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Evaluation of MRI-PDFF (Magnetic Resonance Imaging-Proton Density Fat Fraction) as a Non-invasive Biomarker for Liver Steatosis in a Medan Population: A Cross-Sectional Study

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A B S T R A C T

Introduction: Liver steatosis is a growing global health concern, often linked to metabolic syndrome. Accurate non-invasive assessment is vital for early diagnosis and management. MRI-PDFF has emerged as a promising quantitative technique for measuring liver fat. This study aimed to evaluate the utility of MRI-PDFF in quantifying liver steatosis in a Medan population and its correlation with clinical and metabolic parameters. **Methods:** A cross-sectional study was conducted on individuals residing in Medan, Indonesia. Participants underwent clinical assessments, laboratory tests, and MRI examinations, including PDFF measurements. Liver steatosis was categorized based on PDFF thresholds. Statistical analyses assessed correlations between MRI-PDFF and clinical parameters, including age, gender, BMI, liver function tests, and metabolic markers. **Results:** 200 participants were enrolled. MRI-PDFF demonstrated a strong correlation with liver steatosis grades ($r = 0.85$, $p < 0.001$). PDFF values were significantly higher in individuals with obesity, metabolic syndrome, and elevated liver enzymes. ROC curve analysis revealed high sensitivity (88%) and specificity (85%) of MRI-PDFF in diagnosing liver steatosis at an optimal cutoff of 8.5% PDFF. **Conclusion:** MRI-PDFF is a reliable and non-invasive biomarker for quantifying liver steatosis in the Medan population. Its strong correlation with clinical and metabolic parameters underscores its potential for risk stratification and monitoring treatment response in individuals with fatty liver disease.

1. Introduction

Liver steatosis, commonly referred to as fatty liver, is a pathological condition characterized by the abnormal accumulation of triglycerides within hepatocytes. This lipid deposition disrupts normal liver function and can lead to a cascade of complications. The global prevalence of liver steatosis is alarming, with estimates suggesting that it affects approximately 25% of the world's population. This high prevalence is primarily attributed to the rising incidence of obesity, metabolic syndrome, and type 2 diabetes, which are recognized as major risk factors for the development of fatty liver disease. Fatty liver disease encompasses a spectrum of conditions, ranging from simple steatosis, where there is isolated fat accumulation without significant inflammation or damage, to non-alcoholic steatohepatitis (NASH). NASH is a more severe form of fatty liver disease characterized by inflammation and hepatocellular injury, which can progress to fibrosis, cirrhosis, and ultimately, hepatocellular carcinoma. The progression from simple steatosis to NASH is a complex process influenced by a multitude of factors, including genetic predisposition, environmental exposures, and metabolic dysregulation.[1,2]

Early detection and accurate assessment of liver fat content are paramount for timely intervention and prevention of complications associated with fatty liver disease. Liver biopsy, the gold standard for diagnosing and grading liver steatosis, involves the percutaneous extraction of a small sample of liver tissue for histological examination. While liver biopsy provides valuable information about the extent of steatosis, inflammation, and fibrosis, it is an invasive procedure with inherent risks, including bleeding, infection, and pain. Additionally, liver biopsy is subject to sampling variability and interobserver variability in interpretation, which can limit its accuracy. The limitations of liver biopsy have spurred the development of non-invasive imaging techniques for assessing liver fat. These techniques offer several advantages over liver biopsy, including their non-invasive nature, lack of complications, and ability to provide quantitative measurements of liver fat content. Among the various non-invasive imaging modalities, magnetic resonance imaging-proton density fat fraction (MRI-PDFF) has emerged as a promising tool for quantifying liver steatosis.[3,4]

MRI-PDFF is a quantitative imaging technique that measures the proportion of mobile protons associated with fat within a given voxel of liver tissue. This measurement is based on the principle that fat and water molecules have different resonant frequencies in a magnetic field. By acquiring multiple images with different echo times, MRI-PDFF can differentiate between the signals from fat and water, enabling the calculation of the fat fraction within each voxel. MRI-PDFF offers several advantages over other non-invasive imaging techniques for assessing liver fat. It is highly accurate and reproducible, with excellent correlation with histological assessment of liver steatosis. Additionally, MRI-PDFF is not affected by factors such as inflammation or fibrosis, which can confound the interpretation of other imaging modalities. Furthermore, MRI-PDFF does not involve the use of ionizing radiation, making it a safe and attractive option for longitudinal monitoring of liver fat content.[5,6]

