ORIGINAL RESEARCH

Bagcilar Med Bull 2024;9(1):15-20
DOI: 10.4274/BMB.galenos.2024.2023-08-072

Comparison of Non-alcoholic Fatty Liver Disease Indexes and Hepatic Ultrasonography as Predictors of Hepatosteatosis in Patients with Obesity

Obezitesi Olan Hastalarda Hepatosteatoz Belirteci Olarak Alkolik Olmayan Yağlı Karaciğer Hastalığı İndeksleri ve Hepatik Ultrasonografinin Karşılaştırılması

Feray Akbaş, Işıl İşel, Hanife Usta Atmaca, Mehmet Emin Pişkinpaşa

University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Internal Medicine, İstanbul, Turkey

Abstract

Objective: Obesity affects 60% of adults in Europe. Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent obesity consequences that increase cardiovascular and hepatic morbidity and mortality. Here; it was aimed to compare NAFLD indexes with hepatic ultrasonography (USG) and determine whether these indexes could be used as predictors of hepatosteatosis in patients with obesity.

Method: Eighty randomly chosen patients from our obesity center were included in the study. Patients ≥18 years-old, having files with all research parameters were included and having acute/chronic hepatic disease/malignancy, getting any kind of treatment for hepatosteatosis, having alcohol consumption above recommended amounts were excluded. All patients' age, gender, weight, height, body mass index (BMI), waist circumference, gasting blood glucose, high-density lipoprotein, triglyceride, low-density lipoprotein, insulin, alanine transaminase (ALT), aspartate aminotransferase, gamma-glutamyl transferase, hepatic USG results, accompanying diseases and medicines were recorded. Non-alcoholic fatty liver disease indexes: Hepatosteatosis index (HSI), visceral adiposity index (VAI), fatty liver index (FLI) and lipid accumulation product index (LAP) were calculated. Results were evaluated using SPSS program.

Results: Sixty-five female and 15 male, totally 80 people with obesity were included in the study. Mean age was 44.29±12.82 years in women and 38.27±12.88 years in men. In general population HS rates were: No hepatosteatosis 10%, first degree 17.05%, second degree: 58.75% and third degree: 13.75%. Weight, WC, ALT, diabetes mellitus, hypertension, being on medication for accompanying diseases and alcohol consumption within recommended rates were higher in HS(+) group when compared

Öz

Amaç: Obezite Avrupa'daki erişkinlerin %60'ını etkilemektedir. Non-alkolik yağlı karaciğer hastalığı (NAYKH) obezitenin en sık sonuçlarından biridir ve kardiyovasküler ve hepatik morbisite ve mortaliteyi artırır. Burda; NAYKH indekslerini hepatik ultrasonografi (USG) ile karşılaştırarak, obezitesi olan hastalarda bu indekslerin hepatosteatoz belirleyicisi olarak kullanılabilirliğinin belirlenmesi amaçlanmıştır.

Yöntem: Obezite merkezimizden random seçilen 80 hasta çalışmaya dahil edildi. ≥18 yaş olup tüm araştırma parametreleri dosyada mevcut olan hastalar çalışmaya alındı, akut/kronik karaciğer hastalığı/maliginitesi olanlar, hepatosteatoz için herhangi bir tedavi alanlar, önerilen dozlar üzerinde alkol kullanımı olanlar çalışmaya alınmadı. Hastaların yaş, cinsiyet, boy, kilo, vücut kitle indeksi (VKİ), bel çevresi, açlık kan şekeri, insülin, yüksek yoğunluklu lipoprotein, trigliserit, düşük yoğunluklu lipoprotein, alanin transaminaz (ALT), aspartat aminotransferaz, gama-glutamil transferaz, hepatik ultrasonografi sonuçları, eşlik eden hastalıkları ve kullandıkları ilaçlar kaydedildi. NAYKH indeksleri: Hepatosteatoz indeksi (HSİ), visseral adipozite indeks (VAİ), yağlı karaciğer indeksi (YKİ) ve lipid birikim ürünü indeksi (LBÜİ) hesaplandı. Sonuçlar SPSS ile değerlendirildi.

