units expressed as μmol Fe/g. The results from these mathematical models are reproducible in other machines.[11,13–15]

Relaxometry methods are considered the best ones because they can discriminate all iron overloads and measure the iron concentrations in the myocardium. They are the most widely used in research papers and clinical trials.

The methods of T2 relaxometry are used in spin echo sequences that last for a few minutes. The most important of all is Ferriscan®,[11] approved by the U.S. Food and Drug Administration (FDA) and used in numerous clinical trials. They require prior calibration and cost €200 per patient.

The most widely used T2* relaxometry methods with shorter acquisition sequences in apnea are Garbowski et al.'s method,[9] and Wood et al.'s method.[12]

Methods of signal intensity ratio

In these methods, the correlation between the liver intensity signal and that of paravertebral musculature is measured (Fig. 2), and used as a standard since it is not affected by the iron overload. Various echo gradient sequences are used. The difference between the liver signal intensity and that of the muscle will basically depend on the LIC. When analyzing signal measurements within the same image, the measurements are subtracted from factors other than the LIC, such as the homogeneity of the magnetic field that equally affects both structures. The study needs to be performed without surface antennas and with the antenna mounted on the