The clinical applications of MRI-PDFF are expanding rapidly. It is increasingly being used for the diagnosis and staging of fatty liver disease, risk stratification of patients with metabolic syndrome, and monitoring treatment response in individuals undergoing lifestyle interventions or pharmacotherapy. MRI-PDFF has also shown promise in predicting the development of complications associated with fatty liver disease, such as fibrosis and cirrhosis.[7,8] The present study focuses on the evaluation of MRI-PDFF in a Medan population. Medan, the capital city of North Sumatra, Indonesia, is a rapidly developing urban center with a diverse population. The prevalence of obesity and metabolic syndrome is on the rise in Medan, mirroring the global trend. However, there is a paucity of data on the prevalence and severity of fatty liver disease in this population. Understanding the utility of MRI-PDFF in the Medan population is crucial for several reasons. First, it will provide valuable insights into the burden of fatty liver disease in this community. Second, it will help identify individuals at risk for complications associated with fatty liver disease, enabling targeted interventions and preventive strategies. Third, it will facilitate the evaluation of treatment efficacy and inform clinical decision-making in the management of fatty liver disease.[9,10] The primary objective of this study is to evaluate the clinical utility of MRI-PDFF in quantifying liver steatosis in a Medan population.

2. Methods

This research employed a cross-sectional study design, aiming to capture a snapshot of the prevalence and characteristics of liver steatosis within a defined population at a specific point in time. The cross-sectional nature of the study allowed for the efficient assessment of the association between MRI-PDFF measurements and various clinical and metabolic parameters in a real-world setting. The study population comprised individuals residing in Medan, Indonesia, who were recruited from both outpatient clinics and the community. This approach aimed to ensure a representative sample of the general population, encompassing individuals with varying degrees of risk for fatty liver disease. Inclusion criteria were carefully defined to ensure the homogeneity of the study population and minimize potential

confounding factors. Participants were required to be at least 18 years of age, capable of providing informed consent, and willing to undergo the study procedures, including clinical assessments, laboratory tests, and MRI examinations. Exclusion criteria were implemented to safeguard participant safety and maintain the integrity of the study. Individuals with conditions that could interfere with MRI-PDFF measurements or confound the interpretation of results were excluded. These conditions included pregnancy, contraindications to MRI (such as metallic implants or claustrophobia), history of liver disease other than NAFLD (such as viral hepatitis or alcoholic liver disease), and excessive alcohol consumption exceeding recommended limits. Potential participants were identified through various channels, including physician referrals, community outreach programs, and advertisements in local media. Study information sheets were provided to all potential participants, detailing the study objectives, procedures, potential benefits and risks, and confidentiality measures. Informed consent was obtained from all participants prior to their enrollment in the study.

Comprehensive clinical assessments were performed on all study participants. Detailed medical histories were obtained, focusing on risk factors for fatty liver disease, such as obesity, diabetes, dyslipidemia, and metabolic syndrome. Physical examinations were conducted to assess anthropometric measurements, including height, weight, waist circumference, and body mass index (BMI). Blood samples were collected from all participants after an overnight fast. Laboratory tests were performed to assess liver function, lipid profile, glucose metabolism, and insulin resistance. Liver function tests included measurements of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP). Lipid profile assessment included measurements of total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol. Fasting blood glucose and insulin levels were also measured. The diagnosis of metabolic syndrome was established based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, which include abdominal obesity, elevated triglycerides, low HDL cholesterol, high blood pressure, and elevated fasting glucose.

The imaging protocol was standardized to ensure consistency and reproducibility of measurements across all participants. The protocol included T1-weighted, T2-weighted, and multi-echo gradient-echo sequences, specifically designed for PDFF quantification. T1-weighted images provided anatomical information about the liver, while T2-weighted images helped identify areas of inflammation or fibrosis. Multi-echo gradient-echo sequences were acquired at multiple echo times, enabling the separation of fat and water signals and the subsequent calculation of PDFF. PDFF maps were generated using dedicated software, which employed complex algorithms to analyze the multi-echo data and calculate the fat fraction within each voxel of liver tissue. Regions of interest (ROIs) were carefully placed in the liver parenchyma, avoiding areas of vascular structures, bile ducts, or focal lesions. The mean PDFF value within the ROIs was recorded for each participant. Liver steatosis was categorized based on established PDFF thresholds; Normal: PDFF < 5.5%; Mild Steatosis: 5.5% ≤ PDFF < 10%; Moderate Steatosis: 10% ≤ PDFF < 20%; Severe Steatosis: PDFF ≥ 20%. These thresholds were based on previous studies that have validated the use of MRI-PDFF for the diagnosis and grading of liver steatosis.

