Research Article

Validation of MRI Quantification of Liver Fat, Keeping CT Liver Attenuation Index (LAI) as Gold Standard

Faryal Ijaz[*,1], Samina Khan[1], Muhammad Salman Rafique[1], Sana Kundi[1], Tahir Malik[1], Ahmad Karim Malik[2]

[1]Department of Radiology, Pakistan Kidney and Liver Institute and Research Center (PKLI & RC), Lahore, Pakistan.
[2]Department of Gastroenterology and Hepatology, Pakistan Kidney and Liver Institute and Research Center (PKLI & RC), Lahore, Pakistan.

Abstract: Background: Non – Alcoholic Fatty Liver Disease (NAFLD) is emerging as a considerable health problem in patients visiting gastroenterology clinics. It is of crucial importance to evaluate the extent of hepatic steatosis in potential candidates for living donor liver transplantation (LDLT) to ensure donor safety as well as optimum graft regeneration.

Objective: To validate the MRI quantification of liver fat keeping CT liver attenuation index as gold standard.

Materials and Methods: This cross-sectional study was carried out in the department of Diagnostic Radiology, Pakistan Kidney and Liver Institute and Research Centre from 10th October, 2022 to 10th December, 2022. We determined the sample size using WHO sample size calculator. The MR fat fraction sequence was acquired as a part of the obligatory MRCP in 70 potential liver donors who undertook CT abdomen. Liver Attenuation Index (LAI) and MR fat fraction were determined separately by two radiologists who were blinded to each other. LAI was calculated as: Mean liver attenuation - mean splenic attenuation. MRI fat fraction from seven areas of liver were taken and their mean calculated to determine the percentage of liver fat. SPSS version 20 was employed for statistical analysis and Pearson's Correlation was applied.

Results: Among the 70 donors 42 were males and 28 were females (M: F= 1.5: 1). The hepatic fat fraction values on MR were correlated with the liver attenuation index on CT using a two - tailed Pearson correlation test. The results showed a very strong negative correlation between the two; the lower the LAI, the higher the MR fat fraction (Pearson correlation coefficient $r = -0.932$, $p<0.05$).

Conclusion: Strong correlation was found between MRI estimation of liver fat and CT LAI fat estimation. MRI is safer than CT as it does not involve ionizing radiation, is quicker to perform, and hence can be recommended as future method of choice.

Keywords: Non – Alcoholic Fatty Liver Disease, hepatic steatosis, Magnetic resonance cholangiopancreaticography, Magnetic Resonance spectroscopy.

INTRODUCTION

Non – Alcoholic Fatty Liver Disease (NAFLD) is emerging as a considerable disease in patients visiting gastroenterology clinics [1]. NAFLD is defined as the abnormal intracellular fatty infiltration, predominantly triglycerides, in the hepatic parenchyma which exceeds 5% on histological examination [2, 3]. The secondary causes and a daily consumption of alcohol ≥ 30g for men or ≥ 20g for women should be ruled out for the diagnosis of NAFLD [4]. Nonalcoholic fatty liver disease (NAFLD) involves spectrum of disease ranging from just steatosis (Non - alcoholic steatohepatitis NASH) to advanced stage of fibrosis/ cirrhosis (NAFLD - related liver cirrhosis) with both increasing the risk of liver cancer development. Unlike disease states that are irreversible, NAFLD can be managed by weight loss, and diabetic control with insulin and antioxidant agents. Therefore, timely diagnosis and observing the progress of the disease has great clinical importance.

