

Epidemiology of Hepatic Steatosis at a Tertiary Care Center: An MRI-based Analysis

Tyler J. Fraum, MD, Daniel R. Ludwig, MD, Scott Kilian, BS, William A. Curtis, MD, Thomas K. Pilgram, PhD, Claude B. Sirlin, MD, Kathryn J. Fowler, MD

Abbreviations

BMI
body mass index
CI
confidence interval
LIC
liver iron concentration
MRI
magnetic resonance imaging
NAFLD
nonalcoholic fatty liver disease
OR
odds ratio
PDFF
proton density fat fraction
RF-CA subgroup
patients with ≥ 1 cancer-related risk factor
RF-CLD subgroup
patients with ≥ 1 risk factor for chronic liver disease not related to NAFLD
RF-NAFLD subgroup
patients with ≥ 1 risk factor for NAFLD
RF-None subgroup
patients not belonging to any of the groups above
ROI
region of interest
tBILI
total serum bilirubin

Rationale and Objectives: Little is known about the frequency and risk factors of hepatic steatosis in the tertiary care setting. Such knowledge is essential to clinicians making decisions about testing for this condition. Thus, our aim was to describe the epidemiology of hepatic steatosis, as captured by magnetic resonance imaging (MRI), at a tertiary care center.

Materials and Methods: A near-consecutive cohort of 1006 adult patients underwent standard-of-care liver MRIs. Images were retrospectively processed to derive proton density fat fraction (PDFF) maps. Data from three spatially distinct regions of interest (ROIs) were aggregated to derive overall hepatic PDFF values. Demographic, anthropometric, clinical, and laboratory variables were included in a multivariate analysis to determine predictors of hepatic steatosis grades (based on established PDFF cutoffs). Hepatic steatosis grades derived from single vs aggregated ROIs were compared.

Results: Hepatic steatosis was observed in 25% of patients (19% grade 1; 3% grade 2; 3% grade 3). Controlling for all other variables, the odds of hepatic steatosis increased by 7%–9% ($P < .001$) for each whole point increase in body mass index (BMI), whereas elevated serum bilirubin was associated with lower odds of hepatic steatosis ($P = .002$). Race, diabetes mellitus, dyslipidemia, and metabolic syndrome were not independently predictive of hepatic steatosis when controlling for other variables (eg, BMI). Employing single ROIs (rather than three aggregated ROIs) resulted in incorrect steatosis grading in up to 8.0% of patients.

Conclusion: Many adult patients undergoing liver MRI at a tertiary care center have hepatic steatosis, with larger BMIs as the only independent predictor of higher grades. This information can be used by clinicians at such centers to make evidence-based decisions about when to test for hepatic steatosis in their patients.

Key Words: Hepatic steatosis; fat quantification; proton density fat fraction (PDFF); hepatic siderosis; iron quantification.

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From the Mallinckrodt Institute of Radiology, Washington University School of Medicine, 510 S. Kingshighway Blvd, Campus Box 8131, Saint Louis, MO 63110 (T.J.F., D.R.L., W.A.C., T.K.P., K.J.F.); Southern Illinois University School of Medicine, Springfield, Illinois (S.K.); Liver Imaging Group, Department of Radiology, San Diego School of Medicine, University of California, La Jolla, California (C.B.S.). Received September 1, 2017; revised October 16, 2017; accepted October 16, 2017. **Address correspondence to:** T.J.F. e-mail: tylerjfraum@wustl.edu

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INTRODUCTION

Hepatic steatosis, the abnormal accumulation of lipids within hepatocytes, is a common condition affecting roughly 20%–30% of the population in Western countries (1). Etiologies of hepatic steatosis have typically been partitioned into nonalcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease. Importantly, the prevalence of NAFLD, which has been linked to nonalcoholic steatohepatitis and cirrhosis, has risen sharply in recent decades, in tandem with the obesity epidemic (2). Even in the absence of cirrhosis, hepatic steatosis is a risk factor for the development of hepatocellular carcinoma (3) and is associated with insulin resistance and cardiovascular disease (4,5).

