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Diagnostic Performance of Tissue Attenuation Imaging for Hepatic Steatosis Quantification in People Living with HIV

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Abstract

Background

Non-alcoholic fatty liver disease (NAFLD) is a common comorbidity among people living with HIV (PLWH), and routine screening is recommended. Conventional ultrasonography (US) has limited sensitivity and cannot quantify steatosis. Tissue attenuation imaging (TAI) is a quantitative US technique not previously studied in PLWH. We evaluated the diagnostic performance of TAI and compared NAFLD prevalence with HIV-negative controls.

Methods

In this retrospective study, PLWH aged ≥18 years were evaluated with conventional ultrasonography, TAI and elastography. Historical HIV-negative controls were matched for sex, body mass index and metabolic syndrome by propensity scores. TAI was compared with ultrasonographic steatosis grade using ROC analysis. In PLWH at risk of NAFLD, elastography, FIB-4, NAFLD fibrosis score (NFS) and APRI were compared.

Results

Of 243 participants (123 PLWH, 120 controls), 56.1% of PLWH had any-grade NAFLD. In the matched cohort, grade ≥2 NAFLD prevalence was similar in PLWH and controls (30.0% vs. 37.5%, p=0.316). The area under the curve of TAI was 0.88 for any steatosis and 0.92 for grade ≥2 steatosis (optimal cut-offs 0.67 and 0.75 dB/cm/MHz). Among 95 PLWH at risk of NAFLD, significant fibrosis or high fibrosis risk was 3.2%, 1.1%, 3.1% and 5.2% by elastography, FIB-4, NFS and APRI, respectively. FIB-4 and NFS were strongly correlated (rho=0.750, p<0.001).

Conclusions

NAFLD was common among PLWH, with a prevalence comparable to metabolically matched HIV-negative individuals. TAI showed high agreement with conventional US grading and may be a practical quantitative screening tool. Fibrosis estimates varied by method, supporting combined use of non-invasive tests.

Keywords

HIV infections, Non-alcoholic fatty liver disease, Tissue attenuation imaging, Quantitative ultrasound, Hepatic steatosis, Liver fibrosis

Background

In liver histology or imaging, fatty infiltration of the liver (hepatic steatosis involving >5% of hepatocytes) caused by factors other than alcohol consumption, hepatotoxic drugs, toxins, viral infections, and genetic factors is defined as non-alcoholic fatty liver disease (NAFLD).(1) NAFLD can lead to progressive liver disease such as non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and even liver cancer.(2) The prevalence of NAFLD is increasing due to the rising incidence of obesity, type 2 diabetes, and metabolic syndrome. (3) Prevalence of NAFLD in the general population is 25-30%.(1) NAFLD is a clinically significant comorbidity caused by ongoing chronic inflammation among people living with HIV (PLWH). The reported prevalence of NAFLD in PLWH ranges from 33% to 43%.(4) HIV management guidelines recommend that PLWH also be monitored for NAFLD.

Ultrasonography (US) is the first recommended method for diagnosing NAFLD.(5) Although standard US can detect hepatic steatosis, it is not sufficient as a tool to identify hepatic steatosis due to low sensitivity across the NAFLD spectrum.(1) Where possible, elastography can be used as an alternative method for diagnosing HIV-related NAFLD. Whenever imaging tools are not available, serum biomarkers and scores are acceptable alternatives for the diagnosis.(1) Quantitative US methods have excellent utility for diagnosing and evaluating the degree of hepatic steatosis.(6,7) Tissue attenuation imaging (TAI) is determined based on the attenuation properties of different frequency components in the tissue, and the spectrum of radiofrequency signals provides a downshift of the center frequency according to depth. The TAI parameter indicates the slope of the US center frequency downshift.(6) However, there is no published article about the diagnostic value of TAI in PLWH. This study aimed to compare the prevalence of NAFLD in PLWH with a control group, and to evaluate the diagnostic value of the fat quantification method to NAFLD.

Materials and methods

Study design

This was a retrospective, cross-sectional study from February 2022 to November 2023. The study was approved by the Gazi University Clinical Research Ethics Committee. (Application number: b95c6962-6a19-4e25-9917-

2a868c04d081, Approval date:14.01.2025) Helsinki Declaration has been followed for involving human subjects in the study. The requirement for informed consent was waived due to the retrospective design of the study.