*Address correspondence to this author at the Department of Radiology, Pakistan Kidney and Liver Institute and Research Center (PKLI & RC), Lahore, Pakistan. Email: faryalbajwa11@gmail.com

NAFLD diagnosis can be made on different radiological imaging, liver biopsy, and simpler non - specific fat measurements, such as body weight, abdominal girth, and body mass index but these cannot characterize fat location [5]. Generic serum markers of liver disease, such as aminotransferases are not very sensitive and specific for the detection of hepatic steatosis [6]. Currently, different imaging modalities are used for the evaluation of fat content in the liver including ultrasonography (USG), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI). Each one of these has its own advantages and disadvantages. Most of the time the diagnosis of NAFLD is incidental on abdominal ultrasound imaging, which despite being readily available and inexpensive, has the limitation of being operator dependent and gives only qualitative information. Moreover, it may underestimate the presence of hepatic steatosis in cases with hepatic fat infiltration <20% [3]. Computed tomography is associated with the risk of increased radiation exposure as well as it has a limited role in the recognition of mild steatosis. MRI is considered highly reliable in the evaluation of even milder forms of hepatic steatosis. It is considered the most sensitive and specific technique for evaluation of liver fat content [7]. Many MRI techniques including in phase (IP) and out phase

doi.org/10.21089/njhs.82.0080

(OP) imaging, chemical shift imaging (CSI), fat-suppressed imaging, MRI estimated fat fraction (MRI-PDFF) and Multi Echo Dixon (m DIXON) have been established for assessment of hepatic steatosis [8]. Nevertheless, its limited availability especially in comparison to USG, and increased cost might be its potential limitation for fat quantification. Liver biopsy has been considered the traditional gold standard method to diagnose and quantify hepatic steatosis, and helps differentiate simple steatosis from NASH [9]. However, it is an invasive procedure which is associated with potential complications such as bleeding, procedure related mortality (although quite low) and small sample volume of hepatic parenchyma. These procedures related complications make it difficult to repeat liver biopsy as follow up in NAFLD monitoring during the course of the disease [3]. So, there is need for quantitative assessment of NAFLD using non-invasive methods. Therefore, the present study is aimed to validate MRI estimation of liver fat, a non-invasive and radiation-free method, considering LAI on CT as the gold standard. The aim of this study is to validate MRI estimation of liver fat, a non-invasive and radiation-free method, considering LAI on CT as the gold standard.

MATERIALS AND METHODS

The approval of the research was taken from Institutional Review Board (IRB) No. PKLI-IRB/AP/79. This cross-sectional study was prospective and carried out in the department of Diagnostic Radiology, Pakistan Kidney and Liver Institute and Research Centre from 10th October, 2022 to 10th December, 2022. According to the WHO sample size calculator, 70 potential liver donors were included.

These were all healthy individuals, free from any underlying medical condition, had been accepted as potential living donors, and sent to the radiology department by the primary team for CT and MRI imaging as part of their essential radiological work-up. Patients with a history of alcoholism or taking drugs that could cause steatosis were excluded.

Those donors (35 in number) who were rejected by the department of hepatobiliary surgery because of hepatic steatosis diagnosed on CT LAI, were requested for a complimentary MRI sequence after proper consent. The fat fraction sequence on MR was already a component of the compulsory magnetic resonance cholangiopancreaticography (MRCP) carried out on all liver donors with an LAI of greater than zero. Thus, the rest of the 35 potential liver donors who undertook CT abdomen for LAI estimation had their MR fat fraction and therefore no consent was required for these 35 liver donors. The liver fat estimation on CT and MR were determined separately by two radiologists blinded to each other.

LAI was determined as:

LAI = Average hepatic density – Average splenic density (Fig. **1A, 2A**).

MRI fat fraction was estimated by drawing regions of interest on seven different parts of liver, and then calculating their mean (Fig. **1B, 2B**).

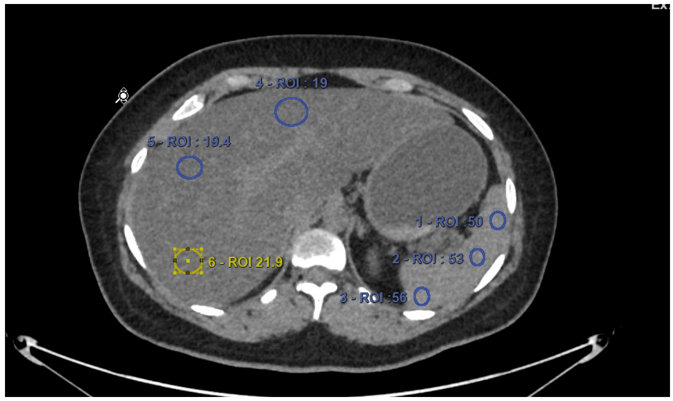

Fig. 1(A). NECT Showing Different Regions of Interest (ROI) from the Liver and Spleen in a Patient with Diffuse Hepatic Steatosis.

