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ORIGINAL ARTICLE

Comparison of hepatic steatosis index as noninvasive diagnostic tool and liver ultrasound for non-alcoholic steatosis in the adult population

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ABSTRACT

Aim: This study aimed to evaluate hepatic steatosis index (HSI) as a non-invasive tool in diagnosing and predicting nonalcoholic fatty liver disease (NAFLD) and to compare it with abdominal ultrasound as the gold standard tool.
Background: NAFLD is a general term attributed to the deposition of adipose tissue in the liver leading to hepatitis, fibrosis, cirrhosis, and also hepatocellular carcinoma (HCC). Rapid and valid screening can remarkably prevent the progression of this disease.
Methods: A total of 464 people were included in the present study based on inclusion criteria. Patients were evaluated for body mass index (BMI), AST, ALT, and ALP indices. The liver echogenicity of patients was evaluated by abdominal ultrasound technique.
Results: The results showed that out of 464 people included in the study, 32.33% represented fatty liver. It was found that 79.1% of patients were female. There was no significant difference between the two groups in terms of age. Furthermore, it was found that ALT, AST, and ALP levels were significantly increased in the two groups of patients compared to the control group. It was determined that out of 150 patients, 75.3% were grade I and 24.7% were grade II NAFLD cases; no grade III cases were observed. The mean HSI for the NAFLD- group was 35.51±5.72 and for the NAFLD+ group was 42.84±5.70, a significant difference. The receiver operating characteristic (ROC) curve also showed that the area under the curve (AUC) of HSI was 0.833 (95% CI, 0.796-0.870) for detecting NAFLD patients. At the cutoff point of > 36.0, the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were 88.7% (95% CI, 82.5–92.5), 63.4% (95% CI, 57.9–68.5), 92.1%, and 53.6%, respectively. Pearson correlation showed a direct and significant correlation between ultrasound data and HSI values.
Conclusion: Overall, the present study results showed that HSI as a non-invasive and non-imaging tool can diagnose NAFLD.

Keywords: Non-alcoholic fatty liver disease, Steatohepatitis, Fatty liver.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a general term for many liver diseases that affect people with or without alcohol consumption. As the name implies, the main feature of NAFLD is the excess lipid storage in liver cells (1-3). NAFLD consists of two main diseases including the non-alcoholic fatty liver (NAFL) attributed to the steatosis of the liver, involving greater than 5% of parenchyma, with no evidence of hepatocyte injury and non-alcoholic steatohepatitis (NASH) histologic terms, that is a necroinflammatory process whereby the liver cells become injured in a background of steatosis (4-6). Pathologically, alcoholic and non-alcoholic fatty liver disease are very similar; the distinctive parameter is the presence of macrovascular steatosis in individuals with NAFLD (7).

Steatosis is histologically defined by the presence of excess lipid in liver cells. Patients with steatosis are usually asymptomatic but may have mild upper body pain or mild transaminases (8). The most widely used

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tool for diagnosing hepatic steatosis is abdominal ultrasound, which has been approved as a tool for screening NAFLD in the general population. The underlying mechanism of hepatic steatosis diagnosis through ultrasound is based on increased liver echogenicity due to accumulation of intracellular lipid droplets that are more reflective in ultrasound. In severe steatosis, visualizing the underlying structures is difficult due to the weak penetration of sonic radiation in the liver (9-11).

Screening asymptomatic individuals using imaging techniques, such as ultrasound and computed tomography (CT), however, does not appear to be cost-effective for mass screening (12). Therefore, a simple, non-invasive test is needed to identify patients at risk for NAFLD and NASH and to aid in establishing an appropriate screening program (3). The hepatic steatosis index (HSI) is a screening tool aimed at optimizing NAFLD and NASH management. The HSI index has been used as a test for NAFLD screening in epidemiological studies and is helpful in the diagnosis of NAFLD in adults. This indicator can help physicians identify liver ultrasound candidates and those who need lifestyle and diet modification (13-15).