Study population and Setting

This study was conducted by analyzing the hospital records of patients followed up at the Infectious Diseases and Radiology outpatient clinics of Gazi University Faculty of Medicine. All PLWH aged ≥18 were consecutively included in the study. Patients with HBV or HCV co-infections, hepatosteatosis-related comorbidities (Wilson disease, abetalipoproteinemia, hypobetalipoproteinemia, lipodystrophy, LCAT deficiency, etc.), patients using alcohol (20 gr/day for women, 30 gr/day for men) and drugs (corticosteroids, amiodarone, methotrexate, total parenteral nutrition, high-dose tetracycline, valproate, tamoxifen, 5-FU, etc.) that may cause hepatosteatosis were excluded from the study. The study's control group consisted of a historical cohort of HIV-seronegative individuals previously evaluated for hepatic steatosis using the same imaging methods.(8,9)

Study protocol and Definitions

Demographic data and biometric measurements of the study group, including age, weight, height, waist circumference, BMI, and also blood pressure, were recorded. Laboratory data within a period of a maximum of 2 weeks with radiological imaging were used for the analyses. HIV RNA, CD4 levels, hemoglobin, WBC, platelets, AST, ALT, albumin, total cholesterol, HDL and LDL cholesterol, triglyceride, and creatinine results were recorded. According to the National Cholesterol Education Program Adult Treatment Panel 3 (NCEP ATP III) definitions; those who meet 3 or more criteria (blood pressure over 130/85 mmHg or antihypertensive drug use, triglyceride level over 150 mg/dl or drug treatment for elevated triglyceride, HDL cholesterol level less than 40 mg/dl for men and 50 mg/dl for women, fasting blood glucose over 100 mg/dl or treatment for elevated glucose, BMI over 30 or waist circumference over 102 cm in men or 88 cm in women) were considered to have metabolic syndrome. (10) With a BMI of 24.9 and below was categorized as normal, between 25 and 29.9 as overweight, and above 30 as obese. Antiretroviral treatment (ART) regimens and durations were recorded for each patient.

Diagnosis of NAFLD

In our institution, all PLWHs are followed according to the EACS Guidelines recommendations for NAFLD.(5) These patients were evaluated for NAFLD using BMI, metabolic syndrome, liver function tests, and radiological methods according to the guidelines' recommendations. Standard and quantitative ultrasound (QUS) imaging using TAI

tools and elastography was performed on all patients. For each patient, both standard US-based hepatosteatosis grades (G0-3) and TAI measurements were recorded.

Diagnosis of hepatic fibrosis

Liver stiffness was assessed with elastography, and the calculated METAVIR (Meta-analysis of Histological Data in Viral Hepatitis) scores (F0-4) and kPa values were also recorded. Fibrosis scores based on serum biomarkers such as FIB-4 (fibrosis-4), NFS (NAFLD fibrosis), APRI (AST/platelet index) score, and elastography were used to predict liver fibrosis. FIB-4 ((Age x AST) / (Platelets x √(ALT)) groups were defined as low risk for significant fibrosis with a cutoff point ≤ 1.30 (≤ 2 for ≥ 65 years), uncertain 1.30-2.67, and high risk for significant fibrosis > 2.67.(1) Cut-offs for NFS (-1.675 + (0.037*age [years]) + (0.094*BMI [kg/m²]) + (1.13*IFG/diabetes [yes = 1, no = 0]) + (0.99*AST/ALT ratio) – (0.013*platelet count [×109/L]) – (0.66*albumin [g/dl])) were ≤-1.455 (≤ 0.12 for ≥65 years), -1.455 – 0.675, and > 0.675 for low, indeterminate, and high risks, respectively.(1) For APRI scores ≤0.5, 0.5-1.5, and ≥1.5 were cut-offs for low probability of significant fibrosis, indeterminate, and high probability for fibrosis, respectively.(1) All fibrosis scores were calculated and recorded as both total scores and grouped as low, indeterminate, and high fibrosis risk. Based on the EACS guideline recommendations, 95 PLWH patients with NAFLD on US and additional metabolic risk factors (metabolic syndrome, overweight/obesity, or elevated ALT) were categorized as at risk for liver fibrosis and underwent fibrosis risk assessment.