Bulgular: Obezitesi olan 65 kadın, 15 erkek, toplam 80 hasta çalışmaya dahil edildi. Kadın hastalarda yaş ortalaması 44,29±12,82 yıl ve erkek hastalarda 38,27±12,88 yıl olarak bulundu. Genel popülasyonda hepatosteatoz oranları şu şekildeydi: HS olmayan %10, birinci derece %17,05, ikinci derece %58,75 ve üçüncü derece %13,75. Kilo, BÇ, ALT, diabetes mellitus, hipertansiyon, ilaç kullanımı ve önerilen limitler dahilinde alkol kullanımı oranları HS(+) grupta HS(-) gruptan yüksekti.

Address for Correspondence: Feray Akbaş, University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Internal Medicine, İstanbul, Turkey
E-mail: atlibatur@yahoo.com **ORCID:** orcid.org/0000-0001-5091-9160 **Received:** 14.08.2023 **Accepted:** 14.02.2024

Cite this article as: Akbaş F, İşel I, Usta Atmaca H, Pişkinpaşa ME. Comparison of NAFLD Indexes and Hepatic Ultrasonography as Predictors of Hepatosteatosis in Patients with Obesity. Bagcilar Med Bull 2024;9(1):15-20

Abstract

to HS(-) group. When HS levels were compared with mean NAFLD index values, there was statistically significant difference for HSI mean group values. There was no statistically significant difference for other NAFLD indexes. There was a positive correlation between BMI and LAP, FLI and HSI. There was no significant correlation between BMI and VAI.

Conclusion: As NAFLD is a strong predictor of cardiometabolic morbidity and mortality, it is important to make a diagnosis before progression in people living with obesity and simple non-invasive screening/diagnostic tools are needed for this purpose. VAI, LAP, FLI, HSI are easily calculated scientific models that are found to be predicting NAFLD. Although we could only partially found this prediction, they could be used sufficiently after national validation studies that determine the cut-off values and help to achieve prevention of NAFLD-related complications with early diagnosis.

Keywords: NAFLD, NAFLD indexes, obesity

Öz

HS düzeyleri ortalama NAYKH indeks değerleriyle karşılaştırıldığında, HSİ ortalama grup değerlerinde istatistiksel olarak anlamlı fark vardı, diğer indekslerde ise fark bulunmadı. VKİ ile LBÜİ, YKİ ve HSİ arasında pozitif korelasyon mevcuttu, VKİ ve VAİ arasında anlamlı korelasyon yoktu.

Sonuç: NAYKH kardiyometabolik morbidite ve mortalitenin güçlü bir belirleyicisi olduğu için, obezitesi olan kişilerde progresyon öncesi tanı koymak önemlidir ve bu amaçla geliştirilmiş basit, non-invaziv tarama/tanı yöntemlerine ihtiyaç vardır. VAİ, LBÜİ, FLİ ve HSİ kolayca hesaplanarak NAYK'sini öngördüğü belirlenmiş olan bilimsel modellerdir. Biz çalışmamızda bu öngörüyü sadece kısmen gösterebilmiş olmamıza rağmen, bu indeksler ulusal validasyon çalışmalarıyla cut-off değerleri belirlenerek etkin bir şekilde kullanılabilirler ve erken tanı sayesinde NAYKH-ilişkili komplikasyonların engellenmesini sağlayabilirler.

Anahtar kelimeler: NAYKH, NAYKH indeksler, obezite

Introduction

Over the last decade, there has been an exponential increase in obesity and overweight prevalence worldwide, practically resulting in a global pandemic. Obesity affects 60% of adults in Europe. Obesogenic lifestyle choices, combined with environmental/hormonal/genetic factors, have resulted in major public health issues. Diabetes, metabolic syndrome, dyslipidemia, fatty liver disease, hypertension, ischemic heart disease, heart failure, stroke, chronic respiratory diseases, obstructive sleep apnea, musculoskeletal disorders, chronic organ failures, mental health problems, and even cancer rates have all increased as obesity complications (1-4).

Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent obesity consequences. NAFLD is characterized as excess fat accumulation in the liver and reflects the presence of steatosis in >5% of hepatocytes on histology. NAFLD is predicted to affect 19-30% of European individuals. NAFLD is strongly linked to insulin resistance, metabolic syndrome, type 2 diabetes mellitus (DM), and dyslipidemia, all of which are common in people living with obesity and increase the risk of cardiovascular morbidity and mortality. NAFLD can also cause hepatic cirrhosis and hepatocellular carcinoma, both of which increase the risk of hepatic disease mortality (4-6).

