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Journal

Journal of Clinical Gastroenterology and Hepatology, 2(3)

ISSN

2575-7733

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Publication Date

2018

DOI

10.21767/2575-7733.1000045

Peer reviewed

HHS Public Access

Author manuscript

J Clin Gastroenterol Hepatol. Author manuscript; available in PMC 2019 July 30.

Published in final edited form as:

J Clin Gastroenterol Hepatol. 2018 ; 2(3): . doi:10.21767/2575-7733.1000045.

A Comparison of the Liver Fat Score and CT Liver-to-Spleen Ratio as Predictors of Fatty Liver Disease by HIV Serostatus

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Abstract

Background and Aim: Non-alcoholic fatty liver disease (NAFLD) is common among HIV-infected (HIV+) adults. The Liver Fat Score (LFS) is a non-invasive, rapid, inexpensive diagnostic tool that uses routine clinical data and is validated against biopsy in HIV-uninfected (HIV−) persons. CT liver-to-spleen (L/S) attenuation ratio is another validated method to diagnose NAFLD. We compared NAFLD prevalence using the LFS versus L/S ratio among Multicenter AIDS Cohort Study participants to assess the LFS's performance in HIV+vs. HIV−men.

Methods: In a cross-sectional analysis of men reporting<3 alcoholic drinks daily (308 HIV+, 218 HIV−), Spearman correlations determined relationships between LFS and L/S ratio by HIV serostatus. Multivariable regression determined factors associated with discordance in LFS- and L/S ratio-defined NAFLD prevalence.

Results: NAFLD prevalence by LFS and L/S ratio were 28%/15% for HIV+men and 20%/19% for HIV−men, respectively. Correlations between LFS and L/S ratio were weaker among HIV +than HIV−men, but improved with increasing BMI and exclusion of HCV-infected men. LFS and L/S ratio discordance occurred more frequently and across BMI strata among HIV+men, but predominantly at BMI<30 kg/m^2 among HIV−men. In multivariate analysis, only lower total testosterone levels were significantly associated with discordance.

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Conclusion: NAFLD prevalence was similar by LFS and L/S ratio identification among HIV −men, but dissimilar and with frequent discordance between the two tests among HIV+men. As discordance may be multifactorial, biopsy data are needed to determine the best non-invasive diagnostic test for NAFLD in HIV+persons.

Keywords

Hepatic steatosis; Non-alcoholic steatohepatitis; Human immunodeficiency

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the Western world [1]. NAFLD is associated with risk for progression to steatohepatitis, cirrhosis and liver cancer, as well as the development of cardiovascular disease and the metabolic syndrome [2,3].

NAFLD prevalence in HIV-monoinfected patients is 35% according to a recent systematic review, and HIV-infected persons with NAFLD may have higher rates of progression to steatohepatitis than HIV-uninfected persons [4–6].

NAFLD can be detected with varying sensitivity using diverse imaging modalities, including ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and Fibroscan with controlled attenuation parameter (CAP). On non-contrast CT, healthy liver is denser than the spleen. With steatosis, the liver becomes less dense. A CT-quantified liver-to-spleen (L/S) attenuation ratio<1.0 accurately represents biopsy-proven hepatic steatosis [7]. However, CT scans are costly and time-consuming, and a rapid, more readily available means of assessing for NAFLD in routine clinical care is needed.

The Liver Fat Score (LFS) is a non-invasive diagnostic method that uses clinical data (metabolic syndrome and diabetes diagnoses, insulin and transaminase levels) to identify hepatic steatosis and has been validated against biopsy-proven steatosis in HIV-uninfected populations [8]. The LFS has the highest area under the curve among commonly used non-invasive risk scores for predicting NAFLD in HIV-uninfected persons (0.771), and an affirmative score also imparts a 224% increased risk of cardiovascular and liver-related mortality [9].

To our knowledge, only one study to date has attempted to determine the predictive ability of the LFS among HIV-infected persons. In that study, a LFS>−0.945 was 100% sensitive and 84% specific in HIV-infected persons with ≥ 5% biopsy-proven steatosis (n=9) vs. HIV-uninfected controls with no steatosis by ultrasound (n=19) [10].

