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The prevalence and determinants of NAFLD and MAFLD and their severity in the VA primary care setting

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Abstract

Background & Aims: A recent panel of international experts proposed the disease acronym metabolic (dysfunction) associated fatty liver disease (MAFLD) in lieu of non-alcoholic fatty liver disease (NAFLD). We aimed to estimate the burden of and risk factors for NAFLD and MAFLD, and to examine the concordance between definitions in a Veterans population.

Methods: We conducted a cross-sectional study among randomly selected patients within primary care at the Houston VA. Participants completed a survey, provided blood, and underwent Fibroscan. In the absence of heavy alcohol, HCV and HBV, a CAP median ≥290 dB/m was used to define NAFLD, while MAFLD was defined as CAP median ≥290 dB/m and either BMI ≥25 kg/m^2 or diabetes, or 2 or more of the following: hypertension, high triglycerides, low HDL cholesterol, and high LDL cholesterol.

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Results: The mean age of participants was 50.9 years, 55.4% were women, 42.8% white, and 43.8% Black. The prevalence of NAFLD was 40.6% (82/202). All 82 NAFLD patients had a BMI ≥25 and therefore met our criteria for MAFLD (i.e., 100% concordance). Compared with patients with no metabolic trait, patients with ≥3 traits 48-fold (adjusted OR, 47.6; 95% CI, 11.3–200) higher risk of NAFLD/MAFLD. Overall, 19 participants (9.4% of the total, 15.9% of NAFLD) had at least moderate fibrosis.

Conclusions: NAFLD was present in 40% of veterans registered in primary care; 9.4% of Veterans had at least moderate hepatic fibrosis, with most having concurrent NAFLD. There was perfect concordance between NAFLD and the alternative MAFLD definition.

Keywords

fatty liver; obesity; Veterans; liver cancer

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is defined by excessive fat in the liver presumably related to systematic insulin resistance in the absence of significant alcohol drinking, and is the most common chronic liver disease worldwide.[1] However, it has become apparent that the threshold of current or past alcohol drinking is unclear, that both alcohol and non-alcohol causes of fatty liver can coexist in the same person, and that fatty liver can also occur in the presence of and after the successful treatment of hepatitis C and B. Therefore, in 2020, a panel of international experts proposed the disease acronym metabolic (dysfunction) associated fatty liver disease (MAFLD). However, discussions over nomenclature for NAFLD are ongoing,[2,3] with The American Association for the Study of Liver Diseases (AASLD), The European Association for the Study of the Liver (EASL) and other pan-national liver societies working to produce a DELPHI-based consensus.

MAFLD is defined as the presence of hepatic steatosis (histological, imaging or blood biomarker evidence of hepatic steatosis) plus at least one of three metabolic criteria (overweight/obesity, type 2 diabetes, or evidence of metabolic dysregulation such as dyslipidemia).[4,5] The important distinction between MAFLD and NAFLD is that the MAFLD criteria requires the presence of metabolic dysfunction, but does not require exclusion of patients with concomitant heavy alcohol intake or other chronic liver diseases.[4,5] However, the concordance between NAFLD and MAFLD and hence the additional yield of MAFLD, if any, over NAFLD is unclear. In the primary care setting, where prevalence of active viral hepatitis is low, we expect similar and high concordant prevalence because almost all NAFLD patients are overweight or obese. Findings from a recent analysis of data from the 1988–1994 cycle of the U.S. National Health and Nutrition Examination Surveys (NHANES) show 30% prevalence of both MAFLD and NAFLD in the U.S. general population.[6] Likewise, prevalence estimates for NAFLD and MAFLD were 96.1% concordant in the most recent (2017–2018) NHANES cycle, where NAFLD/MAFLD were defined using Fibroscan.[7]