Recent researchers' attention on HSI for diagnosing fatty liver disease reflects this procedure's importance as a non-invasive method. Given the above background and the importance of HSI, the current study aimed to compare HSI with ultrasound in diagnosing and screening NFLD in an adult population of Tehran in Bumhan Health Center

Patients and Methods

Study population

The present cross-sectional study was performed on 464 participating subjects of the fatty liver project who were referred to Bumhan Health Center. The subjects were selected based on the following inclusion criteria: age over 18 years, no pregnancy or breastfeeding, no history of alcohol consumption or alcohol consumption of less than 10 mg per day in women and less than 20 mg per day in men, and no liver affected with disease such as hepatitis C, B, liver cancer, biliary disease, autoimmune diseases, cancer, or hereditary disorders affecting the condition of the liver (iron, copper, etc.).

Before beginning the study, its objectives and methods were explained to the subjects, and then written informed consent was obtained from the volunteers. This study is registered under ethics code IR.SBMU.MSP.REC.1399.785 in the National Committee for Ethics in Biomedical Research.

Anthropometric and biochemical measurements

Bodyweight and height were precisely measured in bare-footed participants to calculate body mass index (BMI) as (kg)/(m2), and waist circumference was measured midway between the lower costal margin and the iliac crest. These indices were measured by health professionals in health centers using calibrated tolls (meters with millimeter accuracy and permeability with 0.01 gram accuracy).

A total of 7 ml of venous blood has taken in the fasting state and used for laboratory assessment after serum separation All blood tests including liver enzymes and fasting blood sugar (FBS) were measured in a specialized diagnostic laboratory (Gholhak, Tehran, Iran) with a standard method. Moreover, Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) levels were obtained according to routine laboratory measurements performed on blood from all fasting subjects.

HSI and ultrasonic evaluation

The following equation was used to obtain the HSI value:

HSI = 8 × (ALT / AST ratio) + BMI +2, if female; +2, if diabetes mellitus.

All individuals submitted to liver ultrasound (GE Voluson 730 EXpert, GE Healthcare) to diagnose NAFLD based on the percentage of liver fat. Ultrasound operation and evaluation was executed by an ultrasound radiologist who has previously experienced at least 1,000 liver ultrasounds. Fatty liver changes on ultrasound usually appear when at least 20% of the hepatocytes are occupied by fat. After identifying the patients with NAFLD, ultrasound grading of fatty liver changes was performed as follows:

Grade 1: Increased liver echogenicity without fading around the portal vein and diaphragm

Grade 2: Increased liver echogenicity with fading of the portal vein but without fading of the diaphragm
Grade 3: Increased echogenicity of the liver with the disappearance of the portal vein and diaphragm.

Statistical analysis

Data was analyzed using SPSS software version 21. To examine quantitative variables, mean±standard was reported, and the Kolmogorov-Smirnov test was used to determine the normality of data. One-way analysis of variance and Mann-Whitney tests were used for normal data analysis and non-normal distribution data, respectively. The qualitative variables were analyzed as percentages and compared with the chi-square test. Receiver operating characteristic (ROC) curve analyses with the area under the curve (AUC) (95% confidence interval [CI]) was used to determine HSI in NAFLD detection.

Results

Demography information

Of 464 investigated subjects, 150 was diagnosed with NAFLD according to the mentioned grading and the others have been allocated to the control group. The demographic information of patients is shown in Table 1. According to the results, 79.1% of patients were female, and the mean age of all patients was 44.83±11.26. Patients were evaluated for waist circumference and BMI, and their values were 94.99±11.38 and 27.39±4.58, respectively. Due to the normal distribution of data, the Mann-Whitney test was used to compare indexes between NAFLD+ and NAFLD- patients; a significant difference was observed in BMI indices. Furthermore, out of all investigated patients, 50 were positive for diabetes with no differences between groups.

FBS was measured as 95.60±56.10 and 83.50±31.11 for NAFLD+ and NAFLD- respectively (p-value 0.001). ALP level represented a significant increase in NAFLD+ compared to NAFLD- subjects (p-value < 0.003). Moreover, a Pearson correlation and linear regression tests were employed to determine whether there was a correlation between HSI and ALP level. The results revealed no correlation (Pearson Correlation: 035 and p-value 0.447) and no linear relation ($R2= 001$ and p-value 0.439) between HSI and ALP.

In the next step the ALP and HIS have been compared according to the NAFLD grading and the results are shown in Table 2. It has been shown that ALP (p-value 0.036) and HSI (p-value 0.0001) have been significantly higher in Grade II patients compare to Grade I ones.

Liver echogenicity and HSI validation

As mentioned, all subjects were evaluated by

Table 1. Demographic information of investigated subjects.