However, the accuracy of this finding is compromised by the small sample size and failure to match controls using similar techniques for steatosis identification. Despite these limitations, the authors concluded that the LFS is a “reasonably accurate” method for diagnosing hepatic steatosis in HIV-infected persons.

As validation in a larger, well-characterized HIV-infected cohort is needed prior to implementation in clinical practice, we aimed to compare LFS-and L/S ratio-defined NAFLD prevalence among HIV-infected and HIV-uninfected men in the Multicenter AIDS Cohort Study (MACS), as well as to determine the ability of the LFS to accurately identify NAFLD in HIV-infected men.

Research Methodology

Study population

We conducted a cross-sectional study within the MACS, an on-going, multicenter (Pittsburgh, PA; Baltimore, MD/Washington, DC; Chicago, IL; and Los Angeles, CA), prospective, observational cohort study of the natural history of HIV infection in men who have sex with men.

The MACS began in 1984 and includes men with and without HIV-1 infection. The MACS collects biological and behavioral data from study participants every six months through interviews, physical examinations, laboratory testing, and biological specimen collection [4]. Details regarding participant selection, sample characteristics, and study design have been previously published [11].

This analysis includes men enrolled in the MACS CVD2 substudy, who were required to: be 40-70 years of age, not have a history of heart surgery (coronary artery bypass grafting or valve surgery) or coronary angioplasty, weigh ≤300 pounds and be able and willing to provide informed consent.

Outcome measurements

The LFS is defined as

$$LFS = -2.89 + 1.18\left[\begin{matrix}(Yes = 1, No = 0)\\ MetabolicSyndr.\end{matrix}\right] + 0.45\left[\begin{matrix}(Yes = 2, No = 0)\\ TypeIIDM\end{matrix}\right] + 0.15(insulin[mU/L]) + 0.04(AST[U/L]) - 0.94\left[\frac{AST}{ALT}\right]$$

Among participants of the third National Health and Nutrition Examination Survey (NHANES III) aged 20-74 years without other known causes of liver disease, a LFS ≥ 1.257 detects mild steatosis or greater with 95% specificity and 51% sensitivity, whereas a score ≤ −1.413 excludes steatosis with 52% specificity and 95% sensitivity [9].

Single slice, L4-L5 abdominal CT scans were performed locally but interpreted centrally at the Los Angeles Biomedical Research Institute (Torrance, CA) using GE Advantage Workstation® (Version 4.4, GE Healthcare, Milwaukee, WI) by an experienced reader. The mean Hounsfield Unit (HU) value of 3 round regions of interest of each the liver and spleen were used for calculation of L/S density ratios (<10% biopsy-proven steatosis sensitivity 46%, specificity 94%; 10-25% steatosis sensitivity 57%, specificity 88%;>25% steatosis sensitivity 72%, specificity 95%) [12].

Clinical and demographic characteristics

Age, race, level of education, smoking history, medication use, and diagnosis history were assessed by self-report. Current metabolic diagnoses were confirmed by laboratory or medication use. AIDS and other clinical events were confirmed via medical record review. Hepatitis B virus (HBV) infection was defined by HBV surface antigen positivity.

Chronic hepatitis C virus (HCV) infection was defined as plasma HCV RNA positivity. Metabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) definition, which requires the presence of ≥ 3 of the following: systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg, triglycerides ≥ 150 mg/dL, high-density lipoprotein (HDL)<40 mg/dL, fasting plasma glucose ≥ 100 mg/dL, and waist circumference ≥ 102 cm [13,14]

Use of blood pressure-, lipid-, or glucose-lowering medications qualified a participant as meeting the respective criterion. Total testosterone was measured by liquid chromatography mass spectrometry (LCMS). Free testosterone was calculated from total testosterone and sex hormone-binding globulin (SHBG) as previously described [15].

Analytic methods

Cross-sectional analyses were conducted for all participants who reported<3 alcoholic drinks daily. For HIV-infected men, analyses were restricted to persons with undetectable plasma HIV-1 RNA at the time of CT and who were receiving antiretroviral therapy (ART).