In addition, whether the MAFLD criteria performs equally well or better than the NAFLD criteria for identifying patients with at least moderate fibrosis has not been

thoroughly examined. NAFLD encompasses several stages of increasing severity and worsening prognosis, from simple hepatic steatosis to nonalcoholic steatohepatitis (NASH; characterized by liver cell injury). NASH is a progressive condition which can lead to cirrhosis in 20% of patients and is associated with an increase in both hepatic and non-hepatic (e.g., cardiovascular) morbidity and mortality.[8–11] Better identifying severity of fibrosis by applying the MAFLD versus NAFLD definition may help better determine those at highest risk of poor outcomes. A recent study among 765 Japanese patients with fatty liver disease (identified from a larger cohort of health check examinees) found that MAFLD had better ability to identify patients with significant fibrosis than the NAFLD definition.[12] Whether this holds for a U.S.-based population remains unclear. Participants in NHANES who met the definition of NAFLD but not the MAFLD criteria appeared healthier and had low risk of adverse outcomes, but more data are required.[6]

To address further the utility of the MAFLD definition both in its concordance with NAFLD and its accuracy in identifying patients with at least moderate hepatic fibrosis, we performed a cross-sectional study among randomly selected Veterans in primary care to (1) estimate the burden of MAFLD and NAFLD, and (2) examine the accuracy of MAFLD and NAFLD definitions to identify patients with at least moderate fibrosis. Given the Veteran population is disproportionately highly affected with obesity and diabetes, we hypothesize that there is a high proportion of patients with MAFLD in the VA primary care setting, with high concordance of the MAFLD and NAFLD diagnostic criteria.

METHODS

Study Population

We conducted a single center cross-sectional study with prospective recruitment among patients actively registered within primary care at the Michael E. DeBakey Veterans Affairs (VA) Medical Center (MEDVAMC) in Houston, Texas. The study was approved by the Institutional Review Boards for MEDVAMC and Baylor College of Medicine. All participants provided written informed consent to take part in the study. A full description of the study population and procedures are provided in Supplementary Materials.

Fibroscan, and the Diagnosis of Fatty Liver and Hepatic Fibrosis

Participants underwent Fibroscan (Echosens, Paris, France) examination where vibration-controlled transient elastography (VCTE) was used to obtain measurements of liver fat (controlled attenuation parameter [CAP]) and liver fibrosis (liver stiffness measurement [LSM]). Participants were in the supine position during the procedure with the right arm in maximal abduction and the skin exposed in the right upper quadrant. The VCTE probe was positioned in the intercostal space over the right lobe of the liver. For all examinations, the M probe was applied first; however, the operator switched to the XL probe if needed based on the recommendations of the device and the manufacturer's instructions. The trained operator obtained a minimum of 10 measurements from each participant, and the device calculated the median CAP and LSM values along with the interquartile range. All studies were reviewed by a qualified hepatologist to ensure quality. We excluded examinations from analysis if they were unreliable, which was defined as an interquartile range/median ratio

>0.30 when the median LSM was >7 kPa.[13] A success rate of more than 60% and the ratio of the interquartile range to the median of 10 measurements (IQR/M) being 0.3 or less defined successful readings.[14]

Diagnosis of NAFLD and MAFLD

Study participants with hepatic steatosis by Fibroscan were defined as having NAFLD, while those without hepatic steatosis were defined as non-NAFLD controls. We defined MAFLD as participants with hepatic steatosis by Fibroscan who also had either BMI ≥25 kg/m^2 or diabetes, or in the absence of either BMI ≥25 kg/m^2 or diabetes had 2 or more of the following: hypertension, high triglycerides, low HDL cholesterol, and high LDL cholesterol. The non-MAFLD (control) population referred to participants who do not meet the above conditions for MAFLD. According to alcohol consumption, NAFLD was further refined by excluding those with heavy drinking (>14 drinks/week for males and >7 drinks/week for females), and MAFLD patients were further classified as MAFLD with any current alcohol intake and MAFLD without any current alcohol intake. We chose the cutoff values of LSM >7 kPa for at least moderate hepatic fibrosis[15] and cutoff of CAP median ≥290 dB/m for hepatic steatosis.[7,16] In sensitivity analyses, according to recent guidance from EASL,[17] we used a lower cut-off for hepatic steatosis (>275 dB/m) and used a higher cut-off for at least moderate hepatic fibrosis (≥8 kPa).