Statistical analysis

All data were analyzed by IBM SPSS Statistics for Mac, version 25.0 for Mac OS X (IBM Corp., Armonk, N.Y., USA). The normality of the data distribution was determined by the Shapiro-Wilk test, histogram, and Q-Q plots. The categorical values of the patients were expressed as a number and a percentage and were analyzed with a Chi-square test. Continuous variables were presented as a mean and standard deviation (SD) or median values and an interquartile range (IQR) of 25%–75%. The non-parametric values were analyzed using the Mann–Whitney U. To assess the diagnostic utility of fat quantification results according to grades of NAFLD by abdominal US, a receiver operating characteristic (ROC) curve was constructed and the area under the curve (AUC) was calculated. Differences in TAI values across steatosis grades were analyzed with the Kruskal–Wallis test. Correlations between fibrosis scores were assessed with Spearman's rank correlation. Optimal TAI cut-off values were determined using the Youden index. Both groups were matched for sex, BMI, and metabolic syndrome by propensity matching. The p-value < 0.05 was considered statistically significant.

Outcomes

The primary aim of this study was to compare the diagnostic value of the fat-quantification method for NAFLD in PLWH. The secondary aims of the study were to determine the prevalence of NAFLD in PLWH and to evaluate the correlation between hepatic fibrosis prediction scores.

Results

A total of 243 participants, 123 (50.6%) in the PLWH group and 120 (49.4%) in the control group, were included in the study. Demographic data and clinical characteristics of the PLWH group are presented in Table 1.

Table.1 Demographic data and clinical characteristics of the PLWH

Age, med (IQR 25-75%)	38 (30-51)
Female sex, n (%)	15 (12.2)
Comorbidities	
Diabetes mellitus, n (%)	11 (8.9)
Hypertension , n (%)	18 (14.6)
Dyslipidemia, n (%)	86 (69.9)
Coronary heart disease,n (%)	12 (9.8)
Chronic renal failure, n (%)	5 (4.1)
BMI, median (25-75% IQR)	26.3 (23.5- 29.4)
BMI Group, n(%)	
Normal	46 (37.4)
Overweight	53 (43.1)
Obese	24 (19.5)
Metabolic syndrome, n (%)	30 (24.4)
Recent diagnosis, n (%)	23 (18.7)
Duration of HIV infection, months, med (IQR 25-75)	24 (2-56)
ART-naive, n (%)	29 (23.6)
HIV regimens , n(%)	
BIC/FTC/TAF	43 (35)
EVG/c/FTC/TAF	30 (24.4)
EVG/c/FTC/TDF	1 (0.8)
TDF/FTC/RAL	2 (1.6)
TDF/FTC/EFV	5 (4.1)
TDF/FTC/DTG	2 (1.6)
3TC/DTG	4 (3.3)
DTG/ABC/3TC	7 (5.7)

Abbreviations: BMI, body mass index; ART, antiretroviral treatment ; BIC, bictegravir; FTC, emtricitabine; TAF, tenofovir alafenamide; EVG, elvitegravir; c, cobicistat; TDF, tenofovir disoproxil fumarate; RAL, raltegravir; EFV, efavirenz; DTG, dolutegravir; 3TC, lamivudine; ABC, abacavir

Both groups were compared in terms of NAFLD. The frequency of any grade of NAFLD in PLWH and control groups was 56% (n=69) and 77.5% (n=93), respectively (p<0.001). The frequency of ≥ grade 2 NAFLD in PLWH and control groups was 26% (n=32) and 45.8% (n=55), respectively (p=0.001) (Table 2). In the matched cohort, the frequencies of ≥ grade 2 NAFLD in PLWH and control groups were 30.0% (n = 24) and 37.5% (n = 30), respectively (p = 0.316) (Table 2).

Table.2 Comparison of PLWH and control groups for NAFLD						
Variables	All cohorts			Propensity cohort		
	PLWH n=123	Control n=120	p value	PLWH n=80	Control n=80	p value
Age, median (IQR 25-75%)	38 (30-51)	46 (37-56)	0.005	42.5 (34-54)	44 (35-55)	0.691
Female, n (%)	15 (12.2)	49 (40.8)	<0.001	14 (17.5)	14 (17.5)	1.000
BMI group, n(%)						
Normal	46 (37.4)	27 (22.5)	0.002	17 (21.3)	17 (21.3)	1.000
Overweight	53 (43.1)	47 (39.2)		42 (52.5)	42 (52.5)	1.000
Obese	24 (19.5)	46 (38.3)		21 (26.3)	21(26.3)	1.000
Comorbidities, n(%)						
DM	11 (8.9)	27 (22.5)	0.004	7 (8.8)	13 (16.3)	0.151
HT	18 (14.6)	33 (27.5)	0.014	10 (12.5)	17 (21.3)	0.138
Dyslipidemia	86 (69.9)	80 (66.7)	0.586	59 (73.8)	53 (66.3)	0.301
Metabolic syndrome	30 (24.4)	39 (32.5)	0.161	18 (22.5)	18 (22.5)	1.000
Hepatosteatosis						
Grade 0	54 (43.9)	27 (22.5)	0.001	30 (37.5)	17 (21.3)	0.099
Grade 1	37 (30.1)	38 (31.7)		26 (32.5)	33 (41.3)	
Grade 2	22 (17.9)	44 (36.7)		17 (21.3)	25 (31.3)	
Grade 3	10 (8.1)	11 (9.2)		7 (8.8)	5 (6.3)	
G≥2	32 (26.0)	55 (45.8)	0.001	24 (30.0)	30 (37.5)	0.316