		Number	Min	Max	Mean ±SD	P-value*
Age (year)	NAFLD+	150	23	75	45.4±10.9	0.184
	NAFLD-	314	15	80	44.56±11.43	
BMI (kg/m2)	NAFLD+	150	22	44	30.95±4.12	0.0001
	NAFLD-	314	18	42	25.69±3.73	
Waist circumference (cm)	NAFLD+	150	50	128	101.27±10.45	0.0001
	NAFLD-	314	56	117	91.98±10.54	
ALT (U/L)	NAFLD+	150	6	80	26.72±13.36	0.0001
	NAFLD-	314	6	86	18.44±9.91	
AST (U/L)	NAFLD+	150	10	64	21.64±8.28	0.0001
	NAFLD-	314	10	84	18.79±6.23	
ALP (U/L)	NAFLD+	150	59	620	198.39±73.48	0.003
	NAFLD-	314	56	492	181.17±68.75	
FBS	NAFLD+	150	60	422	95.60±56.10	0.001
	NAFLD-	314	60	290	83.50±31.11	

* by Mann Whitney U test

Table 2. ALP and HSI according to NAFLD grading.

		Min	Max	Mean ±SD	P-value*
ALP	Grade I	65	404	191.38±62.44	0.036
	Grade II	59	620	216.76±99.39	
HSI	Grade I	31.40	59	41.88±5.35	0.0001
	Grade II	34.31	55.23	45.87±5.89	

* by Mann Whitney U test

ultrasound technique and their conditions graded. Among 150 patients diagnosed with NAFLD, 75.3% and 24.7% were grades 1 and 2, respectively. The mean HSI was found to be 42.84±5.70 and 35.51±5.72 for NAFLD+ and NAFLD- subjects, respectively, representing a significant difference (p-value < 0.0001). Figure 1 shows an ultrasound image of a grade-II NAFLD patient with an HSI of 46, which represents appropriate compliance between his score and ultrasound outcome.

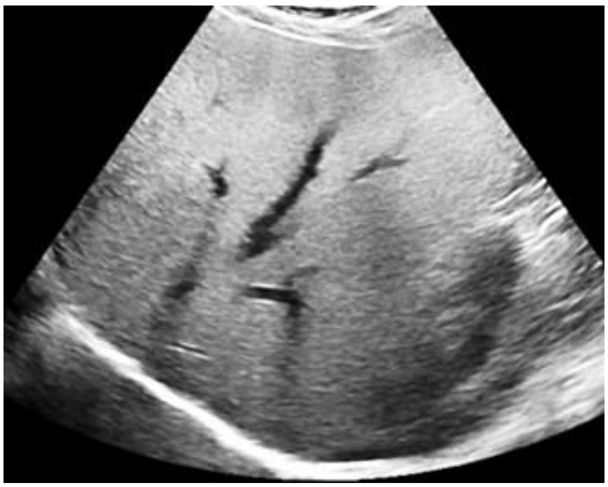

Figure 1. Ultrasound image of a nondiabetic, grade-II NASH+, 48-year-old male patient with an HSI score of 46.

The validation of HSI was evaluated for the diagnosis of NAFLD in all subjects through receiver operating characteristic (ROC). The obtained data revealed the area under the curve (AUC) of HSI to be 0.833 (95% CI, 0.796-0.870) for detecting NAFLD patients (Figure 2). At the cutoff point of > 36.0, the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were 88.7% (95% CI, 82.5-92.5), 63.4% (95% CI, 57.9-68.5), 92.1%, and 53.6%, respectively.

The correlation of ultrasound findings with HSI values was determined using the Pearson correlation test, and a significant positive correlation was revealed (Pearson Correlation: 0.524 and p-value 0.0001).