Statistical analysis

We calculated prevalence of NAFLD, MAFLD and at least moderate fibrosis among the overall study population. Concordance between MAFLD and NAFLD definitions was assessed using Cohen's kappa coefficient (κ) of agreement. κ values <0.20 indicated poor agreement, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial and 0.81–1.0 almost perfect agreement between the two definitions. The Student t-test (for variables normally distributed), the Mann-Whitney U-test (for variables non-normally distributed or sample size of the group is too small to have adequate power for testing normality), the Chi-squared test (for categorical variables) and the Fisher's exact test (for categorical variables with expected small cell counts) were used to examine for differences between patients with and without NAFLD/MAFLD and with and without at least moderate fibrosis. We used unconditional multivariate logistic regression to calculate odds ratios (ORs) and associated 95% confidence intervals (95% CIs) for associations with risk of MAFLD/NAFLD. The final multivariate models included age, sex and race/ethnicity, as well as factors associated with MAFLD/NAFLD in univariate analyses. Because it is common for an individual to have multiple metabolic traits (diabetes, hypertension, dyslipidemia, obesity), we modeled them as additive indicators (as number of traits, from 0 to 4). We also examined the independent association of MAFLD/NAFLD with risk of at least moderate fibrosis in a logistic regression model adjusted for age, sex and race/ethnicity. All analyses were conducted using Stata 16.1 (StataCorp LP, College Station, TX) and all tests for statistical significance two-sided at $\alpha = 0.05$.

RESULTS

We consented 300 participants, of these 298 had complete surveys, 295 had research blood samples, and 226 had liver Fibroscan (214 had informative results) at the time of the current analysis. Twelve participants were subsequently eliminated from analysis after completing the study activities, 9 because of excessive alcohol consumption reported on the survey and 3 because of HBV or HCV infection detected in the study blood sample (i.e., met exclusion criteria only determined after study activities were completed). The characteristics of the remaining 202 with informative Fibroscan results are shown in Table 1. The mean age of participants was 50.9 years (standard deviation, 12.0; range 23–70) and 112 (55.4%) were female. The racial/ethnic distribution was 42.8% white, 43.8% Black, and 13.4% were of other race/ethnicity. Self-reported ethnicity was Hispanic in 15.8% and non-Hispanic white in 34.2%. The mean BMI was 31.6 kg/m^2, and the percent of participants with overweight or obesity, diabetes and hypertension were 85.1%, 25.3%, and 45.1%, respectively. Over half (56.9%) of participants were current alcohol drinkers (Table 1), with an average consumption of 0.35 drinks per day.

The prevalence of NAFLD was 40.6% (82 of 202 participants) (95% CI, 33.8%–47.4%). Because all 82 patients with CAP median score ≥290 also had a BMI ≥25, all NAFLD patients were also classified as having MAFLD (i.e., 100% concordance between NAFLD and MAFLD; $\kappa = 1.0$). Thus, a total of 120 participants did not meet either NAFLD or MAFLD diagnostic criteria. When using the lower threshold of >275, we found that 96 (47.5%) patients had NAFLD and all 96 also met the MAFLD diagnostic criteria (Supplementary Table 1). Among MAFLD patients, 51.2% were current alcohol drinkers and 48.8% were without any current alcohol intake. Compared to participants without NAFLD/MAFLD, those with NAFLD/MAFLD were older on average (mean age, 53.8 vs. 48.9 years; $p<0.01$), and more likely to be male (54.9% vs. 37.5%; $p=0.02$). There were no differences between those with and without NAFLD/MAFLD in terms of race/ethnicity, current smoking status, or current alcohol use (Table 1). As expected, participants with NAFLD/MAFLD had a worse metabolic profile, including significantly higher frequencies of diabetes ($p<0.01$), dyslipidemia ($p<0.01$) and hypertension ($p=0.01$) as well as higher levels of liver enzymes (ALT and AST) compared to participants without NAFLD/MAFLD. Similarly, liver stiffness was higher in the NAFLD/MAFLD group (Table 1). Compared to MAFLD patients without any alcohol use, those with any current alcohol use were younger, on average, were less likely to have diabetes (33.3% vs. 45.0%) and less likely to have hypertension (47.6% vs. 70.0%) but were more likely to have LSM ≥8 (11.9% vs. 7.5%).

