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Grading of Fatty Liver Based on Computed Tomography Hounsfield Unit Values versus Ultrasonography Grading

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Abstract: Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) ranges from hepatic steatosis to nonalcoholic steatohepatitis and may lead to liver cirrhosis. This study aimed to assess the feasibility of numerical grading MASLD using noncontrast computed tomography (NCCT). **Methods:** In a retrospective study of 166 patients diagnosed with MASLD between June 2020 and January 2024, MASLD was graded by ultrasonography, and liver density was measured on NCCT. The MASLD grades and NCCT densities were compared. **Results:** The MASLD grades were distributed as follows: grade 0 (n = 79, 47.6%), grade 2 (n = 48, 28.9%), grade 1 (n = 25, 15.1%), and grade 3 (n = 14, 8.4%). The mean liver density was 57.75 Hounsfield units (HU) ± 6.18 (range: 48.9–78.2), 51.1 HU ± 4.7 (range: 41.4–59.7), 39.3 ± 6.4 (range: 21.4–48.9), and 22.87 ± 7.5 (range: 12–36.4) in the grade 0, grade 1, grade 2, and grade 3 patients, respectively. An analysis of variance test showed significant variance in the distribution of mean liver density in the different MASLD grades ($p < 0.001$). **Conclusions:** After ultrasonography diagnosis of MASLD, NCCT offers an objective, numerical, and calculable method for MASLD grading that is available for radiologists, radiologic technologists, and interested physicians away from experience dependence. NCCT determined that grade 2 had a specific density from 36.4 to 41.4 HU that significantly overlapped with grade 1 (41.4–48.9) HU and with grade 3 (21.4–36.4 HU). Grade 1 showed a significant overlap with the normal liver (48.9–59.7 HU).

Keywords: metabolic dysfunction-associated steatotic liver disease (MASLD); ultrasonography grading of MASLD; computed tomography Hounsfield units (CT HU); liver density (HU); grading of MASLD

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1. Introduction

Steatotic liver disease is the accumulation of triglycerides and other fat in the liver cells. Metabolic dysfunction-associated steatotic liver disease (MASLD) is the latest name for steatotic liver disease associated with metabolic syndrome, formerly known as nonalcoholic fatty liver disease (NAFLD), which is a liver condition mimicking alcoholic hepatitis that can progress to liver cirrhosis in persons without excessive alcoholic consumption [1]. Steatotic liver disease was originally described by Addison in 1836. Subsequently, pathologists have spent decades comparing liver histology changes in people with diabetes, extremely obese persons, and alcoholics. Liver steatosis was originally described by Addison in 1835. In 1838, Rokitansky determined that fat accumulation in the liver might be a cause of liver cirrhosis [2].

MASLD is estimated to be more than 25% of the general adult population globally and is closely linked to obesity, type 2 diabetes mellitus, and related disorders such as hyperlipidemia [3]. In Saudi Arabia, the prevalence of MASLD is predicted to exceed 30%

of the population in 2023, and obesity and diabetes mellitus have been strongly associated with MASLD [4]. By 2030, there will be an estimated 12,534,000 MASLD cases, and the prevalence of compensated liver cirrhosis and advanced liver disease is projected to at least double, with an annual incidence of 4800 deaths in Saudi Arabia [5]. According to the American Heart Association, MASLD is a risk factor for atherosclerotic cardiovascular diseases, end-stage liver disease, and hepatocellular carcinoma [6]. The severity of MASLD is closely associated with subclinical atherosclerosis, with significant linear trends [7].

The risk phases for the progression of MASLD include the following: (1) steatosis, which can create a proinflammatory environment leading to cellular injury and necroinflammation; (2) steatohepatitis in up to 59% of MASLD patients; and (3) advanced fibrosis in up to 25% of MASLD patients [8].

Since MASLD is a reversible health problem in its early stages, early detection and quantitative evaluation are important to avoid serious complications. Liver biopsy is the gold standard for the diagnosis and quantification of hepatic steatosis and is a unique, reliable method to differentiate simple steatosis from nonalcoholic steatohepatitis. However, biopsy is an invasive procedure with complications such as bleeding, and repeated biopsy for monitoring the disease course is not feasible [9]. Ultrasonography is used to diagnose and grade MASLD by scoring liver brightness, the blurring of vessels, and the diaphragm [10]. Ultrasonography can be used for grading MASLD using a four-point scale as follows: normal liver echogenicity (grade 0), diffusely increased liver echogenicity and appreciable periportal and diaphragm echogenicity (grade 1), diffusely increased liver echogenicity obscuring periportal and appreciable diaphragm echogenicity (grade 2), and diffusely increased liver echogenicity obscuring periportal and diaphragm echogenicity (grade 3) [11]. However, simple grayscale ultrasonography is subjective and operator-dependent, and its accuracy is affected by multiple ultrasound machine parameters, such as ultrasound frequency and gain [12].