Two different methods were compared for NAFLD in the PLWH group. The fat quantification method was compared with standard US results to determine its diagnostic value**.** TAI results according to NAFLD grade were: Grade 0, TAI=0.64 dB/cm/MHz (0.61-0.68); Grade 1 TAI=0.71 dB/cm/MHz (0.68-0.75); Grade 2, TAI=0.79 dB/cm/MHz (0.74-0.82); Grade 3 TAI=0.95 dB/cm/MHz (0.87-1.02) (p< 0.001, Kruskal Wallis test) (Figure 1)

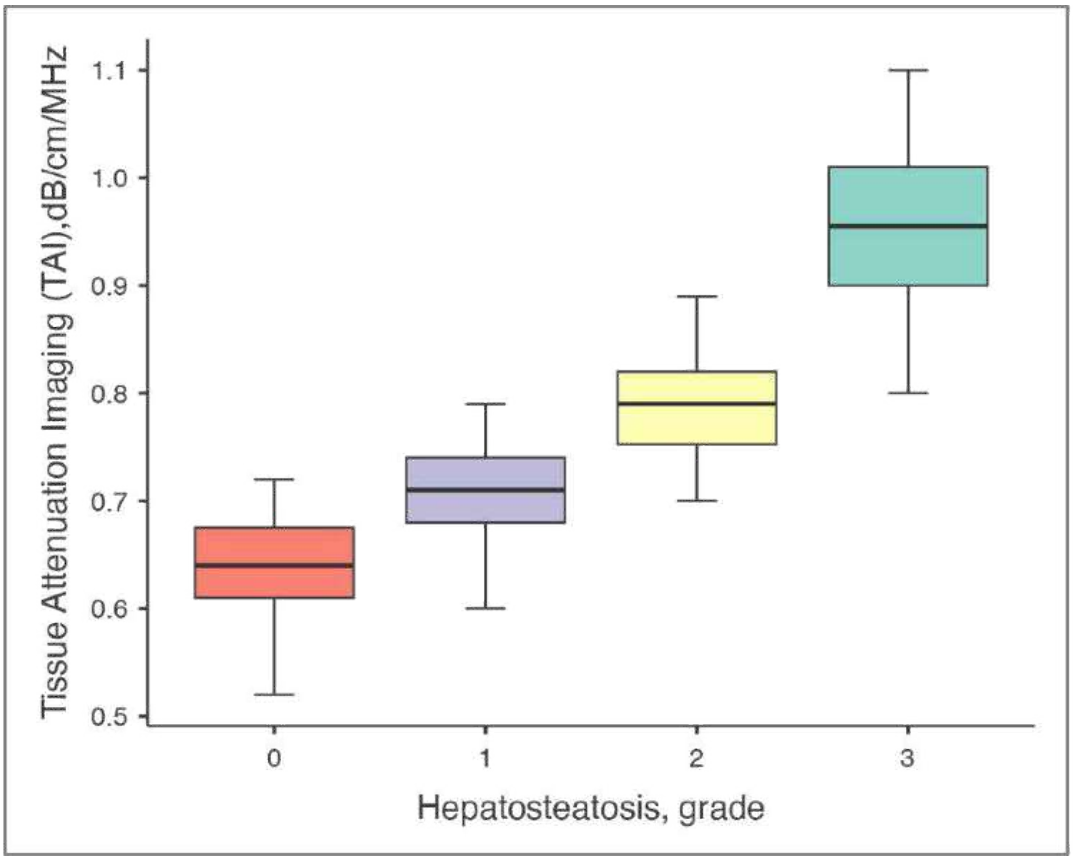

Figure 1. TAI results according to NAFLD grade

The cut-off values and diagnostic values of the fat quantification method according to different NAFLD grades were presented in the table3. In predicting grade ≥2 NAFLD in the PLWH population, the area under the curve (AUC) of the fat quantity determination method at the 0.75 dB/cm/MHz cutoff point was 0.916 (0.85-0.97, P<0.001) (Figure 2).