In the multivariable models, male sex was associated with over 2-fold higher risk of NAFLD/MAFLD and non-Hispanic Black race/ethnicity was associated with lower risk of NAFLD/MAFLD, while there was no difference between Hispanic and non-Hispanic whites (Table 2). When examining each metabolic trait separately, and when simultaneously adjusted, obesity (adjusted OR, 9.36; 95% CI, 4.29–20.5), diabetes (adjusted OR, 2.54; 95% CI, 1.08–5.97), and dyslipidemia (adjusted OR, 2.22; 95% CI, 1.02–4.84) were independently associated with increased risk of NAFLD/MAFLD. However, there was no association with hypertension (adjusted OR, 1.54; 95% CI, 0.71–3.35). Compared with participants with no metabolic traits, the risk of NAFLD/MAFLD was 5-fold (adjusted OR,

5.26; 95% CI, 1.39–19.9), 11-fold (adjusted OR, 10.5; 95% CI, 2.71–40.7), and 48-fold (adjusted OR, 47.6; 95% CI, 11.3–200) higher for participants with 1, 2, and ≥3 traits, respectively (Table 2). Similar associations were observed in sensitivity analyses defining hepatic steatosis at a lower threshold (Supplementary Table 2).

In 202 participants with informative liver Fibroscan results, 19 (9.4%) had at least moderate hepatic fibrosis. Among participants with at least moderate fibrosis, most (68.4%) had NAFLD/MAFLD, compared to 37.7% of those without at least moderate fibrosis. NAFLD/MAFLD status was associated with 4-fold higher risk of at least moderate fibrosis (adjusted OR, 3.65; 95% CI, 1.25–10.7). The distributions of age, sex, race/ethnicity, current smoking status and current alcohol use were no different between participants with and without at least moderate hepatic fibrosis (Table 3); participants with at least moderate hepatic fibrosis had higher number of metabolic traits (≥2 traits, 88.9% vs. 48.2%, p=0.09). Overall, 6 patients had LSM 8–12 and 3 had LSM >12. Using LSM ≥8 to define at least moderate fibrosis, 9 (4.5%) met the criteria (Supplementary Table 3).

DISCUSSION

The main findings of our study, conducted in a random age and sex stratified sample of U.S. Veterans, are that (1) NAFLD is present in almost 40% of Veterans registered in primary care; (2) there is very high concordance of NAFLD and MAFLD definitions (100% in this study) in a primary care setting where the prevalence of heavy alcohol, HCV and HBV is low, but prevalence of overweight/obesity is very high; (3) approximately 9% of Veterans had at least moderate hepatic fibrosis and more than two thirds (68.4%) of these also had NAFLD/MAFLD; and (4) In addition to male sex, which was associated with 2-fold higher risk of NAFLD/MAFLD, we also found that a higher burden of metabolic traits (in particular, obesity, diabetes, and dyslipidemia) was linked with higher risk of NAFLD/MAFLD. Compared to non-Hispanic whites, we found lower risk of NAFLD/MAFLD for non-Hispanic Blacks.

The 40% NAFLD/MAFLD prevalence that we detected by CAP is consistent with recent data from the U.S. general population.[7,18] Likewise, our estimate of 9% prevalence of at least moderate hepatic fibrosis Veterans in primary care is similar to reports from other U.S.-based general population studies.[18] Our finding of high concordance between NAFLD and MAFLD in the primary care setting, where prevalence of viral hepatitis is low, overweight/obesity is higher, and after excluding patients with heavy alcohol use, is consistent with prior population-based studies in the U.S. Lin et al., analyzing data from NHANES III (1988–1994), found that 31.2% of participants had ultrasound-diagnosed NAFLD compared with 33.2% having MAFLD.[6] Overall, approximately 5% of patients meeting the criteria for NAFLD in that study did not meet the criteria for MAFLD. Had we kept the 9 patients with heavy alcohol use according to our study survey, 100% of participants in our study with NAFLD would still have also met the MAFLD definition since all 9 had concurrent overweight/obesity. Using data from the latest cycle of NHANES (2017–218), Ciardullo et al. showed that 37.1% of participants met the NAFLD criteria while 39.1% met the MAFLD criteria. Overall agreement was 96.1% between definitions, with only 2.7% of participants with NAFLD not meeting the MAFLD criteria.[7] Because overall concordance between the