The limitations of liver biopsy and ultrasonography in assessing MASLD create the need to develop a non-invasive and quantitative method for grading MASLD. Aiming to fill the gap and develop a new numerical calculable method for grading and risk stratifying MASLD, we hypothesized that computed tomography (CT) Hounsfield unit (HU) values would provide an accurate, numerically calculable method for grading MASLD. We hypothesized that CT HU would be <60 HU in mild MASLD, <40 HU in moderate MASLD, and <30 HU in severe MASLD. Measuring the CT HU of fatty livers would provide an accurate, numerically calculable method for grading MASLD. This study will add a quantitative and easily calculable method for grading fatty liver away from the subjective ultrasonography grading, which is operator-dependent. To date, no previous studies have thoroughly investigated this idea.

2. Methods

2.1. Study Population

This was a retrospective study of patients diagnosed with MASLD between June 2020 and January 2024 conducted at King Salman bin Abdulaziz Medical City, Al-Madinah Al-Munawwarah, Kingdom of Saudi Arabia. Data for this study were retrospectively collected during the period from 15 November 2023 to 10 March 2024. A structured data collection sheet was designed to collect the patients' ages, sex, and liver density, which was calculated in CT HU using stored NCCT images. Two experienced radiologists independently graded MASLD using the stored liver ultrasonography images. A correlation between the MASLD grade using ultrasonography and the calculated CT HU of the same patients was performed. All activities associated with this study were approved by the King Salman bin Abdulaziz Medical City Institutional Review Board (IRB) (Approval No. IRB23-046, issued on 19 October 2023) with a waiver of informed consent to access non-anonymized patient data. All procedures were performed in accordance with the Declaration of Helsinki, revised in 2013, and all applicable standards and laws. Confidentiality of the patient's information was assured during and after the study.

2.2. Sample Size

This study included the stored images of 166 patients who underwent liver ultrasonography and NCCT and had already been diagnosed with MASLD.

2.3. Exclusion Criteria

This study excluded the following patients: (1) patients with no available liver ultrasonography or NCCT in the same period of time (i.e., one month); (2) patients diagnosed with liver cirrhosis, edema, metastasis, or other pathologies; and (3) patients with no compatible grading of MASLD by at least two radiologists (Figure 1).