The detection of hepatic steatosis is important in guiding clinical management. The current gold standard for diagnosing and grading hepatic steatosis is nontargeted percutaneous biopsy with direct histologic visualization (6,7). Although generally safe, percutaneous liver biopsy is an invasive procedure with non-negligible risks of hospitalization (3%) and death (0.01%), with even higher risks of complications in patients with advanced liver disease (8). Moreover, fat deposition within the hepatic parenchyma can exhibit significant spatial heterogeneity, potentially resulting in undergrading or overgrading due to sampling error (9,10). Consequently, there is a need for safe and accurate methods of globally interrogating hepatic fat levels. With the advent of multiecho chemical shift-encoded sequences, magnetic resonance imaging (MRI) has emerged as a reliable, noninvasive means of liver fat quantification (11–13).

Although hepatic steatosis has been studied in the general population, little is known about its frequency and risk factors in the tertiary care setting. Such knowledge is essential to clinicians making decisions about testing for these conditions and for radiologists adopting advanced quantitative imaging techniques in their practices. However, obtaining this information through traditional means (ie, percutaneous biopsy) in a representative sample of patients is likely not feasible. Thus, the primary aim of our study was to describe the epidemiology of hepatic steatosis at a large tertiary care center, as captured by patients presenting for liver MRI for any indication. Secondary aims were to examine the coincidence of hepatic steatosis with hepatic siderosis and to evaluate the spatial heterogeneity of hepatic steatosis, which may result in sampling errors when assessing liver fat and iron levels via percutaneous biopsy.

MATERIALS AND METHODS

Patient Identification

For this retrospective Health Insurance Portability and Accountability Act-compliant study, which was approved by our local institutional review board, we queried our institution's radiology report database to collect reports for all liver MRIs performed between February 2013 and April 2014. We identified 1562 patients with a total of 1753 liver MRIs. For

patients with >1 liver MRI, the earliest imaging study was selected for analysis. Based on a case-by-case image review by two authors (SK, trainee; KJF, 6 years of experience in liver MRI) in consensus, patients with images of inadequate quality due to artifacts were excluded ($n = 6$; 0.4%). Patients without liver-related laboratory values (total bilirubin [BILI], alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase) within 30 days before or after liver MRI were also excluded ($n = 550$; 35.2%).

For all remaining 1006 patients, numerous demographic, anthropometric, clinical, and laboratory parameters were collected from the electronic medical record. Cirrhosis was not included as a variable of interest due to the lack of consistent histologic confirmation of this diagnosis. For patients found to have both hepatic steatosis and hepatic siderosis (per criteria described in the following paragraph), we also collected clinical information related to risk factors for iron deposition, including transfusions, chronic kidney disease, primary hemochromatosis, and several other less common disease entities (14).

For the subsequent analysis, we also defined the following four patient subgroups, based on various related attributes:

- Patients with ≥ 1 risk factor for NAFLD (RF-NAFLD subgroup), including
 - Diabetes mellitus (DM)
 - Dyslipidemia
 - Body mass index (BMI) $> 35 \text{ kg/m}^2$
 - Metabolic syndrome (defined as all three of the above factors)
- Patients with ≥ 1 risk factor for chronic liver disease not related to NAFLD (RF-CLD subgroup), including
 - Alcohol abuse, current or within the 12 months before MRI
 - Active viral hepatitis infection (B or C)
- Patients with ≥ 1 cancer-related risk factor (RF-CA subgroup), including
 - Liver metastases
 - Chemotherapy, current or within the 6 months before MRI
- Patients not belonging to any of the groups above (RF-None subgroup)

Image Acquisition

All imaging was performed on one of nine 1.5 T or 3.0 T Siemens (Erlangen, Germany) MR scanners in our department. All imaging sessions included a two-dimensional low-flip-angle multiecho proton density-weighted gradient-recalled echo sequence for fat and iron quantification, which has been routine for clinical care in all abdominal MRIs at our institution, regardless of the indication, since 2012. At 1.5 T, MR parameters were as follows: flip angle—10 degrees; time to repetition (TR)—122 milliseconds; time to echo (TE)—2.4 milliseconds, 4.8 milliseconds, 7.1 milliseconds, 9.5 milliseconds, 11.9 milliseconds, 14.3 milliseconds; matrix— 168×192 pixels; slice thickness—10 mm; and slice spacing—20 mm. At 3.0 T, MR

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