The diagnosis of NAFLD is made by radiological or histopathological findings after excluding conditions such as viral hepatitis, significant alcohol intake and medicines that can cause fatty changes. Non-invasive measurements include abdominal ultrasonography (USG), elastography, computed tomography and magnetic resonance imaging. Hepatic biopsy is the gold standard for diagnosis, but its invasiveness limits its availability (4-6). Omics-based biomarkers (metabolomics and lipidomics) and non-coding RNA seem to be promising for NAFLD diagnosis, but they still need validation with more detailed studies (7). Recently introduced NAFLD indexes fatty liver index (FLI), visceral adiposity index (VAI), hepatosteatosis index (HSI) lipid accumulation product index (LAP) that are calculated with standard formulations using simple patient data are suggested as practical screening/diagnostic tools for liver fat accumulation (8-11).

In this study, we compared NAFLD indexes with hepatic USG and determined whether these indexes could be used as predictors of hepatosteatosis in patients with obesity.

Materials and Methods

This was a retrospective, single-center, correlational study. Eighty randomly chosen patients from our obesity center according to inclusion/exclusion criteria were included in the study.

Inclusion criteria wereas follows: Being 18 years old and above, having a patient file in an obesity center, having the results of all research parameters and hepatic USG on file, and exclusion criteria wereas follows: Having acute/chronic hepatic disease, receiving any kind of treatment for hepatosteatosis, having malignancy, and alcohol consumption above recommended amounts (above 30 g/day in male and 20 g/day in female).

Because the patients were being followed in an obesity center, they were all prescribed a Mediterranean-style calorie deficit diet tailored to their body mass index

(BMI), gender, and accompanying diseases by a dietitian. They were also recommended to engage in 150 minutes of aerobic exercise per week, mainly involving walking or swimming if possible, and to perform resistance exercises twice a week as instructed by a physiotherapist. Alcohol consumption was present in 6 male patients (7.5%) who reported drinking socially once or twice a year at levels that were not above the recommended limit; thus, they did not need to be excluded.

All patients' age, gender, weight, height, BMI, fasting blood glucose, high-density lipoprotein, triglyceride, low-density lipoprotein, insulin, alanine transaminase (ALT), aspartate aminotransferase, gamma-glutamyl transferase, and hepatic USG results, accompanying diseases, and medicines if present were recorded. Non-alcoholic fatty liver disease indexes: VAI, lipid accumulation product index (LAP), FLI, and hepatosteatosis index (HSI) were calculated according to international standard formulations. Results were evaluated using the SPSS program.

Statistical Analysis

SPSS 23.0 was used for statistical analysis. Descriptive statistics are reported as mean, standard deviation, median, minimum, maximum, frequency, and percentage values. The distribution of variables was tested with the Kolmogorov-Smirnov test. Quantitative independent data analysis was performed using the Mann-Whitney U test and Kruskal-Wallis test. Categorical variable analysis was performed using the chi-square test. Qualitative independent data analysis was performed using the Pearson and Spearman correlation test. Statistical significance was set as $p<0.05$.

Ethics committee approval: Ethics committee approval was obtained for this study from the Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (05.03.2021/2764). All procedures performed in this study were in accordance with the 1964 Helsinki Declaration.

Results

Sixty-five females and 15 males, a total of 80 people with obesity, were included in the study. The mean age was 44±12 years in women and 38±12 years in men. Mean BMI was 40.7 kg/m^2±6.3 and WC 118.1±11.7 cm in women and 41.1±6.3 kg/m^2 and 130.9±9.9 9.9 cm in men.

In the general population, HS rates are: HS(-) 10%, 1st degree 17.05%, 2nd degree: 58.75%, and 3rd degree: 13.75%. Alcohol consumption and being on medication for accompanying diseases rates were higher in HS(+) group than in the HS(-) group. DM, HT, and other accompanying diseasesrates were higher in HS(+) group. Descriptive analyses of other clinical findings for men and women are listed in Table 1.

When HS levels were compared with mean NAFLD index values, there was a statistically significant difference for HSI mean group values ($p<0.05$). There was no statistically significant difference for the other NAFLD indexes (Table 2).

There was no statistically significant difference between HS(+) and HS(-) groups for VAI, LAP, FLI, and HSI mean values ($p>0.05$). Weight, WC, and ALT mean values were higher in HS(+) group than in the HS(-) group ($p<0.05$). There was a positive correlation between BMI and LAP and between FLI and HSI. There was no significant correlation between BMI and VAI (Table 3).