Demographics and clinical characteristics were compared between the two groups using the Wilcoxon Rank-Sum test for continuous variables and the Chi-square test for categorical variables. LFS and L/S ratios were calculated and analyzed as both continuous and categorical variables. LFS was dichotomized at 1.257 and L/S ratio was dichotomized at 1.0. Participants with agreement between LFS and L/S ratio (LFS>1.257 and L/S ratio<1.0 or LFS ≤ 1.257 and L/S ratio ≥ 1.0) were considered to be concordant. Participants for whom the measures disagreed were categorized as discordant. Concordance was summarized overall and by body mass index (BMI) category (≤ 24.9, 25.0-29.9, ≥30 kg/m^2) within HIV serostatus category to determine whether rates of concordance differ by HIV serostatus and/or BMI.

Spearman's correlations quantified the strength of relationships between LFS and L/S ratio overall and by HIV serostatus. Correlations were also conducted by BMI category and for the subset of men who were HCV-uninfected. Multivariable linear regression adjusting for age, race, BMI, LFS components, total testosterone levels (as hypogonadism has been associated with NAFLD) and HIV serostatus determined factors associated with discordance in LFS-and L/S ratio-defined NAFLD prevalence. All statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC) [16,17]. A two-sided p-value<0.05 was considered statistically significant.

Results

Participant characteristics

Among the 526 participants (308 HIV-infected, 218 HIV-uninfected) included in this analysis, the median age was 54 years, and the median BMI was 27 kg/m^2. HIV-infected men had a median CD4+T lymphocyte count of 609 cells/mm^3.

Thirty-eight percent of participants were non-white. A comparison of demographic and clinical characteristics between HIV-infected and HIV-uninfected control men is presented in Table 1. Briefly, HIV-infected men were younger (median age 53 vs. 55 years, p<0.001), had a lower median BMI (26 vs. 27 kg/m^2, p=0.005) and were more likely to have metabolic syndrome (38% vs. 28.9%, p=0.04) and HBV infection (4.5% vs. 0.9%, p=0.02) than HIV-uninfected men.

HIV-infected men also had higher transaminase (AST: 25 vs. 21 IU/mL, p<0.001; ALT: 27 vs. 21 IU/mL, p<0.001) and total testosterone levels (621.7 vs. 511.3 ng/dL, p=0.007), likely due to higher SHBG levels among HIV-infected MACS men [18].

NAFLD prevalence

NAFLD prevalence by LFS and L/S ratio was 28% and 15%, respectively, for FllV-infected men, and 20% and 19% for HIV-uninfected men (Table 2). NAFLD prevalence was significantly higher among HIV-infected men compared to HIV-uninfected men by LFS (p=0.002) but not L/S ratio.

Discordance in identification of NAFLD by LFS vs. CT

More HIV-infected men had NAFLD by LFS ≥ 1.257 (28%) than by L/S ratio<1.0 (15%), representing greater discordance between these two methods in NAFLD identification among HIV-infected men. L/S ratio and LFS discordance in HIV-infected men occurred across all BMI categories, but primarily at BMI<30 kg/m^2 among HIV-uninfected men (Table 3). The correlation between LFS and L/S ratio improved for all men with increasing BMI and with the exclusion of HCV-infected men (Table 4).

In multivariate analysis adjusting for age, race, BMI, LFS components, total testosterone levels and HIV serostatus, only per ng/dL lower total testosterone levels were significantly associated with LFS and L/S ratio discordance (odds ratio [interquartile range] 1.003 [1.00, 1.006], p=0.03) (Table 5). Components of the LFS were included in the multivariate analysis as reasons for metabolic disturbances in HIV-infected men may differ from those in HIV-uninfected men [18]. HIV−infected men with NAFLD by LFS had significantly lower total testosterone levels compared to HIV-infected men without NAFLD by LFS (496 vs. 665 ng/dL, p<0.001) (Table 6). Free testosterone levels were considered for the model but had no statistically significant relationship (data not shown).