NAFLD and MAFLD definitions is likely to be affected by the underlying prevalence of overweight/obesity in the general population, our findings are more aligned with the 2017–2018 NHANES data, with lower concordance in the 1988–1994 data mainly attributable to that cycle having a higher percent of participants with normal weight (44%) compared with 2017–2018 cycle (26.9%) and our study (15.9%). Despite great concordance of NAFLD and MAFLD after excluding the obvious causes active hepatitis and heavy alcohol use, from a clinical standpoint, MAFLD may be more encompassing because about half of NAFLD/MAFLD drink any alcohol and 10% drink more than minimal amounts (1–2 drinks/day).

Consistent with some prior analyses we found that males had higher risk of NAFLD than females and that non-Hispanic Blacks had lower risk of NAFLD than non-Hispanic whites.[18–20] However, unlike prior studies,[20–22] Hispanic ethnicity and smoking status were not associated with increased risk of NAFLD in our study. Our results provide data on the strength and extent of the associations between metabolic traits and NAFLD/MAFLD.[23,24] When considered individually, we found that obesity, diabetes and dyslipidemia were independently associated with increased risk of NAFLD. However, we know that most patients have multiple metabolic traits. We found that, compared to those with no metabolic traits, risk of NAFLD was >12-fold higher for those with 2 or more metabolic traits. Identifying and treating patients with multiple co-occurring traits might have a larger impact on overall incidence of NAFLD/MAFLD.

The strengths of this study include the representative population-based design, the comprehensive surveys on demographics and lifestyle factors ascertained prior to Fibroscan, thus reducing the differential recall bias between participants with and without NAFLD/MAFLD, and that the study population reflects modern exposure patterns among contemporary populations (including higher prevalence of obesity and diabetes). However, our findings should be interpreted considering some limitations. Firstly, we could only estimate the prevalence of steatosis and fibrosis as liver biopsy (the gold-standard technique for the assessment of liver steatosis) is not well suited for large population-based studies. Secondly, there are no universally accepted cut-offs for CAP and LSM.[25,26] In this study, we used a CAP threshold of ≥290 dB/m to define NAFLD in our primary analysis. While threshold selected in other studies have varied, and include a range from 248–302, we used this relatively high threshold to be close to the recent guidelines from the American Gastroenterological Association.[27] We did however use a lower threshold of >275 dB/m in accordance with the EASL guideline and found similar findings in terms of concordance of diagnostic criteria for NAFLD and MAFLD and risk factors. Third, the cross-sectional study design limits causal inference. Fourth, our study included patients with metabolic fatty liver disease who may have also had HCV or HBV or have history of moderate alcohol drinking. However, our findings may nonetheless not reflect the true prevalence of MAFLD as we may have excluded patients with MAFLD at screening for heavy alcohol use or HBV/HCV. While this may be an effect of our selection criteria, we opted for enhanced feasibility and representative primary care sample over generalizability. Also, it is possible that our sampling frame of non-healthcare seeking individuals in whom when steatosis was detected was mostly without fibrosis reflects a selection bias in which overweight/obesity are strong and common risk factors for MAFLD/NAFLD (as compared to clinic-based patient populations with disproportionally higher NASH and fibrosis in whom overweight/

obesity is less of an essential risk factor). Because our study was conducted within a U.S.-based VA population, where prevalence of active viral hepatitis is low, our findings may not be generalizable to other populations, including those in Asia, with high prevalence of HBV infection. There may be some selection bias, as individuals with more significant forms of disease may not participate in our study; however, this bias would result in underestimating the true association between factors and NAFLD/MAFLD. Last, the obvious advantage of MAFLD definition is highlighting and allowing for metabolic risk factors of liver disease in the presence of other concomitant risk factors especially alcohol drinking and viral hepatitis. However, the MAFLD definition is less conducive to understanding pathophysiology since the common lesion (steatosis) is a common pathway of multiple etiologies (metabolic, alcohol, viral). It is also not clear if the clinical course or prognosis is similar among patients with steatosis and each of these underlying etiologies. Greater consideration to these limitations (but also advantages) is needed before wider adoption of the MAFLD definition.