Discussion

NAFLD is attributed to a condition in which fat particles are synthesized in the liver. Non-alcoholic fatty liver (NAFL) and NASH are considered the main subtypes of NAFLD. Patients with NASH present with inflammation and liver damage in addition to the presence of fat in the liver (16, 17). It has also been reported that NASH may progress to advanced liver failure, such as cirrhosis (18). The diagnostic methods

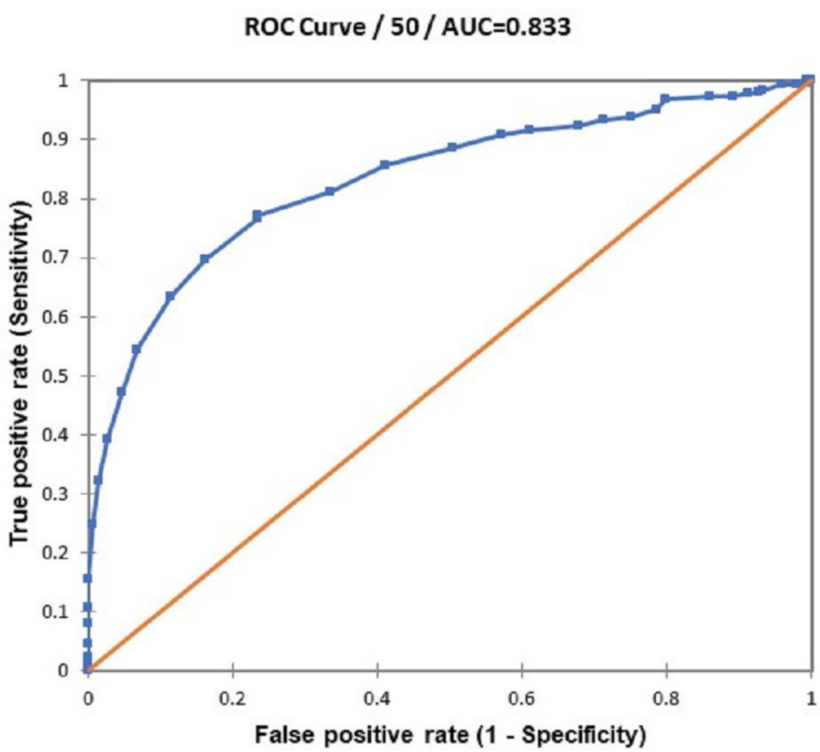

Figure 2. Receiver-operating characteristic (ROC) curve of HSI for detecting NAFLD. The AUC was 0.833. At a cutoff value of 36.0, sensitivity and specificity were 88.7% and 63.4%, respectively.

used for this disease, especially abdominal ultrasound, pose problems and challenges, such as high cost, specialization, and lack of easy access, making finding the disease to prevent its progression challenging (13). Therefore, considering the importance of this disease, it seems necessary to develop valid screening techniques that physicians can efficiently perform without advanced facilities (19). HSI was recently studied as an accurate indicator of NASH, and thus, the present study evaluated the use of this indicator for NAFLD screening (20). It was found that with a cutoff of > 36 with a sensitivity and specificity of 88.7% and 63.40%, respectively, can be used as an effective tool in the clinic. In line with the current study, Murayama et al. recently conducted a study in Japan to investigate several non-invasive non-imaging imaging methods for predicting non-alcoholic fatty liver disease. One of the methods they studied was HSI which, with an AUC of 0.874, had 88.5% sensitivity and 98.5% specificity (21). Although slight differences in the reported values between our study and this group were observed, overall, the results were well matched. The differences between these studies can be attributed to differences in the patient populations, which can affect various parameters such as BMI, AST, and ALT.

Ultrasound is used as the gold standard for diagnosing fatty liver, but it has some limitations, including poor sensitivity and high cost. With an accuracy rate of (67–94%), ultrasound has been declared the standard to compare with HSI (12, 22). According to the current results, HSI significantly correlated with ultrasound output (fatty liver grade). By increasing liver echogenicity in ultrasound, which resembles the degree of hepatic steatosis, HSI represents an elevated value. In line with the current results, Lee et al. found a direct relationship between ultrasound results and the amount of HSI in NAFLD patients. They suggested that ultrasound works for NASH patients as well, which was demonstrated in the current study (13).

Conclusion

In conclusion, the present results showed that HSI can be used as an effective indicator in predicting NAFLD disease in the clinic. Furthermore, no specific relationship between ALP and HSI was identified, although HSI had a significant correlation with ultrasound findings.

This study showed the diagnostic power and screening of HSI index in NAFLD patients with high sensitivity. In general, in comparison with previous studies, it can be suggested that due to NPV, PPV and high sensitivity, this index can be used in the clinic. However, the decision is up to the formal instructions.

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Conflict of interests

The authors declare that they have no conflict of interest.

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