Discussion

In this large and well-characterized group of men participating in the MACS, we observed that NAFLD prevalence did not differ by HIV serostatus when defined using CT L/S ratio,

but was substantially higher among HIV-infected men when defined using the LFS. Accordingly, HIV-infected men were more likely to have disagreement between L/S ratio- and LFS-defined NAFLD identification compared to HIV-uninfected men, in whom both methods performed similarly. Discrepancies between L/S ratio-and LFS-defined NAFLD occurred across BMI strata for HIV-infected men, while such discrepancies among HIV-uninfected men occurred primarily at BMI<30 kg/m^2. Among HIV-infected men, L/S ratio and LFS discordance decreased with increasing BMI and the exclusion of HCV co-infected men. The decrease in discordance with the exclusion of HCV-infected men is consistent with a previously published study demonstrating that the LFS is more sensitive and specific in predicting steatosis in HIV-infected persons without HCV co-infection compared to HIV/HCV co-infected patients [10].

With a CT-defined NAFLD prevalence of 13% among HIV-infected men vs. 19% among HIV-uninfected men, NAFLD prevalence among HIV-infected MACS men is lower than in other published cohorts [4]. An analysis of a subgroup of participants in the Women's Interagency HIV Study (WIHS) and the Study of Visceral Adiposity, HIV, and HCV: Biologic Mediators of Hepatic Steatosis (VAHH) also observed less hepatic steatosis by magnetic resonance spectroscopy among HIV-infected compared to HIV-uninfected women, though no significant difference in liver fat fraction by HIV serostatus was observed in men [19]. However, this study population differs significantly by sociodemographic parameters from the MACS, most notably in that the MACS included only men, has proportionally more Caucasians, and fewer participants with HCV infection or history of injection drug use [19].

However, NAFLD prevalence determined by LFS among HIV-infected MACS men in this analysis (28%) more closely mirrors published prevalence rates among other HIV-infected cohorts in the United States and Europe than the NAFLD prevalence in our cohort determined by L/S ratio (15%). Crum-Cianflone and colleagues observed a NAFLD prevalence of 31% by ultrasound in their cohort of HIV-infected individuals without viral hepatitis co-infection or alcohol abuse [20]. Guaraldi and colleagues observed a NAFLD prevalence of 37% by L/S ratio among patients referred to their HIV metabolic clinic in Modena, Italy who did not have viral hepatitis coinfection or heavy alcohol use [21]. Additionally, a small, prospective study conducted by Sterling and colleagues reported a rate of 65% biopsy-confirmed steatosis in their population of HIV-infected individuals without HBV, HCV, alcohol abuse or diabetes mellitus [22].

There are several reasons that may explain the discordance in LFS and L/S ratio test performance by HIV serostatus. First, it is possible that HIV-infected men may have a greater frequency of mild to moderate steatosis, for which the L/S ratio is less sensitive. CT assessment of NAFLD has been critiqued for its reduced ability to detect mild to moderate steatosis compared to MRI or magnetic resonance spectroscopy, and, although a recent-meta analysis reported that even mild steatosis could be detected on CT, sensitivity remained low when steatosis did not exceed 25% (<10% biopsy-proven steatosis sensitivity 46%, specificity 94%; 10-25% steatosis sensitivity 57%, specificity 88%;>25% steatosis sensitivity 72%, specificity 95%) [12].

Another potential reason for the observed discordance in L/S ratio-and LFS-defined NAFLD prevalence in this analysis could be the differing relationships between insulin resistance and hepatic steatosis among HIV-infected compared to HIV-uninfected persons. Combination ART regimens, particularly those that include protease inhibitors, can cause lipid abnormalities and increased insulin resistance, altering the LFS calculation [23–25]. In addition, older ART medications may contribute to insulin resistance in HIV-infected persons through direct mechanisms or indirectly by causing lipoatrophy [26]. Finally, there may be competing causes of elevated hepatic transaminases in HIV-infected men that could result in greater discordance between LFS and L/S ratio, although we attempted to account for this in our multivariable modeling strategy.