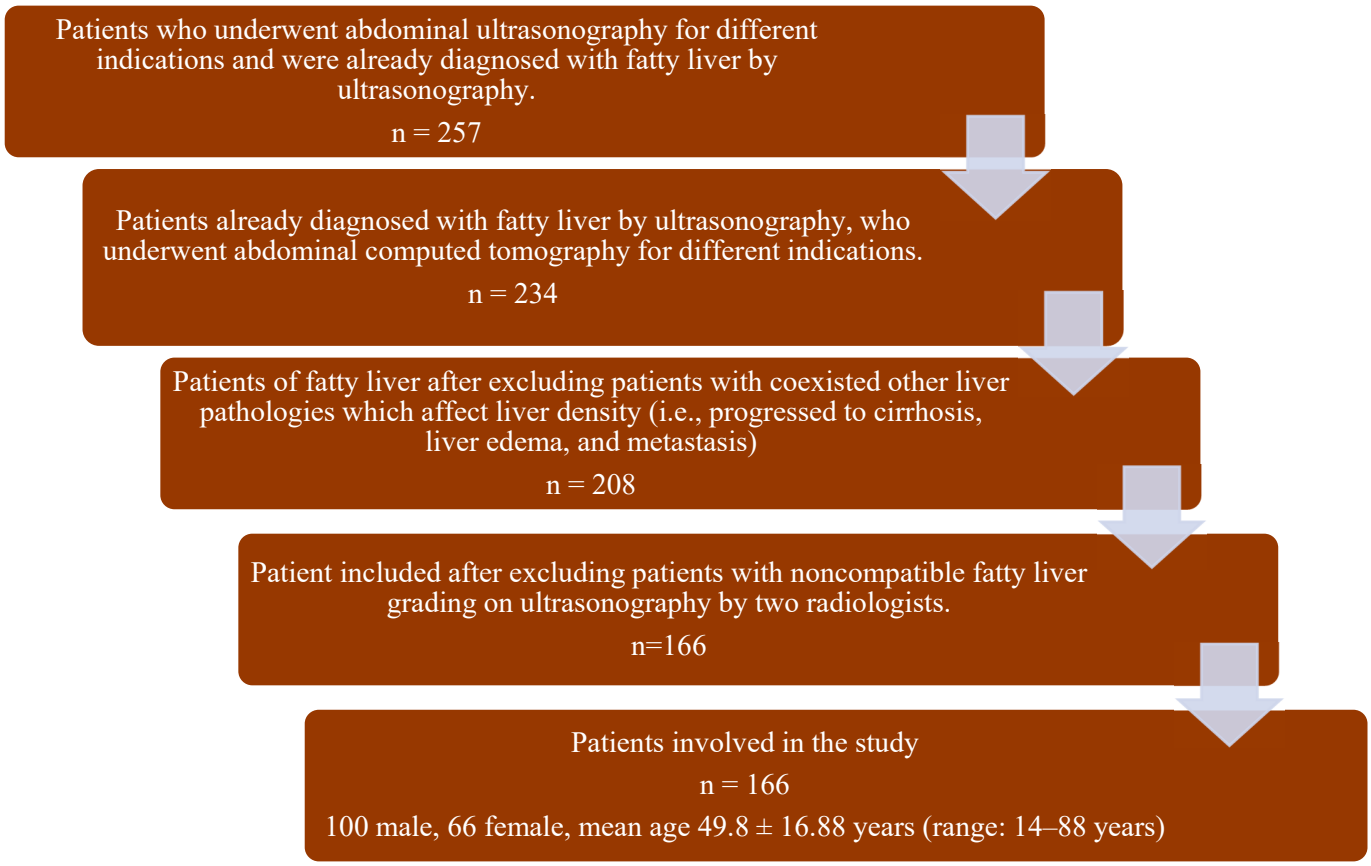


Figure 1. Flowchart of the patient population and study design.

2.4. Ultrasound Image Assessment

Liver ultrasound images stored in the picture archiving and communication system (PACS) were used in this study. High-resolution ultrasonography images of the whole liver with no artifacts were used to grade the fatty liver. Partially imaged liver and unclear images were excluded. Two experienced radiologists independently assessed each ultrasound image. Each radiologist assessed the presence of MASLD (Figure 2) and graded it for each patient. We selected patients diagnosed with grade 0 or grade 1 when the two radiologists agreed on the diagnosis and grading (Figure 3). Cases diagnosed as grade 2 and grade 3 were checked by a third radiologist. We selected the patients diagnosed as grade 2 or grade 3 by at least two of the three radiologists. All patients who met the inclusion criteria were enrolled in this study.

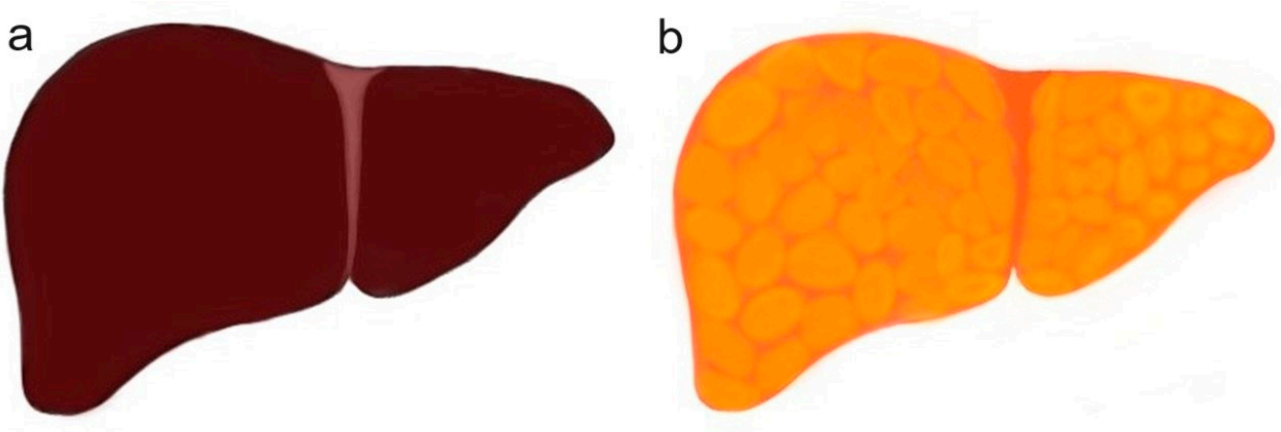


Figure 2. Diagram of the liver: (**a**) normal liver; (**b**) fatty liver disease with fatty infiltration inside the liver cells changing the liver density.