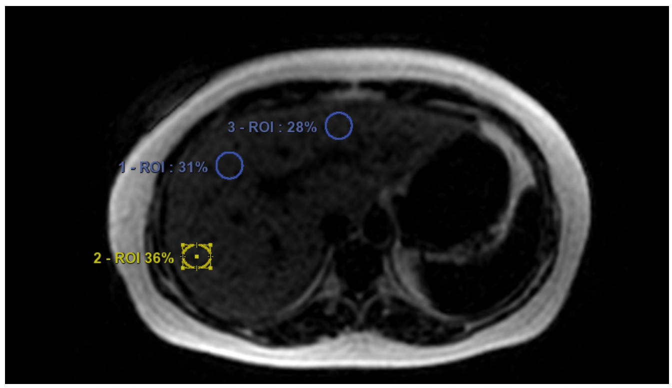

Fig. 1(B). MRI Abdomen Showing Different Regions of Interest (ROI) from Liver Showing Fat Fraction in the Liver in a Patient with Diffuse Hepatic Steatosis.

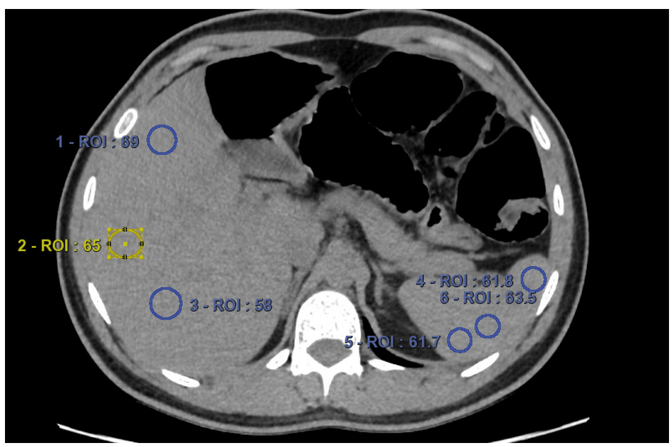

Fig. 2(A). NECT Showing Different Regions of Interest (ROI) from the Liver and Spleen in a Patient with a Healthy Liver.

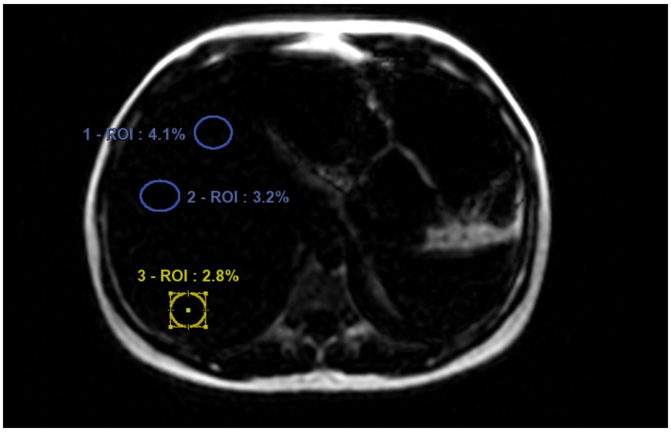

Fig. 2(B). MRI Abdomen Showing Different Regions of Interest (ROI) from Liver Showing Fat Fraction in the Liver in a Patient with a Healthy Liver.

STATISTICAL ANALYSIS

Sample size was approximately 70, calculated according to the correlation formula using Fisher's z-transformation.

True correlation (r) = 0.637 [10].
Correlation under null hypothesis = 0.
Alpha = 0.002.
Power = 0.998.
Sample Size (N) = 67.