While individual effect sizes for the variables included in our multivariate analysis were small, cumulative effect sizes could be large. Of note, in the present analysis, lower testosterone levels were associated with greater discordance between L/S ratio and LFS. However, HIV-infected men in our cohort had statistically higher testosterone levels compared to HIV-uninfected men. While the reason for this discrepancy is unknown, higher SHBG levels in HIV-infected men in this cohort may have resulted in apparently higher testosterone levels among HIV-infected men [18]. Further, differential rates of exogenous testosterone use may have existed by HIV serostatus.

This study has several limitations, notably its cross-sectional design and its relatively homogenous population. This analysis included only men, limiting the generalizability of the results to women. In addition, neither LFS nor L/S ratio are a gold standard for NAFLD diagnosis, and, ultimately, liver biopsy data are needed to confirm whether L/S ratio or LFS is a more accurate NAFLD diagnostic tool in the setting of HIV infection. However, these data are provocative, and strengths of our analysis include our large sample size, the well-characterized nature of both the HIV-infected and HIV-uninfected men and the fact that imaging and labs were obtained as part of a research protocol and not in response to the need for clinical evaluation.

Conclusion

In conclusion, LFS and CT L/S ratio provided similar estimates of NAFLD prevalence among HIV-uninfected men, as would be expected given the previous validation of both techniques against biopsy-confirmed hepatic steatosis in the general population. However, NAFLD prevalence was much higher in HIV-infected men by LFS vs. L/S ratio, and we identified a high frequency of within-person discordance between LFS-and L/S ratio-defined NAFLD among HIV-infected men. Future studies that include liver biopsies are needed to determine the optimal tool for non-invasive NAFLD diagnosis in HIV-infected persons.

Acknowledgments

Grant Support

NIH grants U01 AI035040, K23AI110532 to JEL, K23AG050260 and R01AG054366 to KME, K24AI120834 to TTB and R01HL095129 to WSP, as well as American College of Gastroenterology Junior Faculty Development Award to JCP. This work was also supported by grants to the Multicenter AIDS Cohort Study (MACS): Johns Hopkins University Bloomberg School of Public Health (Joseph Margolick, Todd Brown), U01-AI35042;

Northwestern University (Steven Wolinsky), U01-AI35039; University of California, Los Angeles (Roger Detels, Oto Martinez-Maza), U01-AI35040; University of Pittsburgh (Charles Rinaldo), U01-AI35041; and the Center for Analysis and Management of MACS at Johns Flopkins University Bloomberg School of Public Health (Lisa Jacobson, Gypsyamber D'Souza), UM1-AI35043. The MACS is funded primarily by the National Institute of Allergy and Infectious Diseases, with additional co-funding from the National Cancer Institute, the National Institute on Drug Abuse, and the National Institute of Mental Health. Targeted supplemental funding for specific projects was also provided by the National Heart, Lung, and Blood Institute and the National Institute on Deafness and Communication Disorders. MACS data collection is also supported by UL1-TR001079 (JHU ICTR) from the National Center for Advancing Translational Sciences (NCATS) a component of the National Institutes of Health (NIH), and the NIH Roadmap for Medical Research. The contents of this publication are solely the responsibility of the authors and do not represent the official views of the NIH, Johns Hopkins ICTR or NCATS. The MACS website is located at http://aidscohortstudy.org/.

Abbreviations:

ART:
Antiretroviral Therapy

BMI:
Body Mass Index

CAP:
Controlled Attenuation Parameter

CT:
Computed Tomography

HBV:
Hepatitis B Virus

HCV:
Hepatitis C Virus

HDL:
High-density Lipoprotein

HIV:
Human Immunodeficiency Viru

HIV+:
HIV-infected

HIV−:
HIV-non-infected

HU:
Hounsfield Unit

LCMS:
Liquid Chromatography Mass Spectrometry

LFS:
Liver Fat Score

L/S:
Liver-to-Spleen

MACS:
Multicenter AIDS Cohort Study

MRI:
Magnetic Resonance Imaging

NAFLD:
Non-alcoholic Fatty Liver Disease

NCEP ATP III:
National Cholesterol Education Program Adult Treatment Panel III

NHANES III:
Third National Health and Nutrition Examination Survey

SHBG:
Sex Hormone-Binding Globulin

Study of Visceral Adiposity HIV and HCV:
Biologic Mediators of Hepatic Steatosis (VAHH)

WIHS:
Women's Interagency HIV Study

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Table 1:

Demographic and clinical characteristics *.