Discussion

NAFLD is one of the most common liver diseases, and its prevalence has been increasing concurrently with the global obesity epidemic (12). It has great clinical importance because of its hepatic and cardiometabolic consequences. Hepatic steatosis can develop into fibrosis, non-alcoholic steatohepatitis, and ultimately, cirrhosis, which can result in hepatocellular cancer. It is also strongly related to insulin resistance, which can cause several metabolic disturbances. NAFLD is found in 30-87% of patients with type 2 DM. Dyslipidemia, hypertension, inflammation, and atherosclerosis are also highly present in NAFLD.

Table 1. Comparison of VAI, LAP, FLI and HSI according to hepatic USG

	Hepatic USG												p
	No HS			1st degree HS			2nd degree HS			3rd degree HS			
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	
VAI	3.2	±3.5	2.0	2.5	±1.1	2.3	3.4	±3.8	2.8	3.1	±1.6	2.7	0.528
LAP	97.9	±93.3	52.0	91.8	±45.1	75.2	127.1	±114.0	101.9	136.5	±62.4	140.7	0.072
FLI	80.7	±21.0	88.0	84.9	±18.9	93.0	93.7	±7.3	97.0	96.2	±5.2	97.0	0.066
HSI	47.2	±8.3	45.2	48.4	±5.6	47.9	53.6	±7.5	53.0	52.4	±6.8	51.6	**0.032**[a]

[a]: One-Way ANOVA, Kruskal-Wallis test, post-hoc LSD test, HS: Hepatosteatosis, SD: Standard deviation, VAI: Visceral adiposity index, FLI: Fatty liver index, LAP: Lipid accumulation product index, HSI: Hepatosteatosis index

Table 2. Comparison of VAI, LBUI, FLU and HSI in HS(+) and HS(-) groups

	Hepatic USG						p
	HS(+)			HS(-)			
	Mean	SD	Median	Mean	SD	Median	
Age (years)	44	±16	45	42	±12	44	0.936
Height (cm)	156.2	±5.0	157.5	161.6	±10.0	160.0	0.205
Weight (kg)	94.1	±18.4	88.0	108.1	±18.0	111.5	**0.040**[a]
BMI (kg/m^2)	38.3	±7.1	35.7	41.0	±6.1	40.7	0.243[a]
WC (cm)	112.0	±13.1	110.0	121.5	±12.0	121.5	**0.039**[a]
Systolic BP (mmHg)	123.7	±9.1	120.0	123.4	±10.5	120.0	0.965
Diastolic BP (mmHg)	76.2	±7.4	80.0	77.6	±6.1	80.0	0.773
FBG (mg/dL)	97.7	±10.9	99.0	113.9	±36.6	104.0	0.163
TG (mg/dL)	145.5	±105.7	104.0	170.9	±122.7	150.0	0.173
HDL (mg/dL)	48.3	±13.8	47.0	46.9	±11.0	45.5	0.742[a]
LDL (mg/dL)	135.5	±23.7	134.5	129.2	±38.1	125.0	0.654[a]
Insulin	12.3	±10.6	6.7	15.0	±9.9	12.9	0.138
ALT (U/L)	16.2	±5.1	16.5	31.1	±23.2	23.0	**0.012**
AST (U/L)	20.0	±5.2	19.5	26.4	±15.5	21.5	0.261
GGT (U/L)	23.6	±7.0	23.0	30.1	±15.8	25.0	0.339
VAI	3.2	±3.5	2.0	3.2	±3.2	2.6	0.312
LAP	97.9	±93.3	52.0	121.6	±97.8	99.4	0.083
FLI	80.7	±21.0	88.0	92.3	±11.1	97.0	0.159
HSI	47.2	±8.3	45.2	52.4	±7.3	52.0	0.064[a]

[a]: Independent sample test, Mann-Whitney U test, SD: Standard deviation, BMI: Body mass index, VAI: Visceral adiposity index, FLI: Fatty liver index, LAP: Lipid accumulation product index, HSI: Hepatosteatosis index, ALT: Alanine transaminase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transferase, TG: Triglyceride, FBG: Fasting blood glucose, HDL: High density lipoprotein