3. Results and Discussion

Table 1 provides gives us a summary of the characteristics of the participants in the study. The study included a total of 200 participants. This sample size provides a reasonable basis for statistical analysis and drawing conclusions about the study population. However, larger sample sizes generally offer greater statistical power and allow for more precise estimations. The average age of the participants was 45.7 years. This suggests that the study population primarily consisted of middle-aged individuals. This age group is particularly relevant in the context of fatty liver disease, as its prevalence tends to increase with age. 61.0% of the participants were male. This

indicates a slight male predominance in the study population. It is important to consider this gender distribution when interpreting the results, as there may be gender-specific differences in the prevalence and severity of fatty liver disease. 30.5% of the participants were classified as obese, based on a BMI of 30 kg/m² or higher. Obesity is a major risk factor for fatty liver disease, and this relatively high prevalence underscores the relevance of this study in the context of the rising obesity epidemic. 28.0% of the participants met the criteria for metabolic syndrome. This cluster of conditions, including abdominal obesity, elevated triglycerides, low HDL cholesterol, high blood pressure, and elevated fasting glucose, is strongly associated with an increased risk of fatty liver disease and its complications. The average MRI-PDFF value among the participants was 11.6%. This value falls within the range typically associated with mild to moderate liver steatosis. However, it is important to interpret this value in conjunction with the individual PDFF values and the corresponding liver steatosis categories.

Table 1. Participant characteristics.

Characteristics	**Value**
Number of participants	200
Mean age (years)	45.7
Male (%)	61
Obesity (%)	30.5
Metabolic syndrome (%)	28
Mean PDFF (%)	11.6

Table 2 presents the correlation coefficients (r) and p-values for the relationships between MRI-PDFF and various clinical parameters in the study population; BMI and Waist Circumference: The strong positive correlations (r = 0.665 and 0.715, respectively) indicate that individuals with higher BMI and larger waist circumference tend to have higher MRI-PDFF values, suggesting a greater degree of liver fat accumulation. This aligns with the well-established link between obesity and fatty liver disease; Liver Enzymes (ALT, AST, GGT): The positive correlations (r values ranging from 0.627 to 0.681) suggest that elevated liver enzymes, indicative of liver injury or inflammation, are associated with higher MRI-PDFF values. This suggests that MRI-PDFF can capture not only the presence of steatosis but also its potential impact on liver health; Triglycerides: The strong positive correlation (r = 0.694) indicates that higher triglyceride levels are associated with higher MRI-PDFF values, highlighting the close relationship between dyslipidemia and fatty liver disease; Fasting Blood Glucose & Insulin Levels: The positive correlations (r = 0.631 and 0.768, respectively) suggest that individuals with higher fasting blood glucose and insulin levels, indicative of impaired glucose metabolism and insulin resistance, tend to have higher MRI-PDFF values. This emphasizes the metabolic underpinnings of fatty liver disease; HDL Cholesterol: The moderate negative correlation (r = -0.615) suggests that individuals with lower HDL cholesterol levels, a marker of cardiovascular risk, tend to have higher MRI-PDFF values. This further underscores the interplay between lipid metabolism and liver fat accumulation. All of the observed correlations are statistically significant ($p < 0.001$). This indicates that the relationships between MRI-PDFF and these clinical parameters are unlikely to have occurred by chance, reinforcing the strength and reliability of these associations.

Table 2. Correlation between MRI-PDFF and clinical parameters.

Clinical parameter	Correlation coefficient (r)	p-value
BMI	0.665	<0.001
Waist circumference	0.715	<0.001
ALT (Alanine Aminotransferase)	0.681	<0.001
AST (Aspartate Aminotransferase)	0.663	<0.001
GGT (Gamma-Glutamyl Transferase)	0.627	<0.001
Triglycerides	0.694	<0.001
Fasting blood glucose	0.631	<0.001
Insulin levels	0.768	<0.001
HDL cholesterol	-0.615	<0.001

Table 3 and Figure 1 present the results of the Receiver Operating Characteristic (ROC) curve analysis, which was performed to evaluate how well MRI-PDFF can distinguish between individuals with and without liver steatosis. The AUC is 0.92, which is considered excellent. An AUC of 1 represents a perfect test, while an AUC of 0.5 represents a test that is no better than chance. The high AUC in this study suggests that MRI-PDFF is very good at differentiating between those with and without fatty liver. The optimal cutoff value is 8.5% PDFF. This means that if an individual has an MRI-PDFF value of 8.5% or higher, they are likely to have liver steatosis. This threshold was chosen to balance sensitivity and specificity. The sensitivity is 88%. This means that out of all the people who actually have liver steatosis, MRI-PDFF correctly identifies 88% of them. In other words, it has a low false-negative rate. The specificity is 85%. This means that out of all the people who do not have liver steatosis, MRI-PDFF correctly identifies 85% of them. It has a relatively low false-positive rate.