Table 3. Diagnostic values of fat quantification method according to different NAFLD grades

	Cut-off point TAI (dB/cm/MHz)	Sensitivity, (%)	Specificity, (%)	PPV	NPV	AUC
G0 vs. G1-3	0.67	91.3	74.1	81.8	87.0	0.88
G0-1 vs G2-3	0.75	84.4	88.0	71.1	94.1	0.92
G3 vs G0-2	0.80	100	86.73	40	100	0.97

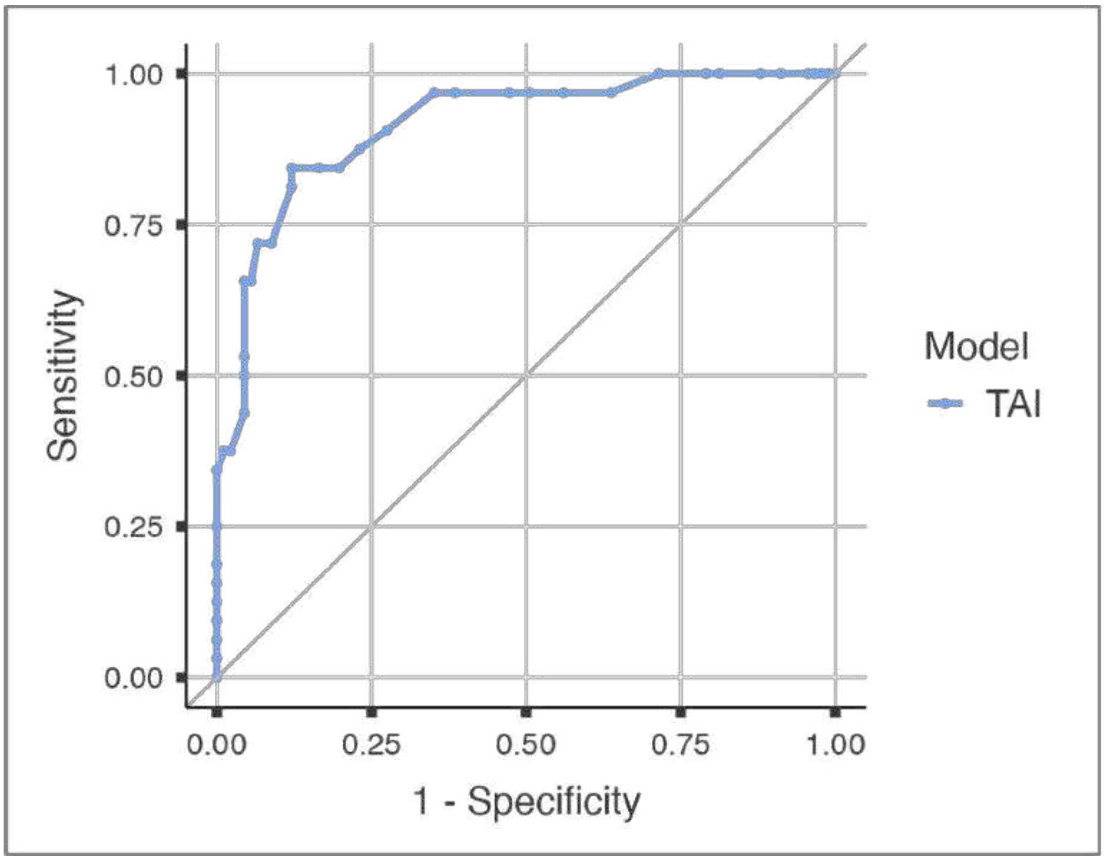

Figure 2. ROC analysis result of TAI to predict >2 Grade of NAFLD

77.2% (n=95) of people living with HIV were at risk of NAFLD. According to the METAVIR scoring system based on elastographic imaging of the at-risk group, 1.1% (n=1) had grade 0 fibrosis, 95.8% (n=91) had grade 1 fibrosis, 2.1% (n=2) had grade 2 fibrosis, and 1.1% (n=1) had grade 3 fibrosis.