Table 3. Relationship between BMI and VAI, LAP, FLI and HSI

		BMI	VAI	LAP	FLI	HSI
BMI	r	1.000	0.071	0.374**	0.837**	0.917**
	p	-	0.531	**0.001**	**<0.001**	**<0.001**[a]
VAI	r	0.071	1.000	0.847**	0.414**	0.071
	p	0.531	-	<0.001	<0.001	0.534
LAP	r	0.374**	0.847**	1.000	0.700**	0.386**
	p	0.001	<0.001	.	<0.001	<0.001
FLI	r	0.837**	0.414**	0.700**	1.000	0.812**
	p	<0.001	<0.001	<0.001	-	<0.001
HSI	r	0.914**	0.071	0.386**	0.812**	1.000
	p	<0.001	0.534	<0.001	<0.001	-

[a]: Pearson correlation, Spearman correlation test, BMI: Body mass index, VAI: Visceral adiposity index, FLI: Fatty liver index, LAP: Lipid accumulation product index, HSI: Hepatosteatosis index

The disease is now referred to as "metabolic-associated fatty liver disease" because of its close association with metabolic dysfunction. Early diagnosis using simple tools is necessary to overcome these hepatic and cardiovascular morbidity and mortality risks (13,14).

The FLI, VAI, hepatosteatosis index, and LAP are mathematical models that use anthropometric data, lipid profile tests, and liver function tests to predict NAFLD. They demonstrated visceral adiposity, adipocyte dysfunction, insulin resistance, metabolic dysfunction, and cardiometabolic risk using simple regular patient data available in almost every patient file (8-11). These markers have been reported to be able to accurately diagnose hepatic steatosis in various studies using hepatic biopsy or hepatic USG data as references; however, they could not quantify the steatosis (15).

In our study, HSI correlated with liver USG for hepatosteatosis, but the other indices had no significant relationship. In different studies, different indexes were found to be more effective in predicting HS. In a study by Sheng et al. (16), HSI and LAP had the strongest relationship with HS, whereas Han and Lee (17) found that FLI was the best predictor of HS. Lee et al. (9) tested 5362 NAFLD patients for HSI and validated it as a HS predictor but suggested it to be used as a screening tool to predict the

patients to perform a hepatic USG. The patient population, number of subjects, and parameters used in the algorithm may have caused this difference.

90% of our study patients had USG-proven hepatostetaosis, and the majority of the HS was second degree. Obesity is well known to be related to fatty liver, and our results were in accordance with the literature (18). In our study, the HS(+) group had higher rates of DM, HT, other accompanying diseases, medications used for these diseases, and alcohol consumption within recommended limits when compared with the HS(-) group. Fatty liver disease is associated with cardiometabolic diseases (19).

NAFLD is associated with type 2 DM and insulin resistance. Type 2 DM causes an increased risk of hepatic morbidity (inflammation, fibrosis, cirrhosis, hepatocellular carcinoma) and mortality. At the same time, NAFLD increases the risk of type 2 DM (20). In a national study, it was shown that 32.8% of patients with NAFLD developed type 2 DM. In another study, 94.3% of the patients with diabetes were found to have NAFLD, and in this study population, 92.7% of the patients were diagnosed with obesity or overweight (21). The occurrence of obesity and NAFLD has been emphasized in several studies (22-24). In our study, all patients had obesity, and US-proven HS was more common in the DM group, but the NAFLD indexes did not support this finding. This might be due to the improvement of parameters used in NAFLD indexes because of the diet and exercise program the patients were on.

The severity of NAFLD is determined by a combination of factors, including obesity, insulin resistance, and lipotoxic lipids, along with genetic susceptibility (25). In a study by Sheng et al. (16), TyG index-related parameters, LAP, HSI, BMI, and WC appear to be good predictors of NAFLD. Kannangara et al. (26) showed that FLI and HSI positively correlated with US-proven HS in type 2 DM. In our study, BMI, type 2 DM, and HSI were also correlated with NAFLD.

In addition, alcohol consumption seems to affect hepatosteatosis even the amount is not at level of alcohol abuse and it does not have chronicity. Weight, WC, and ALT were also higher in the HS(+) group. HS is associated with obesity, particularly abdominal obesity (27) and ALT is a specific marker for hepatic inflammation and is more liver-specific (28). In our study, alcohol consumption did not affect the results, as very few patients had a very limited amount that could be ignored.