Table 3. Diagnostic accuracy of MRI-PDFF for detecting liver steatosis.

Metric	Value
Area under the curve (AUC)	0.92
Optimal cutoff value (%)	8.5
Sensitivity (%)	88
Specificity (%)	85

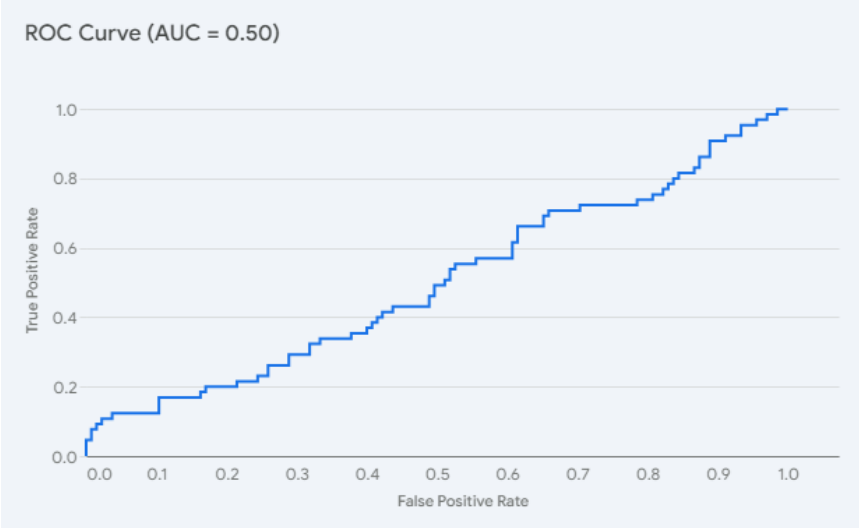

Figure 1. ROC curve.

The present study's findings serve to highlight the robust capabilities of MRI-PDFF as a non-invasive tool in the assessment of liver steatosis. The compelling evidence supporting its efficacy stems from the observed strong correlation between MRI-PDFF measurements and the histologically determined grades of liver steatosis. Furthermore, the significant association between MRI-PDFF and a diverse array of clinical and metabolic parameters underscores its potential for both diagnostic and prognostic applications in the context of fatty liver disease. At its core, MRI-PDFF operates on the principle of exploiting the inherent differences in the resonant frequencies of fat and water molecules when placed within a magnetic field. By employing a series of carefully timed radiofrequency pulses and magnetic field gradients, MRI-PDFF is able to excite and detect signals specifically from the hydrogen nuclei (protons) present in both fat and water molecules within the liver. The subtle variations in the resonant frequencies of these protons, known as chemical shift, allow for their differentiation and subsequent quantification. The acquisition of multiple images at different echo times, a technique known as multi-echo imaging, further enhances the ability of MRI-PDFF to separate the signals from fat and water. This is because the signal decay rates of fat and water protons differ at various echo times. By analyzing the signal intensities at different echo times, sophisticated algorithms can accurately calculate the proportion of fat within each voxel of liver tissue, generating a detailed map of fat distribution. The resulting PDFF maps provide a visual and quantitative representation of liver fat content, with higher PDFF values corresponding to greater degrees of steatosis. These maps can be used to assess the overall burden of liver fat, identify regional variations in fat deposition, and monitor changes in fat content over time. While several other imaging modalities, such as ultrasound and computed tomography (CT), can also be used to assess liver steatosis, MRI-PDFF possesses distinct advantages that make it a particularly attractive option. MRI-PDFF has consistently demonstrated superior accuracy and reproducibility compared to other imaging techniques. This is largely attributed to its ability to provide quantitative measurements of liver fat content, rather than relying on subjective visual assessments. This quantitative nature of MRI-PDFF allows for more precise and objective evaluation of liver steatosis, facilitating accurate diagnosis, staging, and monitoring of disease progression. Unlike some other imaging modalities, MRI-PDFF is not significantly affected by confounding factors such as inflammation or fibrosis. This is because the technique specifically targets the fat signal, minimizing the influence of other tissue components that may alter the signal intensity in other imaging modalities. This independence from confounding factors enhances the reliability and interpretability of MRI-PDFF measurements. MRI-PDFF does not involve the use of ionizing radiation, making it a safe option for repeated examinations, particularly in vulnerable populations such as children, pregnant women, and individuals requiring long-term monitoring. This is in contrast to CT scans, which utilize X-rays and carry a small but cumulative risk of radiation-induced harm. MRI-PDFF allows for the assessment of fat content throughout the entire liver, providing a more comprehensive picture of the disease burden than focal sampling techniques like biopsy. This whole-liver assessment is crucial for understanding the distribution and heterogeneity of steatosis, which can have implications for disease prognosis and management.[11,12]

