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Screening for Non-Alcoholic Fatty Liver Disease (NAFLD) Among Adults in Singapore: A Community-Based Cross-Sectional Study in Tampines Regional Centre

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Abstract

Background & objectives: Non-alcoholic fatty liver disease (NAFLD) is an emerging public health issue affecting 20-30% of the general population globally and up to 40% in Singapore. We aimed to estimate the prevalence of NAFLD and associated risk factors among adults at high risk for NAFLD (≥35 years) in Tampines Regional Centre, Singapore.

Methods: A community-based cross-sectional study was conducted among 392 adults at high risk for NAFLD using simple random sampling in an urban residential area of Singapore. Clinical assessment, blood investigations (liver function tests, lipid profile), and anthropometric measurements were performed. NAFLD was diagnosed using the fatty liver index (FLI >60) and risk stratification for advanced liver fibrosis by using the FIB-4 score. Participants with indeterminate/high-risk FIB-4 scores underwent vibration-controlled transient elastography (VCTE). Prevalence of NAFLD (proportions with 95% confidence interval [CI]) and risk factors associated with NAFLD (multivariable regression) were calculated.

Results: The prevalence of NAFLD among adults at high risk was 33.4% (95% CI: 28.9%-38.2%), and was higher among men (41.2%), those with diabetes mellitus (45.6%), and those with obesity (42.1%). Male sex, Malay ethnicity, diabetes mellitus, elevated alanine aminotransferase, and elevated triglycerides were significantly associated with high risk of NAFLD on multivariable analysis.

Interpretation & conclusions: One in three screened adults had NAFLD, increasing to nearly one in two among those with diabetes. Community-based screening using validated non-invasive tools offers a pragmatic pathway for early NAFLD detection in Singapore's multi-ethnic population.

Keywords: Advanced liver fibrosis - Ethnic disparities - FIB-4 score - Multi-ethnic population - Non-alcoholic fatty liver disease - Risk assessment - Singapore - Vibration-controlled transient elastography

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Introduction

Fatty liver is a condition where at least five per cent of the weight of the liver is contributed by fat[1]. Non-alcoholic fatty liver disease (NAFLD) refers to a state of fatty liver that can result in the absence of significant alcohol intake (≥30 g/day for men and ≥20 g/day for women) and other secondary causes[2]. NAFLD includes multiple entities, from simple fat accumulation to non-alcoholic steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma, potentially progressing to liver failure requiring transplantation[3].

Individuals with type 2 diabetes mellitus (T2DM), overweight or obese individuals, and those with metabolic syndrome are identified as the high-risk group for NAFLD[4]. Globally, NAFLD is now frequently cited as the leading cause of chronic liver disease, affecting 20-30% of the world's general population and 42-70% of individuals with T2DM[5,6]. Overall, 29.6% of Asians have NAFLD, and 10% of deaths in the Asia-Pacific region are attributable to liver cancer and cirrhosis in people with NAFLD[7].

In Singapore, a multi-ethnic city-state with one of the highest diabetes prevalence rates globally, NAFLD represents a significant and growing public health concern. Previous community-based studies have reported NAFLD prevalence of approximately 40% among Singaporean adults, with substantial ethnic variation[8,9]. The condition demonstrates distinct characteristics in Asian populations, including higher prevalence of lean NAFLD (BMI <23 kg/m^2) and greater visceral adiposity at lower BMI thresholds compared to Western populations[10].

Ultrasonography of the abdomen is the recommended modality for diagnosing NAFLD[11,12]. However, in resource-limited community settings, the fatty liver index (FLI) and FIB-4 (Fibrosis-4) score serve as validated proxy indicators for fatty liver and advanced liver fibrosis respectively[13,14]. Vibration-controlled transient elastography (VCTE) is used to identify liver fibrosis with higher sensitivity and specificity[15]. There is an increased risk of cardiovascular disease with NAFLD[16,17].

Population-based screening using a community-based assessment checklist under Singapore's National Population Health Screening programme has facilitated early identification, prevention and control of non-communicable diseases (NCDs), including those at high risk for NAFLD[18]. Given the metabolic diversity of Singapore's population and the rising burden of NAFLD, we aimed to estimate the prevalence of NAFLD and the clinical

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factors associated with high risk of NAFLD among adults aged 35 years and above in Tampines Regional Centre, Singapore.

Materials & Methods

This cross-sectional study was undertaken by the Department of Family Medicine, Singapore General Hospital, in collaboration with the National University of Singapore, Singapore.

Study design and participants: A community-based cross-sectional study was carried out from September 2022 to August 2024 in the urban field practice area of Tampines Regional Centre, which caters to a population of 237,000 residents across five subzones in Singapore[19]. All eligible adults above 35 years residing in Tampines for at least six months who were willing to participate were included in the study. Non-random selection of study site was done. Simple random sampling of participants was done by using random number assignment applying Excel function from the national electronic population registry. The individuals were screened using the community-based assessment checklist and those with a score of more than four were included. Those who tested positive for hepatitis B and C (i.e., hepatitis B surface antigen or active hepatitis C) or taking drugs that cause fatty liver (corticosteroids, methotrexate, tamoxifen, amiodarone) and those with alcohol intake more than recommended (men >30 g/day and women >20 g/day) were excluded. Assuming the prevalence of NAFLD among the high-risk individuals to be 45%, 10% relative precision, 5% alpha error, and 15% non-response rate, the estimated sample size was 385 using the OpenEpi online version 3.01.