In conclusion, NAFLD was highly prevalent (40%) in an unselected primary care population. Importantly, we found that 9% of patients had at least moderate hepatic fibrosis. The overall concordance of diagnostic criteria for NAFLD and MAFLD is high in the U.S. population, characterized by a high prevalence of overweight/obesity and type 2 diabetes. The recent focus on MAFLD vs. NAFLD did not affect the prevalence of the condition in the Veteran population; however, given that the yield is similar, MAFLD may be preferable and easier to be operationalized and better targets the underlying risk factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of interest:

RL serves as a consultant to Aardvark Therapeutics, Altimmune, Anylam/Regeneron, Amgen, Arrowhead Pharmaceuticals, AstraZeneca, Bristol-Myer Squibb, CohBar, Eli Lilly, Galmed, Gilead, Glympse bio, Hightide, Inipharma, Intercept, Inventiva, Ionis, Janssen Inc., Madrigal, Metacrine, Inc., NGM Biopharmaceuticals, Novartis, Novo Nordisk, Merck, Pfizer, Sagimet, Theratechnologies, 89 bio, Terns Pharmaceuticals and Viking Therapeutics. In addition his institutions received research grants from Arrowhead Pharmaceuticals, Astrazeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galectin Therapeutics, Galmed Pharmaceuticals, Gilead, Intercept, Hanmi, Intercept, Inventiva, Ionis, Janssen, Madrigal Pharmaceuticals, Merck, NGM Biopharmaceuticals, Novo Nordisk, Merck, Pfizer, Sonic Incytes and Terns Pharmaceuticals. Co-founder of LipoNexus Inc. All other authors disclose no conflicts of interest.

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What You Need to Know

Background:

Metabolic dysfunction-associated fatty liver disease (MAFLD) is a new terminology updated from non-alcoholic fatty liver disease (NAFLD). The burden of NAFLD/MAFLD and their concordance in high-risk Veteran populations is unknown.

Findings:

We found perfect concordance between NAFLD and MAFLD, and that 40% of veterans in primary care can be diagnosed as MAFLD. 10% of Veterans had at least moderate hepatic fibrosis.

Implications for patient care:

The recent focus on MAFLD vs. NAFLD nomenclature did not affect the prevalence estimate. Given the yield is similar, MAFLD may be easier to operationalize and use clinically.

Table 1.