RESULTS

The sample size was 70, according to the WHO sample size calculator. Of these, 35 individuals had an LAI above 0 and 35 had an LAI value below 0. Regarding the gender distribution, 42 were male and 28 were female. The age range was 18 to 46 years with a mean of 32.15. The hepatic MR fat fraction values were noted in the range of 2% to 40.60% with a mean of 12%, whereas the minimum CT liver attenuation index was -45.9 and maximum was 14 with a mean of -3.7. The hepatic MR fat fraction values were correlated with the CT liver attenuation index using a two-tailed Pearson correlation test. The results showed a very strong negative correlation between the two; the lower the LAI, the higher the MR fat fraction (Pearson correlation coefficient r= -0.932, p<0.05). Fig. (**3**) shows the graphic representation of this correlation between the MR fat fraction and LAI, using an X-Y scatter-type line chart.

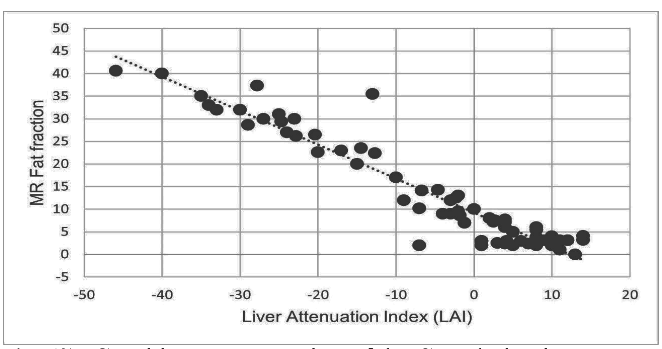

Fig. (3). Graphic Representation of the Correlation between MR Fat Fraction and LAI.

DISCUSSION

Nonalcoholic fatty liver has become a global health problem and has largely affected developed countries. NAFLD is the most common cause of fat infiltration of the liver and is linked with metabolic disorders and cardiovascular diseases.

The role of noninvasive imaging has become crucial considering the invasive nature of liver biopsy. These include ultrasonography, computed tomography (CT), and Magnetic Resonance Imaging (MRI).

Ultrasonography (USG) is the initial investigation in assessment and hepatic steatosis is usually found as an secondary feature. Ultrasound is cost-effective and easily available. However, ultrasonography has a limited role in mild steatosis and in cases of chronic liver disease and fibrosis because fibrosis also increases the hepatic parenchymal echogenicity and can alter the sonographic interpretations [2]. Computed Tomography (CT) is a simple and accurate modality for the assessment of hepatic steatosis and is measured in terms of Hounsfield units (HU). The diagnostic criteria for hepatic steatosis in CT is that the liver attenuation should be at least 10 HU less than spleen attenuation or absolute attenuation of liver to be less than 40 HU [11]. However, due to it ionizing radiation and limited role in the detection of mild steatosis its efficacy declines.

Magnetic resonance imaging (MRI) has now been considered the most accurate modality for liver fat estimation. It has no radiation exposure so can be safely used for liver fat estimation in potential liver donors and follow-up cases of NAFLD.

MR spectroscopy (MRS), mDixon, and MR proton density fat fraction (PDFF) are different sequences to measure fat fraction. MR spectroscopy is an accurate method for liver fat fraction evaluation. The proportion of water and fat in a tissue can be precisely estimated by MRS. It is considered to be a recommended tool for the quantification of hepatic fat. Various studies show a good correlation between MR spectroscopy with that of histopathology results [2]. However, it has certain limitations which include a limited sample size similar to liver biopsy. Another drawback of this method is that liver fat is inhomogenously distributed throughout the liver parenchyma. Hence a single MRS cannot predict the texture of entire liver parenchyma.

The chemical shift-based water and fat separation Dixon MRI method had been widely used to analyze the characteristics of the resonance frequency difference of hydrogen atoms between water and fat molecules.