Variables	HIV-infected (n=308)	HIV-uninfected (n=218)	p-value
Age (years)	52.8 (48.1, 58.4)	54.7 (50.7, 62.3)	<0.001
Non-white race	39.60%	35.30%	0.36
Current smoking	19.50%	16.80%	0.64
BMI (kg/m^2)	26.1 (23.6, 28.7)	27.0 (24.2, 30.0)	0.005
Waist circumference (cm)	95.5 (89.2, 103.2)	97.0 (88.9, 107.2)	0.05
Hypertension	55.80%	50.00%	0.31
Hyperlipidemia	40.60%	32.60%	0.16
Diabetes	16.60%	13.30%	0.37
Metabolic syndrome [1]	38.00%	28.90%	0.04
Framingham Risk Score ≥ 10%	31.30%	33.80%	0.63
Hepatitis B virus infection [2]	4.50%	0.90%	0.02
Hepatitis C virus infection [3]	10.40%	6.00%	0.1
SGOT/AST (IU/mL)	25.0 (20.0, 33.0)	21.0 (18.0, 26.0)	<0.001
SGPT/ALT (IU/mL)	27.0 (20.0, 39.0)	21.0 (17.0, 30.0)	<0.001
HOMA-IR	3.4 (2.5, 5.0)	2.9 (2.2, 4.7)	0.14
Total testosterone (ng/dL)	621.7 (460.4, 814.3)	511.3 (361.7, 709.9)	0.007
Free testosterone (ng/dL)	86.2 (62.2, 112.3)	87.6 (65.5, 109.8)	0.25
Current CD4+T lymphocyte count (cells/mm^3)	609 (442, 777)	--	--
Nadir CD4+T lymphocyte count (cells/mm^3)	277 (171,382)	--	--
Current PI use	48%	--	--
Current NNRTI use	48%	--	--
Current INI use	19%	--	--
Current NRTI use	89%	--	--
Cumulative PI use (years)	6.3 (1.4, 11.4)	--	--

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Variables	HIV-infected (n=308)	HIV-uninfected (n=218)	p-value
Cumulative NNRTI use (years)	4.3 (1.0, 8.3)	--	--
Cumulative NRTI use (years)	24.4 (17.0, 30.3)	--	--
Cumulative D4T use (years)	0.7 (0.0, 3.8)	--	--

*Median and interquartile range or percent

[1]Defined by NCEP ATP III criteria

[2]Defined by HBV surface antigen positivity

[3]Defined as HCV RNA positivity

BMI: Body Mass Index; SGOT/AST: Serum Glutamic Oxaloacetic Transaminase/Aspartate Aminotransferase; SGPT/ALT: Serum Glutamic Pyruvic Transaminase/Alanine Transaminase; HOMA-IR: Homeostatic Model Assessment Of Insulin Resistance; PI: Protease Inhibitor; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitors; INI: Integrase Inhibitors; NRTI: Nucleoside Reverse Transcriptase Inhibitors; D4T: Stavudine

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Table 2:

NAFLD assessment by LFS and L/S ratio.

Variables	HIV-infected (n=308)		HIV-uninfected (n=218)		
	N	Median (IQR) or percent	N	Median (IQR) or percent	p-value
LFS	-	−0.2 (−1.2, 1.7)	-	−0.8 (−1.6, 0.9)	0.002
LFS>1.257	87	28.20%	44	20.20%	0.02
L/S ratio	-	1.2 (1.1, 1.4)	-	1.2 (1.1, 1.4)	0.33
L/S ratio<1.0	47	15.30%	41	18.80%	0.34
Concordance between LFS and L/S ratio	28	28.70%	19	43.20%	0.15

IQR: Interquartile Range

Table 3:

LFS and L/S ratio concordance by HIV serostatus *.