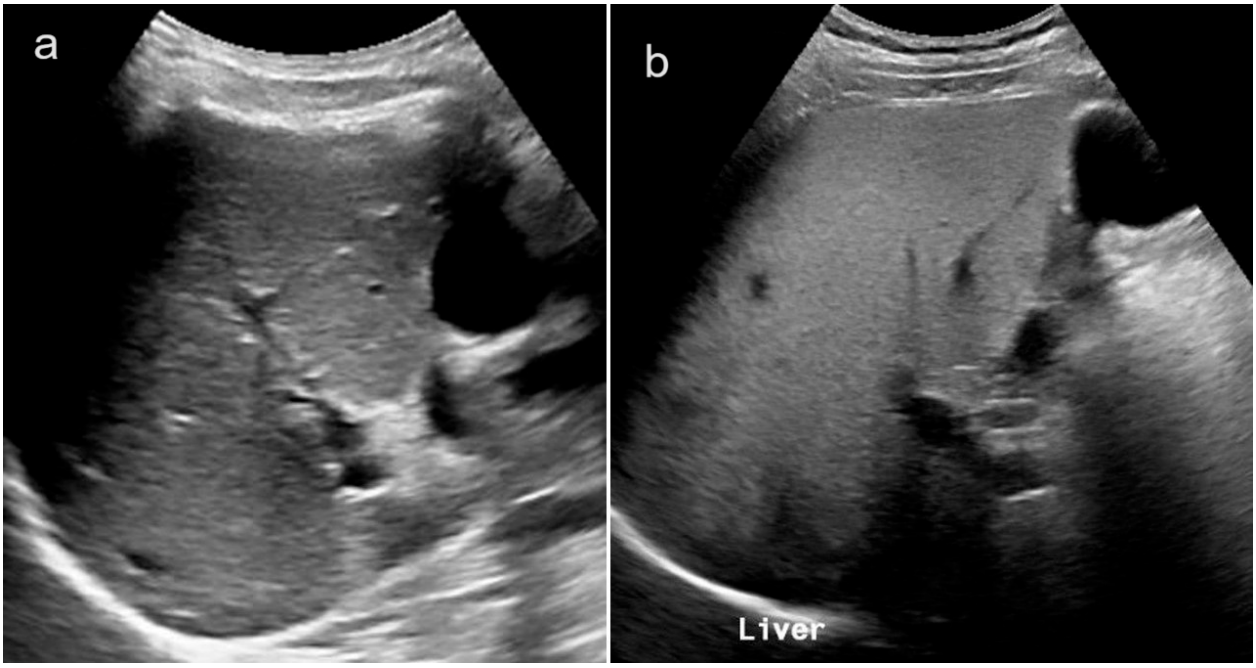


Figure 3. Ultrasonography images from two different patients: (**a**) a normal liver (grade 0) with obvious walls of the portal veins and the diaphragm; (**b**) a fatty liver with increased liver brightness and blurring walls of the portal veins.

2.5. Liver Fat Measurements on CT

Liver NCCT images stored in the PACS system were used in this study. Liver HU attenuation values were measured, taking an area of 100 mm^2 in three regions of interest (ROIs): ROI1 in the right lobe posterior segments, ROI2 in the right lobe anterior segments, and ROI3 in the left lobe. The mean of the three ROIs was calculated for each patient and recorded as the liver HU (Figure 4). Spleen HU attenuation values were measured by taking an area of 100 mm^2 area while taking care to exclude regions of nonuniform parenchymal attenuation to avoid blood vessels. The liver/spleen (L/S) ratio was calculated by dividing the liver HU by the spleen HU, and an L/S ratio < 1 confirmed diagnoses of moderate and severe cases of MASLD [13].