Recently, an innovative MRI technique called magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF) was developed and has powerful correlation and equivalence with MRS. Usually, qualitative imaging requires sampling through 2-3 echoes, unlike quantitative imaging which employs six or more echoes. PDFF expresses the density of mobile protons from triglycerides as a fraction of the total density of moving protons from triglycerides and water. It is stated as an absolute percentage (%) and ranges from 0–100% [12]. The primary advantage of this method is that it allows simple calculation of liver fat from any segment of the liver in a single breath acquisition. MRI-PDFF has effectiveness in the early detection of liver diseases [4].

In our study, we estimated hepatic fat content as fat percentage from seven different regions, averaged and taken as a mean hepatic fat percentage. A strong correlation of MR fat fraction with CT LAI is observed which depicts the more negative LAI value on non-enhanced CT, the higher the fat fraction on MR sequence.

Our results are comparable to those of similar studies done in the past. One study compared magnetic resonance spectroscopy (MRS) with CT fat estimation and found remarkable correlation between MRS and CT observations [13]. However, there are certain limitations of MRS such as it is not widely available, it is time-consuming and involves complicated post-processing and data analysis [14-16]. Furthermore, MR-PDFF is convenient, offers speedy acquisition, estimates liver steatosis in any part, and according to Bonekamp *et al.*, Awai *et al.*, and Harald *et al.* It correlates effectively with MRS ($r2 = 0.98$) [17-19].

Sherif *et al.* declared in their findings that MR-PDFF was an invaluable tool for the quantitative determination of hepatic fat infiltration against histopathology as the gold standard [20]. Chiang *et al.* kept intraoperative liver biopsy as their gold standard. They had similar observations and found MR to be 100% sensitive and 77.1% specific for hepatic steatosis estimation [21].

LIMITATIONS

The limitation of our study includes a small sample size including only potential liver donors. The study can be extended to involve the general population with normal fat fraction and in cirrhotic patients with fibrosis. Secondly, due to limited biopsy of potential liver donors at our institution we were unable to compare our results with histopathology.

In future, correlation with Magnetic spectroscopy (MRS) can also be considered as it also provides a quantitative non-invasive method of measuring hepatic fat content.

CONCLUSION

The use of MRI PDFF sequence accurately measures liver fat fraction. It is a non-invasive technique that can safely be performed on potential liver donors and in follow-up cases of NAFLD. It has a short acquisition time with no radiation exposure. Our study shows a strong correlation of MR fat fraction with CT LAI such that the more negative LAI value on non-enhanced CT, the higher the fat fraction on MR sequence.

AUTHORS' CONTRIBUTION

- **Faryal Ijaz**: Data acquisition.
- **Samina Khan**: Drafting of the article.
- **Muhammad Salman Rafique**: Conception of main idea and design.
- **Sana Kundi**: Intellectual input to the content.
- **Tahir Malik**: Final proof reading and approval.
- **Ahmad Karim Malik**: Data analysis and interpretation.

CONFLICT OF INTEREST

Declared none.

ACKNOWLEDEMENTS

My co-authors and I acknowledge the swift and efficient response from Ms. Maria Baig (In-charge Publications and Editorial Manager Publications, National Journal of Health Sciences). We are grateful to her for regular communications and expert advice.

REFERENCES

[1] Bhat V, Velandai S, Belliappa V, Illayraja J, Halli KG, Gopalakrishnan G. Quantification of liver fat with mDIXON magnetic resonance imaging, comparison with the computed tomography and the biopsy. J Clin Diagn Res 2017; 11(7): TC06-TC10.

[2] Lee DH. Imaging evaluation of non-alcoholic fatty liver disease: Focused on quantification. Clin Mol Hepatol 2017; 23(4): 290-301.

[3] Zhang Y, Wang C, Duanmu Y, *et al.* Comparison of CT and magnetic resonance mDIXON-Quant sequence in the diagnosis of mild hepatic steatosis. Br J Radiol 2018; 91(1091): 20170587.

[4] Lv S, Jiang S, Liu S, Dong Q, Xin Y, Xuan S. Noninvasive quantitative detection methods of liver fat content in nonalcoholic fatty liver disease. J Clin Transl Hepatol 2018; 6(2): 217-21.