Variables	HIV-infected			HIV-uninfected		
	N	Concordant	Discordant	N	Concordant	Discordant
Overall	87	29%	71%	44	43%	57%
BMI (kg/m^2)						
≤24.9	15	13%	87%	3	0%	100%
25.0-29.9	28	32%	68%	16	31%	69%
≥ 30.0	40	33%	68%	25	56%	44%

* Restricted to men with LFS>1.257 or L/S Ratio<1.0. Higher LFS or lower L/S ratio values reflect greater steatosis.

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Table 4:

Correlation between LFS and L/S ratio.

Variables	HIV-infected		HIV-uninfected	
	N	Correlation coefficient (p-value)	N	Correlation coefficient (p-value)
Overall	308	−0.20 (<0.001)	218	−0.37 (<0.001)
HCV-Men Only	275	−0.25 (<0.0001)	205	−0.40 (<0.0001)
By BMI (kg/m2)				
<25.0	119	−0.11 (0.22)	73	−0.02 (0.89)
25.0-29.9	120	−0.14 (0.12)	86	−0.38 (<0.001)
≥ 30	57	−0.29 (0.03)	56	−0.54 (<0.001)
By BMI (kg/m2) in HCV-uninfected Only				
<25.0	108	−0.18 (0.06)	68	−0.20 (0.84)
25.0-29.9	105	−0.16 (0.11)	81	−0.40 (<0.001)
≥ 30	52	−0.36 (0.009)	53	−0.62 (<0.0001)

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Table 5:

Multivariate analysis of factors associated with discordance*.

Variables	OR (95% CI)	p-value
Age (per year)	1.09 (0.99, 1.21)	0.09
White race	0.24 (0.06, 0.98)	0.05
BMI (per kg/m^2)	0.97 (0.83, 1.12)	0.64
Metabolic syndrome	0.44 (0.08, 2.59)	0.37
Diabetes	1.67 (0.52, 5.30)	0.39
Insulin (per microIU/L)	0.98 (0.94, 1.01)	0.22
SGOT/AST (per IU/mL)	1.02 (0.95, 1.10)	0.53
SGPT/ALT (per IU/mL)	0.98 (0.94, 1.02)	0.27
HIV+serostatus	1.94 (0.55, 6.82)	0.3
Total testosterone (per ng/dL)	1.003 (1.000, 1.006)	0.03

* HCV excluded as no HCV in concordant group.

BMI: Body Mass Index, SGOT/AST: Serum Glutamic Oxaloacetic Transaminase/Aspartate Aminotransferase; SGPT/ALT: Serum Glutamic Pyruvic Transaminase/Alanine Transaminase

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Table 6:

Testosterone and NAFLD by LFS and L/S ratio.

Total testosterone (ng/dL)					
Variables	-	**HIV-infected**		**HIV-uninfected**	
		N	**Median (Q1, Q3)**	**N**	**Median (Q1, Q3)**
NAFLD by LFS (LFS > 1.257)	Yes	60	496 (356,684)	23	376 (297,723)
	No	127	665 (512,848)	71	524 (381,711)
	p-value	-	p<0.001	-	0.107
NAFLD by CT (L/S Ratio < 1.0)	Yes	33	518 (404,782)	16	485 (333,695)
	No	154	648 (484,817)	78	511 (363,711)
	p-value	-	0.082	-	0.829
Free testosterone (ng/dL)					
Variables	-	**HIV-infected**		**HIV-uninfected**	
		N	**Median (Q1, Q3)**	**N**	**Median (Q1, Q3)**
NAFLD by LFS (LFS > 1.257)	Yes	60	79 (54,102)	23	76 (54,101)
	No	127	90 (64,118)	71	89 (66,112)
	p-value	-	0.18	-	0.511
NAFLD by CT (L/S Ratio < 1.0)	Yes	33	88 (75,106)	16	89 (70,116)
	No	154	85 (59,115)	78	86 (65,106)
	p-value	-	0.697	-	0.499

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