Characteristics of participants with and without NAFLD

		NAFLD status		
Variable	**Total (N=202) N (%)**	**NAFLD (N=82) N (%)**	**No NAFLD (N=120) N (%)**	**p-value**
Age, years: mean (SD)	50.9 (12.0)	53.8 (10.8)	48.9 (12.4)	<0.01
Sex				
Female	112 (55.4%)	37 (45.1%)	75 (62.5%)	0.02
Male	90 (44.6%)	45 (54.9%)	45 (37.5%)	
Race/Ethnicity				0.51
Non-Hispanic white	69 (34.2%)	33 (40.2%)	36 (30.0%)	
Non-Hispanic Black	83 (41.1%)	29 (35.4%)	54 (45.0%)	
Hispanic	32 (15.8%)	13 (15.9%)	19 (15.8%)	
Other	17 (8.4%)	7 (8.5%)	10 (8.3%)	
Missing	1 (0.5%)	0 (0.0%)	1 (0.8%)	
Smoking status				0.42[≠]
Never	122 (60.4%)	51 (62.2%)	71 (59.2%)	
Former	54 (26.7%)	24 (29.3%)	30 (25.0%)	
Current	25 (12.4%)	7 (8.5%)	18 (15.0%)	
Missing	1 (0.5%)	0 (0.0%)	1 (0.8%)	
Alcohol status				0.34[≠]
Never/Rarely	68 (33.7%)	33 (40.2%)	35 (29.2%)	
Former	18 (8.9%)	7 (8.5%)	11 (9.2%)	
Current	115 (56.9%)	42 (51.2%)	73 (60.8%)	
Missing	1 (0.5%)	0 (0.0%)	1 (0.8%)	
Alcohol (average drinks/day for current drinkers)	0.35 (0.40)	0.33 (0.40)	0.37 (0.40)	0.63
Rarely	1 (0.9%)	0 (0.0%)	1 (1.4%)	0.82[≠]
<1 drink/day	106 (92.2%)	40 (95.2%)	66 (90.4%)	
1-<2 drinks/day	8 (7.0%)	2 (4.8%)	6 (8.2%)	
Diabetes (self-report)	51 (25.3%)	32 (39.0%)	19 (15.8%)	<0.01
Body mass index (kg/m^2)				
Mean (SD)	31.6 (6.2)	35.3 (5.6)	29.1 (5.3)	<0.01
<25	30 (14.8%)	0 (0.0%)	30 (25.0%)	<0.01
25-<30	63 (31.2%)	15 (18.3%)	48 (40.0%)	
≥30	109 (54.0%)	67 (81.7%)	42 (35.0%)	
Dyslipidemia	76 (37.6%)	45 (54.9%)	31 (25.8%)	<0.01
Triglycerides, mg/dL: mean (SD)	141.7 (92.0)	169.4 (97.3)	122.6 (83.4)	<0.01
HDL, mg/dL: mean (SD)	50.7 (15.4)	45.3 (13.4)	54.5 (15.6)	<0.01
LDL, mg/dL: mean (SD)	110.3 (36.9)	106.1 (40.6)	113.3 (34.0)	0.19

		NAFLD status		
Variable	**Total (N=202) N (%)**	**NAFLD (N=82) N (%)**	**No NAFLD (N=120) N (%)**	**p-value**
Total cholesterol, mg/dL: mean (SD)	186.8 (42.0)	181.0 (44.2)	190.8 (40.1)	0.11
Glucose, mmol/L: mean (SD)	113.0 (54.4)	129.2 (66.7)	101.6 (40.4)	<0.01
HbA1c: mean (SD)	6.3 (1.5)	6.8 (1.7)	5.9 (1.2)	<0.01
AST, IU/L: mean (SD)	25.1 (10.7)	27.1 (10.7)	23.7 (10.5)	0.03
ALT, IU/L: mean (SD)	27.5 (14.6)	33.2 (16.5)	23.4 (11.5)	<0.01
Albumin, IU/L: mean (SD)	3.96 (0.33)	3.96 (0.32)	3.96 (0.33)	0.98
Platelet count, (10^9/L): mean (SD)	260.7 (67.5)	263.9 (75.3)	258.6 (61.7)	0.59
Hypertension (self-report)	91 (45.1%)	48 (58.5%)	43 (35.8%)	<0.01
Fibroscan E Median score >7	19 (9.4%)	13 (15.9%)	6 (5.0%)	0.01
MAFLD	82 (40.6%)	82 (100.0%)	0 (0.0%)	<0.01

$^{\neq}$P-value from Fisher's exact test.

Table 2.

Odds ratios and 95% confidence intervals for associations with risk of NAFLD/MAFLD

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Age >50	2.41 (1.34–4.32)	1.74 (0.80–3.81)	1.32 (0.63–2.77)
Male	2.03 (1.15–3.59)	2.85 (1.25–6.54)	2.11 (1.03–4.29)
Race/Ethnicity (ref: Non-Hispanic white)			
Non-Hispanic Black	0.59 (0.30–1.13)	0.44 (0.19–1.01)	0.45 (0.20–0.99)
Hispanic	0.75 (0.32–1.74)	0.45 (0.15–1.39)	0.46 (0.16–1.33)
Other	0.76 (0.29–2.24)	0.64 (0.16–2.56)	0.65 (0.18–2.42)
Current Smoker	0.53 (0.21–1.33)		
Current Drinker	0.68 (0.38–1.19)		
Obese	8.30 (4.23–16.3)	9.36 (4.29–20.5)	
Diabetes	3.40 (1.76–6.59)	2.54 (1.08–5.97)	
Dyslipidemia	3.49 (1.92–6.34)	2.22 (1.02–4.84)	
Hypertension	2.53 (1.42–4.50)	1.54 (0.71–3.35)	
Sum of Metabolic Traits			
1	4.53 (1.23–16.7)		5.26 (1.39–19.9)
2	9.00 (2.44–33.2)		10.5 (2.71–40.7)
3 or 4	44.7 (11.6–173)		47.6 (11.3–200)