[5] Graffy PM, Pickhardt PJ. Quantification of hepatic and visceral fat by CT and MR imaging: Relevance to the obesity epidemic, metabolic syndrome and NAFLD. Br J Radiol 2016; 89(1062): 20151024.

[6] Rehm JL, Wolfgram PM, Hernando D, Eickhoff JC, Allen DB, Reeder SB. Proton density fat-fraction is an accurate biomarker of hepatic steatosis in adolescent girls and young women. Eur Radiol 2015; 25(10): 2921-30.

[7] Zhang YN, Fowler KJ, Hamilton G, *et al.* Liver fat imaging—a clinical overview of ultrasound, CT, and MR imaging. Br J Radiol 2018; 91(1089): 20170959.

[8] Pasanta D, Htun KT, Pan J, *et al.* Magnetic resonance spectroscopy of hepatic fat from fundamental to clinical applications. Diagnostics 2021; 11(5): 842.

[9] Iftikhar R, Kamran SM, Sher F, Wahla MS. Prevalence of non alcoholic fatty liver disease in patients with metabolic syndrome. PAFMJ 2015; 65(5): 616-9.

[10] Paparo F, Cenderello G, Revelli M, *et al.* Diagnostic value of MRI proton density fat fraction for assessing liver steatosis in

chronic viral C hepatitis. BioMed Res Int 2015; 2015: 758164.

[11] Wells MM, Li Z, Addeman B, *et al.* Computed tomography measurement of hepatic steatosis: Prevalence of hepatic steatosis in a Canadian population. Canadian J Gastroenterol Hepatology 2016; 2016: 4930987.

[12] Caussy C, Reeder SB, Sirlin CB, Loomba R. Noninvasive, quantitative assessment of liver fat by MRI-PDFF as an endpoint in NASH trials. Hepatology 2018; 68(2): 763-72.

[13] Kramer H, Pickhardt PJ, Kliewer MA, *et al.* accuracy of liver fat quantification with advanced ct, mri, and ultrasound techniques: Prospective comparison with mr spectroscopy. Am J Roentgenol 2017; 208: 92-100.

[14] Hwang I, Lee J, Lee K, *et al.* Hepatic steatosis in living liver donor candidates: Preoperative assessment by using breath-hold triple-echo MR imaging and 1H MR spectroscopy. Radiology 2014; 271(3): 730-8.

[15] Koplay M, Sivri M, Erdogan H, Nayman A. Importance of imaging and recent developments in diagnosis of nonalcoholic fatty liver diseases. World J Hepatol 2015; 7(5): 769-76.

[16] Vos MB, Castillo-Leon E, Knight-Scott J, *et al.* Validation of MRI-VLFF for the non-invasive measurement of steatosis in children. GastroHep 2020; 2(4): 171-80.

[17] Bonekamp S, Tang A, Mashhood A, *et al.* Spatial distribution of MRI-determined hepatic proton density fat fraction in adults with nonalcoholic fatty liver disease. J Magn Reson Imaging 2014; 39(6): 1525-32.

[18] Awai H, Newton K, Sirlin C, Behling C, Schwimmer J Evidence and recommendations for imaging liver fat in children, based upon systematic review. Clin Gastroenterol Hepatol 2014; 12(5): 765-73.

[19] Harald K, Perry P, Mark K, *et al.* Accuracy of liver fat quantification with advanced CT, MRI, and ultrasound techniques: prospective comparison with MR spectroscopy. Am J Roentgenol 2017; 208: 92-100.

[20] Sherif FM, Elmogy SA, EL-wahab RMA, *et al.* Utility of magnetic resonance proton density fat fraction technique in quantification of liver fat in living donors for liver transplantation. Egypt J Radiol Nucl Med 2019; 50: 58. https://doi.org/10.1186/s43055-019-0061-4.

[21] Chiang HJ, Lin LH, Li CW, *et al.* Magnetic resonance fat quantification in living donor liver transplantation. Transplant Proc 2014; 46(3): 666-8.

Received: January 01, 2023 Revised: June 05, 2023 Accepted: June 07, 2023