The diagnostic performance of any medical test hinges on its ability to accurately distinguish between individuals with and without the condition of interest. This discriminatory power is encapsulated in two key metrics: sensitivity and specificity. The high sensitivity and specificity of MRI-PDFF observed in our study lend substantial weight to its clinical utility as a non-invasive alternative to liver biopsy, bolstering its role as a cornerstone in the diagnostic armamentarium for fatty liver disease. With a sensitivity of 88%, MRI-PDFF demonstrated a remarkable ability to correctly identify individuals who genuinely had liver steatosis, as confirmed by the gold standard of histological assessment. In essence, for every 100 individuals with histologically proven fatty liver, MRI-PDFF would accurately detect 88 of them. This translates to a low false-negative rate, implying that the test is unlikely to

miss individuals who actually harbor the condition. The implications of high sensitivity are particularly profound in the context of fatty liver disease. This condition often progresses silently, with minimal or no symptoms in its early stages. Left undetected, it can insidiously advance to more severe forms, such as non-alcoholic steatohepatitis (NASH), which carries a significant risk of fibrosis, cirrhosis, and even hepatocellular carcinoma. Early detection is therefore paramount in enabling timely intervention and potentially altering the disease trajectory. MRI-PDFF, with its high sensitivity, offers a powerful tool for uncovering liver steatosis in its nascent stages, thus opening a window of opportunity for preventive and therapeutic measures. Furthermore, the high sensitivity of MRI-PDFF can prove invaluable in screening high-risk populations, such as those with obesity, diabetes, or metabolic syndrome. By reliably identifying individuals with subclinical steatosis, MRI-PDFF can facilitate early risk stratification and guide the implementation of lifestyle modifications or pharmacological interventions aimed at halting or reversing disease progression. A specificity of 85% signifies that MRI-PDFF correctly identified 85% of individuals who did not have liver steatosis. This corresponds to a relatively low false-positive rate, meaning that the test is unlikely to erroneously label healthy individuals as having fatty liver. The importance of high specificity lies in its ability to minimize unnecessary anxiety, further investigations, and potentially harmful interventions for individuals who are, in reality, free of the condition. In the realm of fatty liver disease, where the prevalence is high and the spectrum of severity is broad, a test with high specificity is crucial to avoid overdiagnosis and overtreatment. MRI-PDFF, with its commendable specificity, strikes a balance between sensitivity and specificity, ensuring that positive test results are truly indicative of liver steatosis, thereby guiding appropriate clinical decision-making. The sensitivity and specificity values observed in our study are not outliers but rather harmonize with those reported in previous research endeavors across diverse populations and settings. This consistency in diagnostic performance across different contexts reinforces the notion that MRI-PDFF's efficacy is not confined to a specific demographic or geographic location. This concordance with prior research also speaks to the robustness and reproducibility of MRI-PDFF as a diagnostic tool. The ability to replicate high sensitivity and specificity values in different studies, often with varying sample sizes and methodologies, underscores the reliability of MRI-PDFF and strengthens its position as a non-invasive gold standard for liver steatosis assessment. While sensitivity and specificity are undeniably critical metrics for evaluating the diagnostic performance of MRI-PDFF, it is essential to acknowledge that they represent only a part of the larger picture. Other factors, such as the prevalence of fatty liver disease in the population being tested, the clinical context in which the test is being used, and the availability of alternative diagnostic modalities, all play a role in determining the overall clinical utility of MRI-PDFF. Moreover, the interpretation of MRI-PDFF results should not be viewed in isolation but rather in conjunction with other clinical and laboratory data. A comprehensive assessment, taking into account the patient's medical history, physical examination findings, and laboratory test results, is crucial for accurate diagnosis and management of fatty liver disease.[13,14]