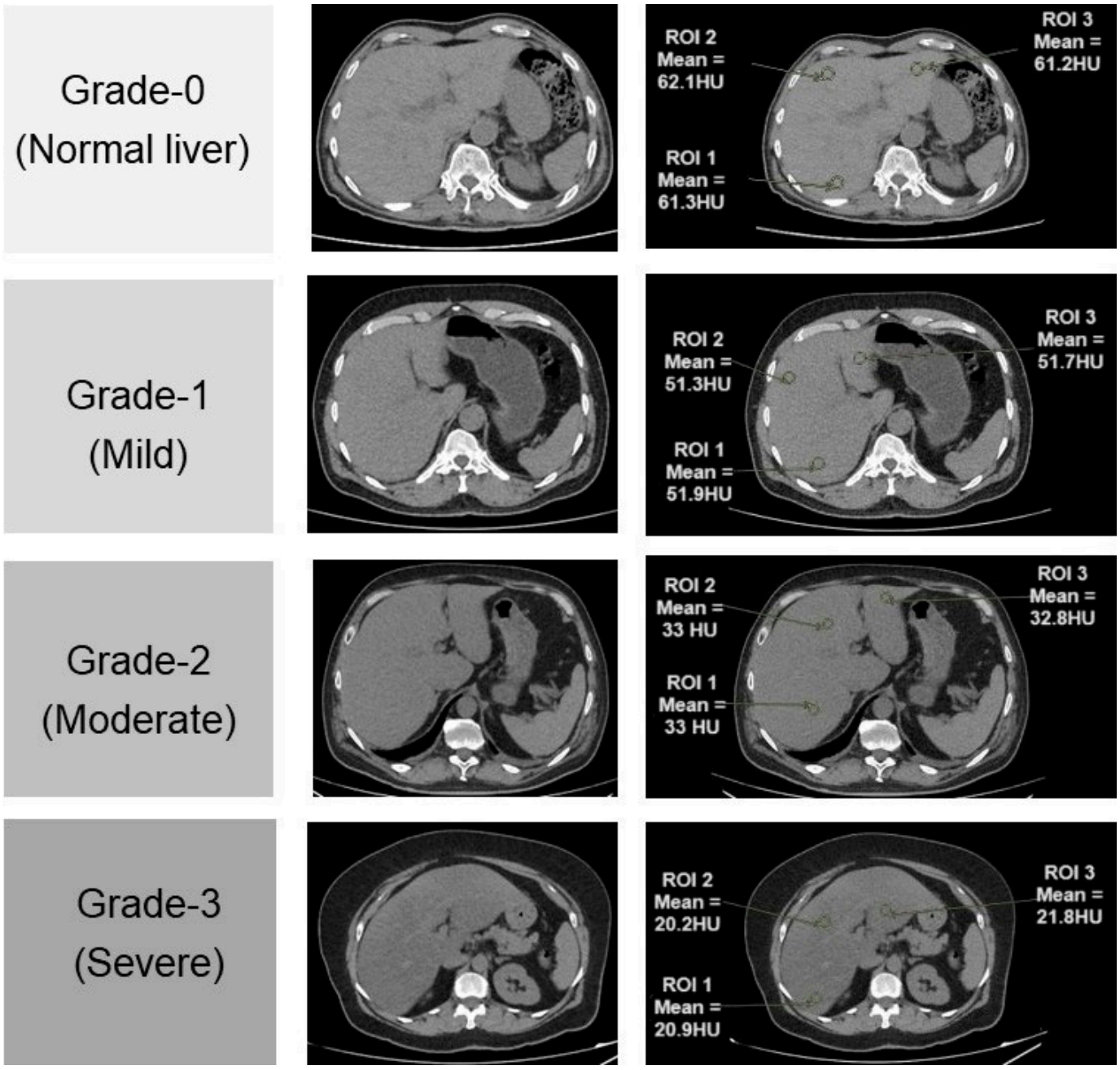


Figure 4. Noncontrast computed tomography images from four different patients. Each image is presented without and with measurements in the three regions of interest, showing (a) a normal liver (grade 0) with an average density of 61.53 HU, (b) a mild (grade 1) fatty liver with an average liver density of 51.63 HU, (c) a moderate (grade 2) fatty liver with an average density of 32.93 HU, and (d) a severe (grade 3) fatty liver with an average liver density of 20.96 HU.

2.6. Statistical Analysis

The collected data were analyzed using the Statistical Package for Social Sciences (SPSS), version 25 (IBM, Armonk, NY, USA). This study reported the liver density (HU) in the different grades of MASLD in patients. Also, we compared the liver density in sex among the patients. Categorical variables were expressed as frequencies and percentages, whereas continuous variables were presented as means with standard deviations. Analysis of variance (ANOVA) test and post hoc analysis of the liver density were used to show

the variation in the distribution of the mean liver density (HU) in the different grades of MASLD, with *p*-values considered significant when less than 0.05.

3. Results

Demographic Data

This study included 166 patients with an average age of 49.8 ± 16.88 years (range: 14–88). Of these, 60.2% (n = 100) were male, and 39.8% (n = 66) were female. The most commonly affected age group was middle-aged adults (n = 73, 43.98%), followed by young adults (n = 44, 26.5%) and old adults (n = 42, 25.3%). The patients' livers were categorized as follows: grade 0 (n = 79, 47.6%), followed by grade 2 (n = 48, 28.9%), grade 1 (n = 25, 15.1%), and grade 3 (n = 14, 8.4%) (Table 1).

Table 1. Sociodemographic data of the patients involved in the study.

Variable	Categories	Number	Percent
Sex	Male	100	60.2%
	Female	66	39.8%
	Total	166	100.0%
Age groups	Young (Less than 20 years)	7	4.2%
	Young adults (From 20 to 40 years)	44	26.5%
	Middle-aged adults (From 41 to 60 years)	73	44%
	Old adults (More than 60 years)	42	25.3%
	Total	166	100%
Grades of MASLD	Grade 0 (Normal liver)	79	47.6%
	Grade 1 (Mild)	25	15.1%
	Grade 2 (Moderate)	48	28.9%
	Grade 3 (Severe)	14	8.4%
	Total	166	100%

The mean measured liver density was 57.75 HU ± 6.18 (range: 48.9–78.2), 51.1 HU ± 4.7 (range: 41.4–59.7), 39.3 ± 6.4 (range: 21.4–48.9), and 22.87 ± 7.5 (range: 12–36.4) in grade 0, grade 1, grade 2, and grade 3 patients, respectively.

An ANOVA test showed significant variance in the distribution of mean liver density (HU) in the different NAFLD grades ($p < 0.001$) (Table 2).

Table 2. Compare the means of the liver density of the patients in different grades of metabolic dysfunction-associated steatotic liver disease (MASLD).