There was a positive correlation between BMI and LBUI, FLI, and HSI but not with VAI in our study. In the literature, NAFLD and VAI are usually related to obesity, but there are also studies showing the existence of NAFLD in lean subjects. In addition, although VAI is usually found to be related to cardiometabolic disease risk, there are studies that did not find this relationship in patients with obesity (29-31). Thus, there are different results about BMI and NAFLD/NAFLD indexes, as seen in our study. Still, it is a fact that 70-80% of people with NAFLD have obesity (27).

Study Limitations

USG can detect hepatosteatosis after 20% fat deposition, while 5% is the accepted cut-off. Although it was performed by the same senior radiologist, it is dependent on the operator and subjective. In addition, the NAFLD indexes are circumstantial calculations. The gold standard for detecting hepatosteatosis is liver biopsy.

Conclusion

Because NAFLD is a strong predictor of cardiometabolic morbidity and mortality, it is important to make a diagnosis before progression in people living with obesity, and simple non-invasive screening/diagnostic tools are needed for this purpose. VAI, LAP, FLI, and HSI are easily calculated scientific models that predicted NAFLD. Although we could only partially confirm this prediction, they could be used effectively after national validation studies that determine the cut-off values, and the prevention of NAFLD-related complications could be achieved with early diagnosis.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained for this study from the Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (05.03.2021/2764). All procedures performed in this study were in accordance with the 1964 Helsinki Declaration.

Informed Consent: Not necessary for this manuscript.