The FIB-4, NFS, and APRI scores of the NAFLD at-risk group in PLWH were presented in table 4.

Table.4	NAFLD at-risk group n=95
FIB-4, median (IQR 25-75%)	0.880 (0.645-1.240)
FIB-4-Groups, n(%)	
Low	74 (77.9)
Indeterminate	20 (21.0)
High	1 (1.10)
NFS, median (IQR 25-75%)	-2.15 (-3.00- -1.380)
NFS group, n(%)	
Low	66 (69.5)
Indeterminate	26 (27.4)
High	3 (3.10)
APRI, median (IQR 25-75%)	0.200 (0.200-0.350)
APRI group, n(%)	
Low	89 (93.7)
Indeterminate	1 (1.10)
High	5 (5.20)

Among the fibrosis prediction scores, there was a high-level correlation between FIB4 and NFS (Rho: 0.750, p<0.001), a low-level correlation between FIB-4 and APRI (Rho: 0.31, p=0.002), and no correlation between NFS and APRI (Rho: 0.02, p=0.851) (Figure. 3).

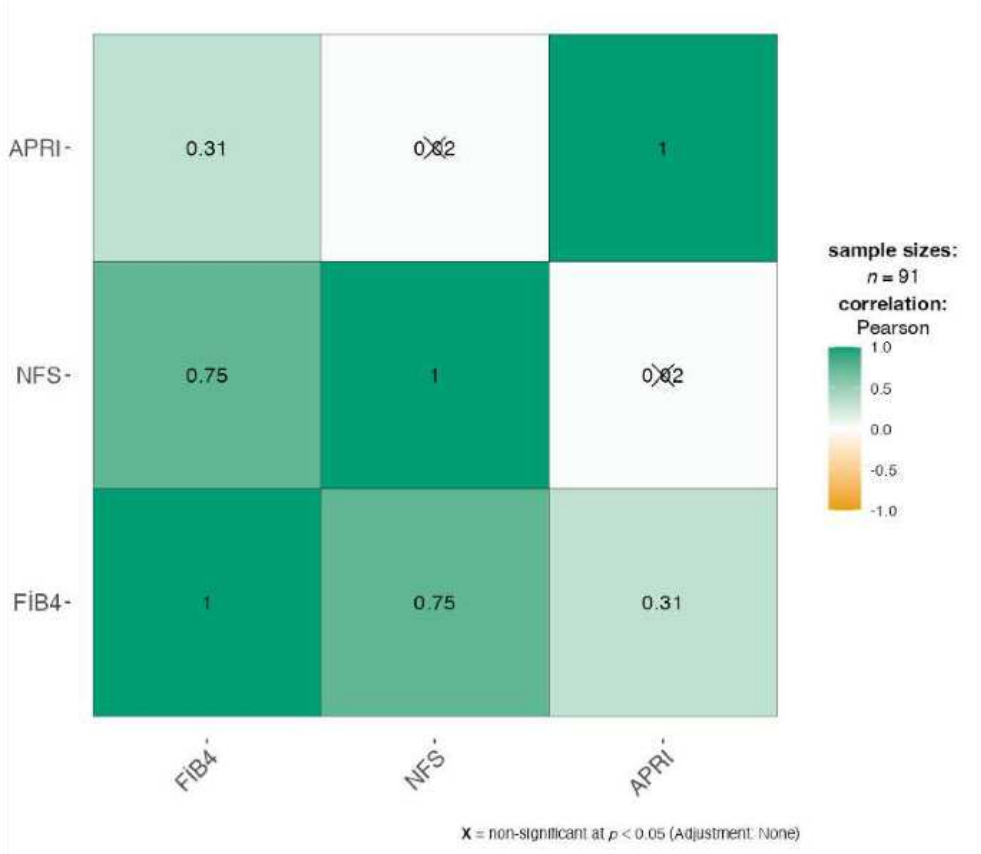

Figure 3. Correlation between different type of non-invasive fibrosis scores

Discussion

The burden of NAFLD and fibrosis is high among PLWH. According to a currently published meta-analysis, the prevalence of any grade of NAFLD in PLWH is 29-48%. (4,11) In contrast, moderate or severe NAFLD prevalence is reported as 11-23%.(11) This prevalence changes across geographic regions. In Europe, the reported pooled prevalence of NAFLD in PLWH reaches nearly 50%.(11) Similarly, there are significant regional variations between countries. While prevalence rates reach 65-75% in Greece or France, Denmark reports a NAFLD prevalence of only 10%. This meta-analysis reports a prevalence between 14% and 40% in Türkiye.(12) However, a few monocenter studies with small sample sizes highlight the knowledge gap on fatty liver in the HIV population in Türkiye.(13,14) The prevalence of any grade of NAFLD we found in our study, at 56%, which is higher than the reported prevalence range in Türkiye, should be considered with the knowledge gap on this issue. In addition to geographic differences, the patient selection criteria led to overestimated or underestimated prevalence in