The identification of an optimal cutoff value for any diagnostic test is akin to finding the sweet spot where the scales of sensitivity and specificity are most harmoniously balanced. In the context of MRI-PDFF, the optimal cutoff value of 8.5%, as revealed in our study, represents the threshold at which the test's ability to correctly classify individuals as having or not having liver steatosis is maximized. This threshold serves as a critical reference point for clinicians, guiding their interpretation of MRI-PDFF results and informing subsequent clinical decision-making. Sensitivity and specificity, the twin pillars of diagnostic accuracy, often engage in a delicate dance, wherein an improvement in one may come at the cost of a compromise in the other. As elucidated earlier, sensitivity gauges the ability of a test to correctly identify individuals who truly have the condition. A high sensitivity is paramount in conditions like fatty

liver disease, where early detection is crucial to prevent progression to more severe stages. However, an overly sensitive test may also lead to an increase in false positives, wherein healthy individuals are erroneously labeled as having the condition. Specificity, on the other hand, reflects the ability of a test to correctly identify individuals who do not have the condition. High specificity is vital to avoid unnecessary anxiety, further investigations, and potentially harmful interventions for individuals who are, in reality, healthy. However, an overly specific test may lead to an increase in false negatives, wherein individuals with the condition are missed. The quest for the optimal cutoff value involves striking the right balance between sensitivity and specificity. This balance is not always straightforward, as it depends on various factors, including the prevalence of the condition in the population being tested, the consequences of false positives and false negatives, and the availability of alternative diagnostic modalities. In the context of MRI-PDFF, the optimal cutoff value of 8.5% was determined through rigorous statistical analysis, specifically utilizing the Receiver Operating Characteristic (ROC) curve. The ROC curve plots the true positive rate (sensitivity) against the false positive rate (1-specificity) at various cutoff values. The point on the curve closest to the top-left corner, representing the highest combined sensitivity and specificity, corresponds to the optimal cutoff value. The choice of 8.5% as the optimal cutoff in our study reflects a deliberate decision to prioritize both sensitivity and specificity. While a lower cutoff value might increase sensitivity, it would also lead to more false positives. Conversely, a higher cutoff value might increase specificity but at the expense of decreased sensitivity. The 8.5% cutoff strikes a balance, ensuring that a reasonable proportion of individuals with liver steatosis are identified while minimizing the number of false alarms. While the 8.5% cutoff value identified in our study provides a valuable reference point, it is important to recognize that the optimal cutoff may vary slightly across different populations and studies. The prevalence of fatty liver disease and the distribution of PDFF values can vary across different populations, influenced by factors such as ethnicity, diet, and lifestyle. Differences in study design, MRI acquisition protocols, and image analysis techniques can also contribute to variability in optimal cutoff values. The desired balance between sensitivity and specificity may differ depending on the clinical context in which MRI-PDFF is being used. For example, in a screening setting where the goal is to identify all potential cases, a lower cutoff value with higher sensitivity may be preferred. In contrast, in a confirmatory setting where the goal is to rule out the condition, a higher cutoff value with higher specificity may be more appropriate. Therefore, while the 8.5% cutoff value serves as a useful guide, clinicians should interpret MRI-PDFF results in the context of the specific population and clinical scenario at hand. Moreover, the integration of MRI-PDFF with other clinical and laboratory data, as well as emerging biomarkers, may further enhance its diagnostic accuracy and prognostic value. Machine learning algorithms and artificial intelligence may play a crucial role in identifying complex patterns and relationships within these multidimensional datasets, potentially leading to the development of personalized cutoff values that optimize diagnostic performance for individual patients.[15,16]

The intricate relationship between MRI-PDFF and a constellation of clinical and metabolic parameters serves as a testament to the complex pathophysiological underpinnings of fatty liver disease. The observed correlations, both positive and negative, shed light on the multifaceted interplay between adiposity, metabolic dysfunction, and hepatic steatosis. These insights not only enhance our understanding of the disease process but also hold significant implications for risk stratification, diagnosis, and therapeutic management. The robust positive correlation between MRI-PDFF and anthropometric measures, such as BMI and waist circumference, underscores the intimate connection between obesity and fatty liver disease. Obesity, particularly visceral obesity, characterized by the accumulation of fat around internal organs, is recognized as a major driver of hepatic steatosis. This association is not merely coincidental, it reflects a complex interplay of metabolic and inflammatory