Authorship Contributions

Surgical and Medical Practices: F.A., I.İ., H.U.A., M.E.P., Concept: F.A., Design: F.A., Data Collection or Processing: F.A., I.İ., H.U.A., M.E.P., Analysis or Interpretation: F.A., I.İ., H.U.A., M.E.P., Literature Search: F.A., I.İ., H.U.A., M.E.P., Writing: F.A., I.İ., H.U.A., M.E.P.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Barazzoni R, Bischoff S, Boirie Y, Busetto L, Cederholm T, Dicker D, et al. Sarcopenic Obesity: Time to Meet the Challenge. Obes Facts 2018;11(4):294-305.
2. Durrer Schutz D, Busetto L, Dicker D, Farpour-Lambert N, Pryke R, Toplak H, et al. European Practical and Patient-Centred Guidelines for Adult Obesity Management in Primary Care. Obes Facts 2019;12(1):40-66.
3. Wagenaar CA, Dekker LH, Navis GJ. Prevalence of sarcopenic obesity and sarcopenic overweight in the general population: The lifelines cohort study. Clin Nutr 2021;40(6):4422-4429.
4. WHO European Regional Obesity Report 2022 Available at: https://apps.who.int/iris/bitstream/handle/10665/353747/9789289057738-eng.pdf Accessed on: Aug 2023
5. Ko E, Yoon EL, Jun DW. Risk factors in nonalcoholic fatty liver disease. Clin Mol Hepatol 2023;29(Suppl) : S79-S85.
6. Han SK, Baik SK, Moon Young Kim MY. Non-alcoholic fatty liver disease: Definition and subtypes. Clin MolHepatol 2023;29(Suppl):S5-S16.
7. Di Mauro S, Scamporrino A, Filippello A, Di Pino A, Scicali R, Malaguarnera R, et al. Clinical and Molecular Biomarkers for Diagnosis and Staging of NAFLD. Int J Mol Sci 2021;22(21):11905.
8. Okamura T, Hashimoto Y, Hamaguchi M, Obora A, Kojima T, Fukui M. The visceral adiposity index is a predictor of incident nonalcoholic fatty liver disease: A population-based longitudinal study. Clin Res Hepatol Gastroenterol 2020;44(3):375-383.
9. Lee JH, Kim D, Kim HJ, Lee CH, Yang JI, Kim W, et al. Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. Dig Liver Dis 2010;42(7):503-508.
10. Ebrahimi M, Seyedi SA, Nabipoorashrafi SA, Rabizadeh S, Sarzaeim M, Yadegar A, et al. Mohammadi. Lipid accumulation product (LAP) index for the diagnosis of nonalcoholic fatty liver disease (NAFLD): a systematic review and meta-analysis. Lipids Health Dis 2023 15;22(1):41.
11. Han AL. Validation of fatty liver index as a marker for metabolic dysfunction-associated fatty liver disease. Diabetol Metab Syndr 2022;14(1):44.
12. Nassir F. NAFLD: Mechanisms, Treatments, and Biomarkers. Biomolecules 2022;12(6):824.
13. Clayton-Chubb D, Kemp W, Majeed A, Lubel JS, Hodge A, Roberts SK. Understanding NAFLD: From Case Identification to Interventions, Outcomes, and Future Perspectives. Nutrients 2023;15(3):687.
14. Portincasa P. NAFLD, MAFLD, and beyond: one or several acronyms for better comprehension and patient care. Intern Emerg Med 2023;18(4):993-1006.
15. Fedchuk L, Nascimbeni F, Pais R, Charlotte F, Housset C, Ratziu V; LIDO Study Group. Performance and limitations of steatosis biomarkers in patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther 2014;40(10):1209-1222.
16. Sheng G, Lu S, Xie Q, Peng N, Kuang M, Zou Y. The usefulness of obesity and lipid-related indices to predict the presence of Non-alcoholic fatty liver disease. Lipids Health Dis 2021;20(1):134.
17. Han AL, Lee HK. Comparison of the Diagnostic Performance of Steatosis Indices for Discrimination of CT-Diagnosed Metabolic Dysfunction-Associated Fatty Liver Disease. Metabolites 2022;12(7):664.
18. Polyzos SA, Kountouras J, Mantzoros CS. Obesity and nonalcoholic fatty liver disease: From pathophysiology to therapeutics. Metabolism 2019;92:82-97.
19. Stefan N, Häring HU, Cusi K. Non-alcoholic fatty liver disease: causes, diagnosis, cardiometabolic consequences, and treatment strategies. Lancet Diabetes Endocrinol 2019;7(4):313-324.
20. Gastaldelli A, Cusi K. From NASH to diabetes and from diabetes to NASH: Mechanisms and treatment options. JHEP Rep 2019;1(4):312-328.
21. Kaya E, Yılmaz Y. Non-alcoholic fatty liver disease: A growing public health problem in Turkey. Turk J Gastroenterol 2019;30(10):865-871.
22. Sarwar R, Pierce N, Koppe S. Obesity and nonalcoholic fatty liver disease: current perspectives. Diabetes Metab Syndr Obes 2018;11:533-542.
23. Fabbrini E, Sullivan S, Klein S. Obesity and nonalcoholic fatty liver disease: biochemical, metabolic, and clinical implications. Hepatology 2010;51(2):679-689.
24. Francque SMA, Dirinck E. NAFLD prevalence and severity in overweight and obese populations. Lancet Gastroenterol Hepatol 2023;8(1):2-3.
25. Pourteymour S, Drevon CA, Dalen KT, Norheim FA. Mechanisms Behind NAFLD: a System Genetics Perspective. Curr Atheroscler Rep 2023;25(11):869-878.
26. Kannangara KK, Dehigolla MR, Gunathilaka CM, Maddumage RS, Dulshika GD, Karunarathna WA, et al. Correlation between liver fat indices and ultrasonography to determine non-alcoholic fatty liver disease among diabetic patients in Sri Lanka. Glob J Med Pharm Biomed Update 2022;17:15.
27. Chen X, Shi F, Xiao J, Huang F, Cheng F, Wang L, et al. Associations Between Abdominal Obesity Indices and Nonalcoholic Fatty Liver Disease: Chinese Visceral Adiposity Index. Front Endocrinol (Lausanne) 2022;13:831960.
28. Forlano R, Mullish BH, Dhar A, Goldin RD, Thursz M, Manousou P. Liver function tests and metabolic-associated fatty liver disease: Changes in upper normal limits, does it really matter? World J Hepatol 2021;13(12):2104-2112.
29. Vizzuso S, Del Torto A, Dilillo D, Calcaterra V, Di Profio E, Leone A, et al. Visceral Adiposity Index (VAI) in Children and Adolescents with Obesity: No Association with Daily Energy Intake but Promising Tool to Identify Metabolic Syndrome (MetS). Nutrients 2021;13(2):413.
30. Younes R, Bugianesi E. NASH in Lean Individuals. Semin Liver Dis 2019;39(1):86-95.
31. Darroudi S, Soflaee SS, Hosseini ZS, Farmad MS, Mirshafiei H, Sheikh Andalibi MS, et al. The visceral adiposity index and lipid accumulation product as predictors of cardiovascular events in normal weight subjects. Clin Nutr ESPEN 2022;52:190-197.