Grading	No. (%)	Minimum	Maximum	Mean	Std. Deviation	Std. Error of Mean	*p*-Value
Grade 0	79 (47.6%)	48.90	78.20	57.7456	6.17708	0.69498	$p < 0.001$
Grade 1	25 (15.1%)	41.40	59.70	51.0560	4.70311	0.94062	
Grade 2	48 (28.9%)	21.40	48.90	39.3104	6.43882	0.92936	
Grade 3	14 (8.4%)	12.00	36.40	22.8714	7.53499	2.01381	
Total	166 (100%)	12.00	78.20	48.4663	12.63925	0.98100	

A post hoc analysis of liver density showed statistically significant differences between the grade 0, grade 1, grade 2, and grade 3 MASLD patients ($p < 0.001$) (Table 3).

Figure 5 shows that liver density decreased significantly with an increasing fatty liver grade.

Table 3. Post hoc multiple comparisons of liver density between different groups of the involved patients.

Dependent Variable: Liver Density (HU)						
Tukey HSD						
(I) Grading	(J) Grading	Mean Difference (I–J)	Std. Error	*p*-Value	95% Confidence Interval	
					Lower Bound	Upper Bound
Grade 0	Grade 1	6.68957 *	1.41890	0.000	3.0063	10.3729
	Grade 2	18.43515 *	1.13158	0.000	15.4977	21.3726
	Grade 3	34.87414 *	1.79300	0.000	30.2197	39.5286
Grade 1	Grade 0	−6.68957- *	1.41890	0.000	−10.3729-	−3.0063-
	Grade 2	11.74558 *	1.52506	0.000	7.7867	15.7045
	Grade 3	28.18457 *	2.06403	0.000	22.8266	33.5426
Grade 2	Grade 0	−18.43515- *	1.13158	0.000	−21.3726-	−15.4977-
	Grade 1	−11.74558- *	1.52506	0.000	−15.7045-	−7.7867-
	Grade 3	16.43899 *	1.87814	0.000	11.5635	21.3145
Grade 3	Grade 0	−34.87414- *	1.79300	0.000	−39.5286-	−30.2197-
	Grade 1	−28.18457- *	2.06403	0.000	−33.5426-	−22.8266-
	Grade 2	−16.43899- *	1.87814	0.000	−21.3145-	−11.5635-

*. The mean difference is significant at the 0.05 level.

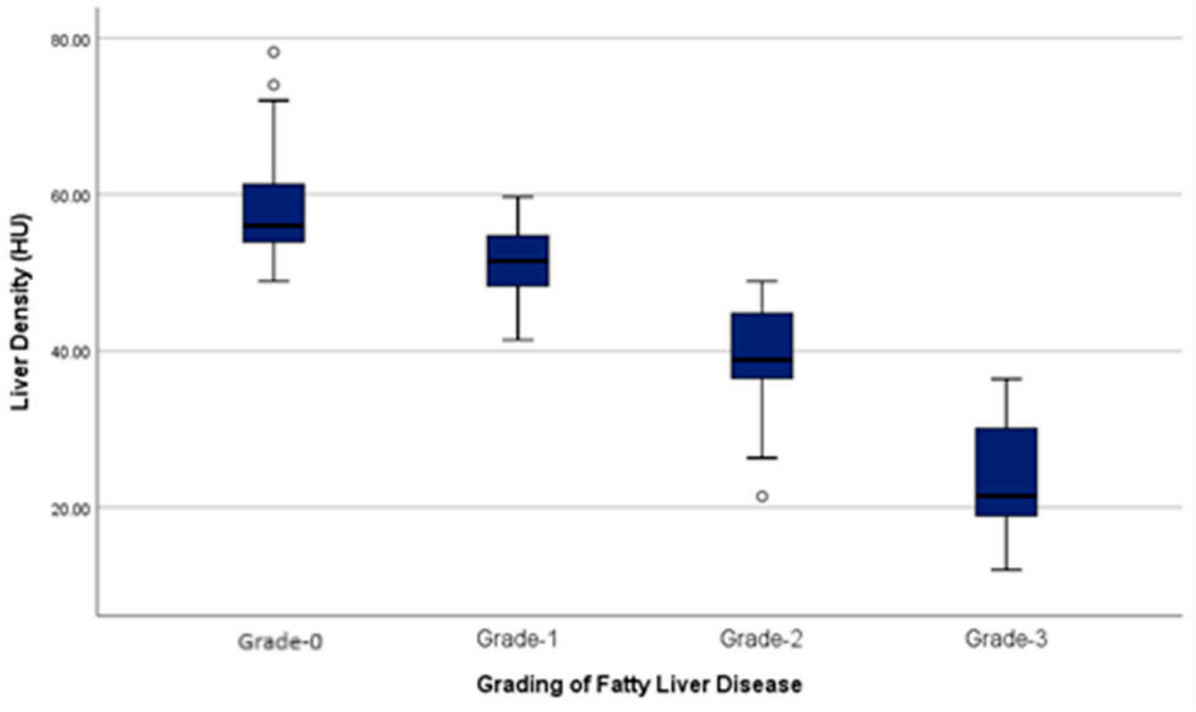


Figure 5. Boxplots showing density distribution in different grades of metabolic dysfunction-associated steatotic liver disease.