CI, confidence interval; IR, odds ratio.

Table 3.

Characteristics of participants with and without moderate hepatic fibrosis

Variable	At least moderate fibrosis (N=19) N (%)	Less than moderate fibrosis (N=183) N (%)	p-value
Age, years: mean (SD)	51.6 (10.9)	50.8 (12.1)	0.79
Sex			
Female	7 (36.8%)	105 (57.4%)	0.09
Male	12 (63.2%)	78 (42.6%)	
Race/Ethnicity			
Non-Hispanic white	5 (26.3%)	64 (35.0%)	0.80[≠]
Non-Hispanic Black	10 (52.6%)	73 (39.9%)	
Hispanic	3 (15.8%)	29 (15.8%)	
Other	1 (5.3%)	16 (8.7%)	
Missing	0 (0.0%)	1 (0.6%)	
Smoking status			
Never	12 (63.2%)	110 (60.1%)	0.78[≠]
Former	4 (21.0%)	50 (27.3%)	
Current	3 (15.8%)	22 (12.0%)	
Missing	0 (0.0%)	1 (0.6%)	
Alcohol status			0.52[≠]
Never/Rarely	5 (26.3%)	63 (34.4%)	
Former	3 (15.8%)	15 (8.2%)	
Current	11 (57.9%)	104 (56.8%)	
Missing	0 (0.0%)	1 (0.6%)	
Alcohol (average drinks/day for current drinkers)	0.16 (0.15)	0.37 (0.41)	0.09
Rarely	0 (0.0%)	1 (1.00%)	1.00[≠]
<1 drink/day	11 (100.0%)	95 (91.4%)	
1-<2 drinks/day	0 (0.0%)	8 (7.7%)	
Diabetes	7 (36.8%)	44 (24.0%)	0.22
Body mass index (kg/m^2)			
Mean (SD)	34.6 (7.3)	31.3 (6.0)	0.03
<25	2 (10.5%)	28 (15.3%)	0.48[≠]
25-<30	4 (21.1%)	59 (32.2%)	
≥30	13 (68.4%)	96 (52.5%)	
Dyslipidemia	13 (68.4%)	63 (34.4%)	<0.01
Triglycerides, mg/dL: mean (SD)	139.7 (71.8)	142.0 (94.0)	0.92
HDL, mg/dL: mean (SD)	43.9 (20.0)	51.4 (14.7)	0.05
LDL, mg/dL: mean (SD)	106.5 (35.0)	110.7 (37.2)	0.64
Total cholesterol, mg/dL: mean (SD)	172.7 (36.2)	188.3 (42.4)	0.14

Variable	At least moderate fibrosis (N=19) N (%)	Less than moderate fibrosis (N=183) N (%)	p-value
Glucose, mmol/L: mean (SD)	135.1 (63.7)	110.6 (53.0)	0.06
HbA1c: mean (SD)	6.9 (1.7)	6.3 (1.5)	0.11
AST, IU/L: mean (SD)	34.0 (15.9)	24.2 (9.6)	<0.01
ALT, IU/L: mean (SD)	39.0 (17.9)	26.2 (13.7)	<0.01
Albumin, IU/L: mean (SD)	3.85 (0.37)	3.98 (0.32)	0.10
Platelet count, (10^9/L): mean (SD)	263.5 (74.4)	260.4 (66.9)	0.85
Hypertension	6 (31.6%)	85 (46.5%)	0.22
MAFLD/NAFLD	13 (68.4%)	69 (37.7%)	0.01

[≠]P-value from Fisher's exact test.