studies included in the meta-analysis. In high-risk groups, the pooled prevalence of NAFLD in PLWH increases to 75% (58-90%).(11) Because of significant differences between risk groups, comparative studies with populations without HIV infection in the same study is essential for an accurate understanding of the risk of NAFLD in PLWH. In our study, a matched population with a high risk for NAFLD was selected as a control group. When compared with this group, there was a similar moderate and severe prevalence of NAFLD in PLWH.

Due to its low cost and availability, standard US is a commonly used diagnostic method for liver steatosis. Although its diagnostic accuracy is high in moderate and severe liver steatosis, in mild cases its diagnostic value is limited.(6) Inability of quantification and low reproducibility rates between different operators are other limitations of this method.(6) For this reason, several non-invasive quantitative diagnostic approaches and new methods based on US or MRI are recommended for diagnosing and monitoring hepatosteatosis.(6) These techniques provide information about the liver fat content by analyzing increased scattering magnitudes or signal attenuation. MRI-based imaging is the recommended noninvasive diagnostic method for NAFLD. Due to its high costs and limited availability, MRI-based imaging is currently still not a useful screening tool and its use remains limited to research.(15) There is still a need for more economical and accessible noninvasive tools. Tissue attenuation imaging (TAI) is a spectral-based technique that measures energy loss as US waves pass through fatty tissue with attenuation coefficient.(6) TAI has high diagnostic accuracy in studies that use magnetic resonance imaging proton density fat fraction as a reference method. Rónaszéki et al. found that the AUC of TAI for the detection of ≥5% MRI-PDFF was 0.89 [CI = 0.83–0.95] with the optimal cutoff value at 0.765 dB/cm/MHz. For the detection of ≥10% MRI-PDFF, the AUC was 0.93 (CI = 0.88–0.98) with a cutoff at 0.845 dB/cm/MHz.(16) In another study with the same study design, for the detection of ≥5% and ≥10% MRI-PDFF, the AUCs were 0.861 (95% CI: 0.786–0.918) with an optimal cutoff value of 0.884 dB/cm/MHz and 0.835 (95% CI: 0.757–0.897) with an optimal cutoff value of 0.980 dB/cm/MHz.(7) Although these results support the good diagnostic value of TAI for hepatic steatosis and assessing its severity in the general population, more data is needed on optimal cutoff value and its diagnostic performance in specific populations. In our study, compared to the standard US method, which is the recommended tool for NAFLD screening in PLWH by international guidelines, the TAI method provides a high AUC of 0.88 for screening. Our finding supported the TAI diagnostic accuracy between different NAFLD groups in PLWH. The optimal threshold value of is unknown for TAI and changes among different studies according to measurement protocols and heterogeneity in the characteristics of the studied cohorts.(17) Previous studies have also reported optimal TAI thresholds for moderate-severe NAFLD in the general population to be between

0.70 and 0.98 dB/cm/MHz. Similarly, in our study, TAI thresholds for different NAFLD grades ranged from 0.67 to 0.80 dB/cm/MHz, while the optimal threshold for predicting moderate-severe NAFLD was 0.75 in PLWH.

The reference standard for prognosis assessment in NAFLD patients is the histological examination of liver biopsy specimens. However, liver biopsies have many limitations, which has restricted their use in routine practice. Therefore, different non-invasive tests (NIT) are used for the same purpose.(18) For staging and risk stratification of NAFLD patients, the use of two or more NITs combining serum biomarkers and/or imaging-based tests are recommended.(18) FIB-4 score, NFS score, and APRI are the most commonly used non-invasive biomarker-based scoring systems. However, FIB-4 is the most validated non-invasive score being used for NAFLD.(1) FIB-4 is commonly available, low-cost, and has good sensitivity at low cut-off values.(19) In a meta-analysis, NFS or FIB-4 are as effective in predicting clinical outcomes and prognosis in patients with NAFLD as histological assessment.(20) The European AIDS Clinical Society (EACS) guideline recommends that PLWH at risk of NAFLD should first be assessed for fibrosis risk using non-invasive biomarkers such as FIB-4 and NFS, followed by elastographic evaluation.(5) In our study, FIB-4 and NFS had high-level correlation, while APRI showed low correlation with other scoring systems.