In a comparison of the females and males with different grades, we found a slight decrease in liver density in the females compared to the males in grades 2 and 3 (Figure 6).

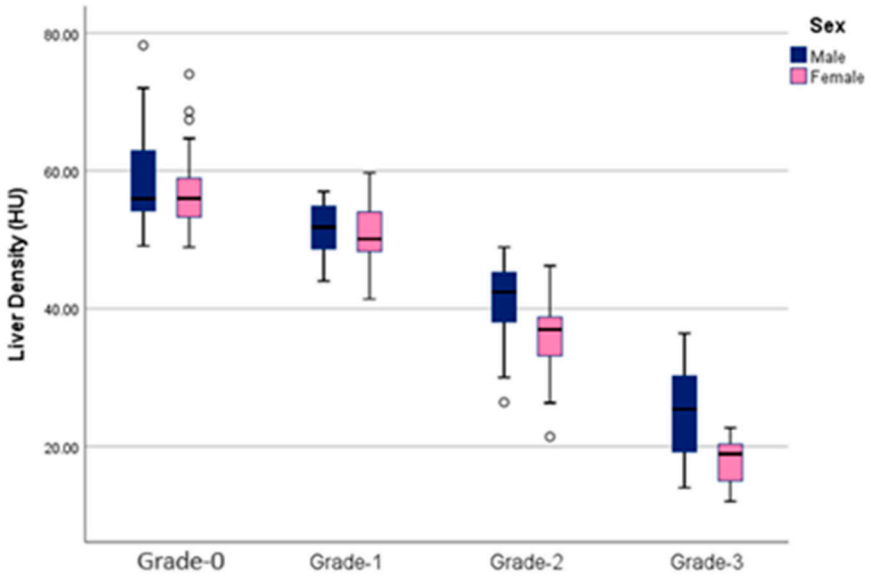


Figure 6. Boxplots showing the difference between males and females in density distribution in different metabolic dysfunction-associated steatotic liver disease grades.

4. Discussion

Optimal diagnosis and grading of MASLD are essential to predict long-term outcomes, prevent progression, and reduce the burden on health services. The focus of the current study was to minimize subjective variation and optimize the accuracy of MASLD grading. This study was designed to create a new numeric, calculable, and objective method for grading MASLD. We measured liver density using NCCT and assessed MASLD grades using ultrasonography, and the liver density was compared with the MASLD grades.

In this study, the most commonly affected age group was middle-aged adults (41–60 years), followed by young adults (21–40 years) and the elderly (>60 years). In Saudi Arabia, the average age of overweight and obese patients is 40.9 ± 3.8 years [14]. MASLD is strongly associated with increased obesity, which explains the predominance of MASLD in middle-aged adults [15]. MASLD affects 50–90% of obese patients and is reported in 65% of patients with grade I and II obesity and in 85% of patients with grade III obesity [16]. In the United States, data from population surveys show that the prevalence of obesity increases progressively from 20 to 60 years old [17]. MASLD incidence is 50–70% in type 2 diabetes mellitus patients [18]. A previous survey-based study reported that the prevalence of diabetes and prediabetes increased with increasing age, from 11.1–40.3% among people aged 40–49 years to 23.9–47.6% among people aged from 60 to 69 years [19].

Brunt et al. proposed grading fatty liver histologically as follows: grade 0 means about 5% of the hepatocytes contain intracellular lipid vacuoles, grade 1 means 5–33% of the hepatocytes contain intracellular lipid vacuoles, grade 2 means 34–66% of the hepatocytes contain intracellular lipid vacuoles, and grade 3 means >66% of the hepatocytes contain intracellular lipid vacuoles [20]. NCCT is an effective modality for diagnosing fatty liver, with a threshold of around 45–50 HU indicating moderate or severe fatty liver, which corresponds to ≥30% lipid content in histologic scoring [21,22]. The X-ray absorption of fat is less than that of normal liver tissue [9,23]. The presence of fat (triglycerides) in liver cells (hepatocytes) leads to decreased attenuation of the liver cells, with an inverse correlation between the measured HU and the histological degrees of fatty liver [20,24,25]. The decrease in tissue attenuation in fat-containing liver cells can be used to diagnose and grade fatty liver using NCCT.