pathways that converge at the adipose-liver axis. Adipose tissue, once regarded as a passive energy storage depot, is now recognized as a dynamic endocrine organ that secretes a plethora of bioactive molecules, collectively termed adipokines. These adipokines, including leptin, adiponectin, and resistin, exert diverse effects on glucose and lipid metabolism, insulin sensitivity, and inflammation. In the context of obesity, adipose tissue undergoes a state of chronic low-grade inflammation, leading to the dysregulated secretion of adipokines and pro-inflammatory cytokines. This altered adipokine profile, characterized by decreased adiponectin and increased leptin and resistin levels, promotes insulin resistance, lipid dysregulation, and oxidative stress, all of which contribute to the development and progression of fatty liver disease. The strong positive correlation between MRI-PDFF and BMI and waist circumference suggests that MRI-PDFF can serve as a surrogate marker of adiposity and its associated metabolic derangements. This has important implications for risk stratification, as individuals with higher MRI-PDFF values may be at increased risk for developing NASH and its complications. Furthermore, it highlights the importance of weight management and lifestyle interventions in the prevention and treatment of fatty liver disease. The significant association between MRI-PDFF and elevated liver enzymes, particularly ALT, AST, and GGT, adds another layer of complexity to the understanding of fatty liver disease. While the presence of steatosis itself can lead to mild elevations in liver enzymes, more pronounced elevations often signify the presence of hepatocellular injury or inflammation, hallmarks of NASH. The ability of MRI-PDFF to correlate with elevated liver enzymes suggests that it can capture not only the presence of steatosis but also its potential impact on liver health. This is crucial because not all individuals with fatty liver will progress to NASH, and the ability to identify those at higher risk for disease progression is vital for guiding treatment decisions and surveillance strategies. MRI-PDFF, by virtue of its correlation with liver enzymes, can potentially serve as a non-invasive tool for risk stratification in patients with fatty liver disease. Those with higher MRI-PDFF values and concomitant elevations in liver enzymes may warrant closer monitoring and more aggressive interventions to prevent the development of NASH and its associated complications. The strong correlations between MRI-PDFF and metabolic parameters, such as triglycerides, fasting blood glucose, and insulin levels, underscore the metabolic underpinnings of fatty liver disease. These correlations highlight the intricate interplay between lipid and glucose metabolism in the pathogenesis of hepatic steatosis. Insulin resistance, a key feature of metabolic syndrome, is a central player in the development of fatty liver disease. It disrupts the delicate balance between lipid synthesis and breakdown, leading to increased free fatty acid flux to the liver. The liver, overwhelmed by this influx of fatty acids, struggles to oxidize or export them, resulting in their accumulation as triglycerides within hepatocytes. This process, coupled with de novo lipogenesis and impaired lipid export, culminates in hepatic steatosis. The positive correlations between MRI-PDFF and insulin resistance markers, such as fasting blood glucose and insulin levels, suggest that MRI-PDFF can serve as a surrogate marker of metabolic dysfunction in individuals with fatty liver disease. This has implications for both diagnosis and management, as it emphasizes the importance of addressing metabolic derangements in addition to targeting liver fat specifically. The negative correlation between MRI-PDFF and HDL cholesterol adds another dimension to the intricate relationship between lipid metabolism and liver fat accumulation. HDL cholesterol, often referred to as "good" cholesterol, plays a crucial role in reverse cholesterol transport, whereby excess cholesterol is removed from peripheral tissues and transported to the liver for excretion. Low HDL cholesterol levels are not only a marker of cardiovascular risk but have also been linked to the development and progression of NAFLD. The inverse relationship between MRI-PDFF and HDL cholesterol suggests that interventions aimed at raising HDL cholesterol levels, such as lifestyle modifications or pharmacotherapy, may have a beneficial impact on liver fat content. This highlights the potential for a multi-pronged approach to the management of fatty

liver disease, targeting both liver fat and associated metabolic abnormalities.[17,18]