This study has several limitations. Its retrospective, single-center design limits generalizability and introduces potential selection bias. NAFLD diagnosis was based on standard US rather than liver biopsy or MRI-PDFF, which may have resulted in misclassification of steatosis severity. The control group consisted of individuals previously referred for the evaluation of hepatic steatosis, which may have resulted in a higher prevalence of steatosis in this group. And despite propensity score matching, residual confounding cannot be excluded. Conventional US and TAI measurements were not performed by blinded operators. In addition, TAI cut-off values were derived and evaluated in the same cohort without external validation, which may have overestimated diagnostic performance.

Conclusion

As a result of our study, NAFLD prevalence was higher than previously reported in Türkiye, underscoring the need for larger, well-designed studies in PLWH. TAI demonstrated high diagnostic accuracy for detecting and grading liver steatosis in PLWH compared with conventional US. With its non-invasive, accessible, and quantitative structure, TAI can be used for practical screening and monitoring of NAFLD. However, more data are needed to determine optimal thresholds in specific groups. The prevalence of liver fibrosis varies depending on the

methods. Therefore, the combined use of imaging and biomarker-based non-invasive methods is essential. In PLWH, FIB-4 and NFS, along with elastography, are more consistent noninvasive tests for identifying liver fibrosis.

List of abbreviations

3TC: Lamivudine

5-FU: 5-Fluorouracil

ABC: Abacavir

ALT: Alanine aminotransferase

APRI: Aspartate aminotransferase-to-platelet ratio index

ART: Antiretroviral therapy

AUC: Area under curve

BIC: Bictegravir

BMI: Body mass index

c: Cobisistat

CI: Confidince interval

DM: Diabetes mellitus

DTG: Dolutegravir

EACS: European AIDS Clinical Society

EFV: Efavirenz

EVG: Elvitagravir

FIB-4: Fibrosis-4 index

FTC: Emtricitabine

HBV: Hepatitis B virus

HCV: Hepatitis C virus

HDL: High-density lipoprotein

HIV: Human immunodeficiency virus

HT: Hypertension

IFG: Impaired fasting glucose

IQR: Interquartile range

LCAT: Lecithin–cholesterol acyltransferase

LDL: Low-density lipoprotein

METAVIR: Meta-analysis of Histological Data in Viral Hepatitis

MRI-PDFF: Magnetic resonance imaging proton density fat fraction

NAFLD: Non-alcoholic fatty liver disease

NASH: Non-alcoholic steatohepatitis

NCEP ATP III: National Cholesterol Education P;rogramme Adult Treatment Panel III

NFS: NAFLD fibrosis score

NIT: Non-invasive test

NPV: Negative predictive value

PLWH: People living with HIV

PPV: Positive predictive value

QUS: Quantitative ultrasound

RAL: Raltegravir

ROC: Receiver operating characteristic

SD: Standard deviation

TAF: Tenofovir alafenamide

TAI: Tissue attenuation imaging

TDF: Tenofovir disoproxil fumarate

US: Ultrasonography

WBC: White blood cell

Declarations

Ethics approval and consent to participate: The study was approved by the Gazi University Clinical Research Ethics Committee. (Application number: b95c6962-6a19-4e25-9917-2a868c04d081, Approval date:14.01.2025) Helsinki Declaration has been followed for involving human subjects in the study. The requirement for informed consent was waived due to the retrospective design of the study. All procedures involving human participants were conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and/or analysed during the current study are not publicly available due to patient privacy and ethical restrictions but are available from the corresponding author on reasonable request.

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Authors' contributions

Methodology,M.B.,S.N.T.,Y.Y,M.N.C.,K.E.,H.N.S.,H.S.O.; Investigation, Data curation, M.B.,Y.Y.,K.E.,H.S.O. Investigation (ultrasonographic and elastographic evaluation, TAI measurements),S.N.T.,M.N.C.,H.N.S.; statistical analysis, M.B., H.S.O.; Writing – review & editing, M.B.,S.N.T.,Y.Y,M.N.C.,K.E.,H.N.S.,H.S.O.

All authors read and approved the final manuscript

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