Quantification of Hepatic Fat and Iron with Magnetic Resonance Imaging

Shane A. Wells, MD

KEYWORDS

• Magnetic resonance imaging • Hepatic steatosis • Fat quantification • Iron overload • Iron quantification • T_2 • R_2^*

KEY POINTS

- Quantitative magnetic resonance (MR) imaging–based biomarkers for liver fat and iron have evolved rapidly over the last decade.
- Quantitative MR imaging–based biomarker techniques are accurate, reproducible, cost-effective, and noninvasive methods to both qualitatively and quantitatively assess liver disease and its related complications.
- The emerging pandemic of nonalcoholic fatty liver disease and the recognition of the role of the metabolic syndrome on the development of chronic liver disease remain driving forces for the ongoing technical development and validation of MR imaging–based biomarkers.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a form of chronic liver disease that encompasses a spectrum of hepatic pathologic abnormalities ranging from isolated steatosis, nonalcoholic steatohepatitis (NASH), fibrosis, and cirrhosis. Abnormal accumulation of fat in hepatocytes, largely in the form of triglycerides (unsaturated fatty acids), provides the foundation for the development of NAFLD. The pathogenesis of steatosis is likely multifactorial, involving genetic, environmental, and nutritional factors regulating lipid metabolism and the corresponding ebb and flow of free fatty acids (saturated fatty acids) from hepatocytes. Unlike isolated steatosis, NASH is characterized by steatosis with superimposed necroinflammation, ballooning degeneration, and fibrosis. Although isolated steatosis may be clinically stable, NASH can progress to cirrhosis in a significant percentage of patients.[1–8] In fact, end-stage NASH accounts for a large percentage of patients with idiopathic or cryptogenic cirrhosis and can result in the development of hepatocellular carcinoma (HCC).[3,9–13] It should be noted that there are several other causes for the excessive accumulation of triglycerides within hepatocytes, including alcohol, viral hepatitides including human immunodeficiency virus, genetic lipodystrophies, and treatment effect following chemotherapy (Fig. 1).

Ferritin dysregulation, excess intestinal iron absorption, and repeated blood transfusions result in elevated hepatic iron content. Increased hepatic iron clearly contributes to cirrhosis and the development of HCC in patients with hereditary hemochromatosis (HH). Evidence also suggests that elevated hepatic iron results in progressive fibrosis in NAFLD and NASH and increases the risk for the development of HCC.[14]

This article reviews magnetic resonance (MR) imaging techniques for the quantification of

Funding Sources: Nil.
Conflict of Interest: Nil.
Department of Radiology and Medical Imaging, University of Virginia Health System, 1215 Lee Street, PO Box 800170, Charlottesville, VA 22908-0170, USA
E-mail address: saw3ah@virginia.edu

Magn Reson Imaging Clin N Am 22 (2014) 397–416
http://dx.doi.org/10.1016/j.mric.2014.04.010
1064-9689/14/$ – see front matter

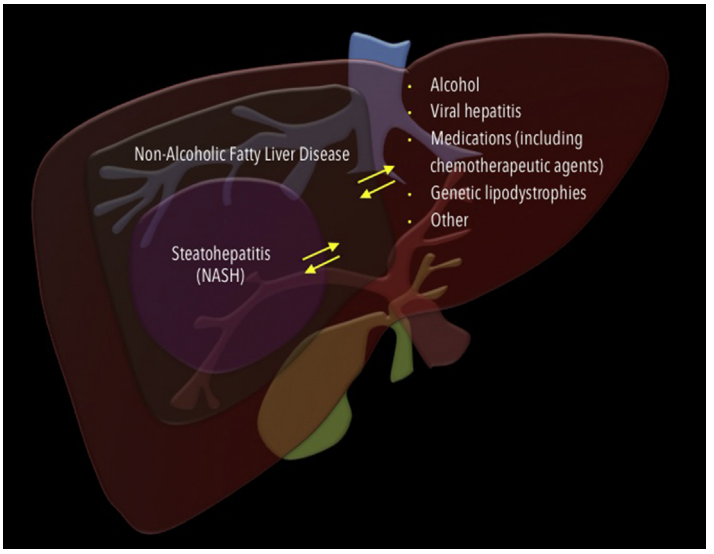

Fig. 1. The dynamic process of NAFLD, including a list of the most common causes. NAFLD and NASH can progress when untreated or regress with the potential for resolution with appropriate therapy (*to and fro arrows*). Notice the morphologic changes of the liver associated with NAFLD and NASH; the liver is enlarged with rounding of the hepatic contour. (*Courtesy of* Juliana M. Bueno, MD, University of Virginia, Charlottesville, VA.)

hepatic fat and iron. The content is divided into the following sections:

- Overview of the dynamic process of NAFLD and important related diseases resulting from elevated liver fat
- Overview of iron metabolism and deposition and important related diseases resulting from elevated liver iron
- Brief review of the qualitative and invasive quantitative assessment of liver fat and iron, with strengths and limitations
- Description of state-of-the-art noninvasive quantification of liver fat and iron with MR imaging

After reading this content, the reader should understand the scope of chronic liver disease related to elevated hepatic fat and iron and the limitations of both liver biopsy and qualitative assessment of liver fat and iron. The reader will become familiar with quantitative noninvasive methods for measuring liver fat and iron with MR imaging.

NAFLD

NAFLD is considered the hepatic manifestation of the metabolic syndrome, a product of insulin resistance. The metabolic syndrome comprises several clinical manifestations, including hypertension, hyperlipidemia, glucose intolerance and type 2 diabetes mellitus (T2DM), and obesity.[1,15,16] NAFLD affects 30% of the adult population (more than 100 million Americans) and up to 80% of obese adults (body mass index >30), particularly the centrally obese (visceral adiposity) and diabetic population.[17–21] In children, fatty liver is regarded as the most common cause of chronic liver disease with a prevalence of 9.6% of 2 to 19 year olds, representing greater than 6.5 million US children and 38% of obese children.[22]

Although the prevalence of NAFLD is most strongly associated with visceral (central) obesity and features of the metabolic syndrome, age, gender, ethnicity, and race also play a role. In general, the rate of NAFLD increases with age with women, demonstrating a later peak, possibly related to hormonal changes of menopause.[23,24] NAFLD more often affects men and in population studies is more common in Hispanic Americans compared with non-Hispanic white and black Americans.[25] Although determining racial differences has been somewhat problematic, several studies suggest that the prevalence of NAFLD may be lower in black Americans.[26,27] Browning and colleagues[28,29] measured hepatic triglyceride content (with MR spectroscopy) in 2287 subjects and found that the incidence of steatosis in black American adults was significantly lower than in Hispanic and non-Hispanic white Americans, independent of obesity or diabetes.

In children, the effects of ethnicity and race may be even more strongly correlated than in adults. Even though non-Hispanic black American children have higher rates of risk factors for fatty liver, such as obesity and insulin resistance, the prevalence of fatty liver (1.5%) is significantly lower