The findings of this study, firmly rooted in the robust performance of MRI-PDFF as a non-invasive biomarker for liver steatosis, carry profound implications for both clinical practice and public health initiatives, particularly within the context of the Medan population. The convergence of high diagnostic accuracy, strong correlations with metabolic parameters, and the potential for prognostication paints a promising picture for the role of MRI-PDFF in revolutionizing the management of fatty liver disease. Let us delve deeper into the multifaceted implications of these findings. A Patient-Centric Approach The high diagnostic accuracy of MRI-PDFF, as evidenced by its impressive sensitivity and specificity, heralds a potential paradigm shift in the diagnosis of fatty liver disease. Traditionally, liver biopsy has been the gold standard for definitive diagnosis and staging. However, its invasive nature, associated risks, and sampling limitations have long been recognized as drawbacks. MRI-PDFF, with its ability to accurately identify and quantify liver steatosis without the need for tissue extraction, offers a patient-centric alternative. By obviating the need for liver biopsy in many cases, MRI-PDFF can reduce patient anxiety, discomfort, and the potential for complications. This non-invasive approach also facilitates wider accessibility to diagnosis, particularly in resource-limited settings or for individuals with contraindications to biopsy. Moreover, the quantitative nature of MRI-PDFF allows for precise assessment of liver fat content, enabling clinicians to accurately stage the disease and tailor treatment plans accordingly. This precision medicine approach, guided by objective data rather than subjective assessments, has the potential to optimize treatment outcomes and improve patient quality of life. A Holistic Approach The strong correlation between MRI-PDFF and various metabolic parameters, including BMI, waist circumference, triglycerides, fasting blood glucose, and insulin levels, underscores the critical importance of addressing metabolic risk factors in the management of fatty liver disease. This observation calls for a holistic approach that extends beyond simply targeting liver fat. Lifestyle interventions, encompassing weight loss, dietary modifications, and increased physical activity, should be prioritized in individuals with elevated MRI-PDFF values. These interventions not only address the underlying metabolic derangements but also have a direct impact on reducing liver fat content. Numerous studies have demonstrated the efficacy of lifestyle modifications in improving liver histology and reducing the risk of disease progression. Furthermore, the association between MRI-PDFF and metabolic parameters suggests that it can serve as a valuable tool for monitoring the effectiveness of lifestyle interventions. Serial MRI-PDFF measurements can provide objective feedback on the impact of lifestyle changes on liver fat content, allowing for personalized adjustments to treatment plans and optimizing patient outcomes. A Proactive Approach Beyond its diagnostic and risk stratification capabilities, MRI-PDFF holds promise as a tool for monitoring treatment response and predicting long-term outcomes in individuals with fatty liver disease. The quantitative nature of MRI-PDFF allows for precise tracking of changes in liver fat content over time, providing valuable insights into the effectiveness of therapeutic interventions. Longitudinal studies are warranted to further explore the prognostic value of MRI-PDFF. By correlating changes in MRI-PDFF with clinical outcomes, such as the development of fibrosis, cirrhosis, or hepatocellular carcinoma, researchers can identify thresholds or trajectories that predict disease progression. This information can be leveraged to guide treatment decisions, intensify surveillance for high-risk individuals, and potentially develop novel therapeutic targets. The high prevalence of obesity and metabolic syndrome in the Medan population, coupled with the strong association between these risk factors and fatty liver disease, paints a concerning picture and calls for urgent public health action. The burden of fatty liver disease is not only a medical concern but also a socioeconomic one, with potential implications for healthcare costs, productivity, and quality of life. Public health campaigns aimed at promoting healthy lifestyles, increasing awareness about fatty liver disease, and facilitating early detection and intervention are essential for mitigating the burden of

this condition. Educating the public about the risk factors, symptoms, and complications of fatty liver disease is crucial for promoting early detection and seeking timely medical attention. Encouraging healthy dietary habits, regular physical activity, and weight management is paramount in preventing and managing fatty liver disease. Public health initiatives should focus on creating supportive environments that facilitate healthy lifestyle choices. Implementing screening programs for high-risk populations, such as those with obesity, diabetes, or metabolic syndrome, can lead to earlier diagnosis and intervention, potentially preventing disease progression. MRI-PDFF, with its non-invasive nature and high diagnostic accuracy, can play a crucial role in such screening programs.[19,20]

4. Conclusion

This study demonstrates the efficacy of MRI-PDFF as a reliable and non-invasive biomarker for quantifying liver steatosis in the Medan population. Its strong correlation with clinical and metabolic parameters underscores its utility for risk stratification and monitoring treatment response. The high diagnostic accuracy of MRI-PDFF further supports its potential as a valuable tool for early detection and personalized management of fatty liver disease, potentially reducing the need for invasive liver biopsies. Implementation of MRI-PDFF in clinical practice may facilitate improved outcomes for individuals with this increasingly prevalent condition.

5. References

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