In NCCT, the mean density of the normal liver (grade 0) is approximately 64 HU, whereas in a moderately fatty liver, it is 42 HU [20]. A threshold of 48 HU has been reported as 100% specific for moderate to severe fatty liver with no false positives [20,22,26]. The

current study results showed that the average density of the liver in grade 1 MASLD patients was 51.10 HU ± 4.70 (range: 41.4–59.7), the mean density of the liver in grade 2 MASLD patients was 39.3 ± 6.4 (range: 21.4–48.9), and the mean density of the liver in grade 3 MASLD patients was 22.87 ± 7.5 (range: 12–36.4). These values are comparable with the values reported by Pamilo et al., who reported 52 HU (range: 39–60 HU), 27 HU (range: 4–46 HU), and 10 HU (range: −6 to 19) for grades 1, 2, and 3, respectively [27]. The variations in our results in grades 2 and 3 can be explained by the small sample size. The heterogeneity of liver HU in different grades of hepatic steatosis can be implemented in clinical practice as a new method for grading MASLD. In the current study, NCCT determined that liver density of more than 48.9 HU is specific for grade 1 or grade 0, and liver density below 48.9 HU is a threshold for grade 2. The determined upper limit of grade 2 and 3 is consistent with the results of Chung et al., who reported that liver density less than 48 HU and attenuation difference between liver and spleen (CTL-S) of −1 were threshold for grade 2 to grade 3 hepatic steatoses with 100% specificity [28]. However, another study reported that a CTL-S of −9 was the threshold for grade 2 to grade 3 hepatic steatoses with 100% specificity [28,29]. Unfortunately, we did not find a previous study that determined the threshold between grade 2 and grade 3 to compare with the current study.

In the current study, the largest value in the grade 2 MASLD cases was 48.9, and the largest value of grade 3 cases was 36.4 HU, which compares well with the threshold reported in the previously mentioned studies. Our results determined 48.9–78.2 HU as the range for a normal liver (grade 0), 41.4–59.7 HU as the range for grade 1 fatty liver, 21.4–48.9 HU as the range for grade 2 fatty liver, and 12–36.4 HU as the range for grade 3 fatty liver. Measurements between 36.4 and 41.4 HU were specific to grade 2 fatty livers, which overlapped significantly with grade 1 (41.4–48.9 HU) fatty liver and overlapped with grade 3 fatty liver (21.4–36.4 HU). However, grade 1 fatty liver showed a significant overlap with grade 0 (normal liver) at 48.9–59.7 HU. A previous study reported that the low accuracy of NCCT in detecting grade 1 fatty liver suggests that CT is not suitable for the evaluation of MASLD patients, who frequently present with grade 1 fatty liver [26]. In line with that study, our results showed that the mean density of the normal liver was 57.75 HU ± 6.18 (range: 48.9–78.2), and the mean density of the liver in grade 1 MASLD patients was 51.1 HU ± 4.7 (range: 41.4–59.7), which reflects a significant overlap between the normal liver (grade 0) and grade 1 NAFLD patients. In contrast, a previous study reported that HU values on CT are feasible for risk stratification of grade 1 fatty liver [30]. Further studies to assess the role of CT density in the diagnosis and risk stratification of grade 1 fatty liver are recommended.

Limitations: This study had several limitations. It was a single-center study with a small sample size (n = 166). In addition, histological confirmation of the liver fat was not performed. Grading of liver steatosis was performed using ultrasonography, which is a good method for assessment of liver steatosis; however, it is subjective and non-digital. We have overcome this problem by independently assessing each patient with two experienced radiologists and selecting the patients when the two radiologists agree on the grading.

Future direction: A prospective study with a large sample size and more than two observers to grade fatty liver using ultrasonography and more than one observer to read the liver density on NCCT images for each patient with available histological confirmation of the liver fat is recommended to create a more accurate scale for grading of MASLD.

5. Conclusions

After an ultrasonography diagnosis of MASLD, NCCT offers an objective, numerical, calculable, and non-invasive method for MASLD grading that is available for radiologists, radiologic technologists, and interested physicians away from experience dependence. In this study, NCCT determined that grade 2 MASLD had a specific area of 36.4–41.4 HU, with a significant overlap with grade 1 (41.4–48.9 HU) and an overlap with grade 3 (21.4–36.4 HU). However, grade 1 showed a significant overlap with the normal liver (48.9–59.7 HU). The

liver density of 48.9 HU was the cut-off separating grade 0/grade 1 and the significantly high grades of steatosis.

Author Contributions: S.A.A. (Sultan Abdulwadoud Alshoabi): study concept, supervision, formal analysis, and writing of the article; R.M.A., R.B.A., S.A.A. (Shahad Abdullah Alahmadi) and M.A.: methodology and data curation; S.F.F. and D.A.: investigation and validation; A.A.Q. and F.H.A.: writing—review and editing; R.M.A. and A.K.A.: resources and writing—review and editing. All authors have read and agreed to the final version of the manuscript.

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Informed Consent Statement: Patient consents were waived by the IRB due to the retrospective nature of the study.

Data Availability Statement: Data are available from the corresponding author upon a reasonable request.

Conflicts of Interest: The authors have declared that no competing interests exist.

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