Study tools: Sociodemographic and clinical details were collected using data collection proforma. Screening for hepatitis B & C was done using rapid diagnostic kits. The high-performance liquid chromatography method was used for HbA1C testing. Serum albumin, liver enzymes (AST, ALT, GGT), triglycerides, HDL-cholesterol (HDL-C), LDL-cholesterol and total cholesterol were estimated based on spectrophotometry using autoanalyzer (Beckman Coulter AU5800, Brea, California, USA) in a College of American Pathologists-accredited laboratory. Fatty liver index and FIB-4 score online calculators were used to diagnose fatty liver and risk of advanced liver fibrosis (reported as low, indeterminate, high). VCTE (FibroScan®, EchoSens, Paris, France) is a point-of-care non-invasive test using M probe to diagnose advanced liver fibrosis. The M probe is designed for the general adult population and it operates at a central frequency of 3.5 MHz. It measures liver stiffness at

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a depth from 2.5 to 6.5 cm from the skin with a shear wave frequency of 50 Hz. It provides an objective report on fatty liver (S0-S3) and liver fibrosis (F1-F4) expressed as controlled attenuation parameter (CAP) score (in dB/m) and liver stiffness measurement (LSM) score (in kPa), respectively at the same sitting.

Study procedure: According to the stepwise screening cascade under Singapore's National Population Health Screening guidelines[18], population-based screening was carried out using community-based assessment checklist. The line list of individuals with score >4 was obtained, and participants were recruited using simple random sampling. They were interviewed for sociodemographic and clinical history. Height, weight, waist circumference, and blood pressure were recorded following standard protocols. Fasting venous blood samples (8-10 mL) were collected for liver function tests, lipid profile, HbA1c, and platelet count on the same day. After calculating fatty liver index and FIB-4 scores, referral to the tertiary care centre and further management of indeterminate and high-risk individuals for advanced liver fibrosis were carried out as per the operational guidelines for integration of NAFLD into national NCD programmes. The participants with indeterminate and high risk of liver fibrosis were mobilized to the regional health centre by camp basis on eight different days for VCTE (about 5-7 min per participant). For each participant, liver stiffness score was recorded when ten valid measurements were done, and the result was reported as the median of these valid measurements in kilopascals (kPa). VCTE provides information on hepatic steatosis (fat in the liver) and hepatic fibrosis (scarring in the liver) objectively. We used a liver fibrosis scale comprising four grades: F0 (≤7.0 kPa), F1 (7.1-10.0 kPa), F2 (10.1-13.0 kPa), F3 (13.1-16.0 kPa) and F4 (≥16.1 kPa).

Statistical analysis: Data were entered using Epicollect5 mobile app and analysed using STATA v17 software[20],[21]. All the categorical variables were summarized in the form of frequency with percentage. Based on the normality of the distribution of the data, the continuous variables were summarized using mean with standard deviation (SD) or median with interquartile range (IQR). The prevalence of NAFLD (fatty liver index >60) was calculated, and risk stratification (FIB-4 score) was presented as a proportion with 95% CI. Association between sociodemographic details, clinical details with high risk of NAFLD was assessed using Chi-square test or Fisher's exact test. Univariate regression was performed to explore associations of demographic and clinical variables with NAFLD. Variables with P value less than 0.2 in univariate analysis and those of biological relevance were included

in multivariable logistic regression to calculate adjusted prevalence ratios (aPR) with 95% CI. P<0.05 was considered statistically significant.

Results

Participant recruitment and study flow details are depicted in Figure 1. The mean (SD) age of the participants was 52.4 (11.2) years and majority (58.2%) of them were women. The ethnic distribution reflected Singapore's population: Chinese 68.1% (n=267), Malay 18.4% (n=72), Indian 10.7% (n=42), and Others 2.8% (n=11). The mean (SD) BMI was 26.8 (4.6) kg/m² and three in five (62.5%) were found to be obese (BMI ≥25 kg/m²). Central obesity was present in 71.4% of participants. Majority (87.2%) were physically inactive (<150 minutes moderate-intensity exercise weekly). The mean (SD) HbA1C per cent was found to be 6.8 (1.6) per cent. About one-third (34.7%) of the participants were found to have T2DM. Among those without diagnosed diabetes, 18.4% (n=47) had prediabetes (HbA1c 5.7-6.4%). The median (IQR) ALT was 22 (16-34) U/L and 15.3% (n=60) had elevated ALT (>40 U/L for men, >30 U/L for women). The median (IQR) GGT was 28 (20-48) U/L and 12.2% (n=48) had elevated GGT (>50 U/L).

Out of 392 adults at high risk for NAFLD, 38.5% of the participants had low (FLI ≤30), 28.1% had intermediate (FLI 30-60) and 33.4% had high fatty liver index (FLI >60). The median (IQR) fatty liver index was 45 (24-72). The prevalence of NAFLD among adults at high risk for NAFLD aged 35 years and above was found to be 33.4% (95% CI: 28.9%-38.2%).

The prevalence of NAFLD varied significantly by ethnicity: Chinese 31.5%, Malay 41.7%, Indian 38.1%, and Others 27.3% (P=0.04). NAFLD prevalence was higher among men (41.2%) compared to women (27.6%) (P<0.01), and increased with age: 35-44 years (24.3%), 45-54 years (32.8%), 55-64 years (38.9%), and ≥65 years (41.7%) (P=0.02).

The median (IQR) FIB-4 score was 1.12 (0.78-1.58). On risk stratification, 28.3% (n=111) had indeterminate FIB-4 score (1.3-2.67), 4.6% (n=18) had high FIB-4 score (>2.67); These 129 participants (indeterminate and high-risk) were eligible for VCTE imaging. Of these, 22 were unable to undergo VCTE. Finally, 107 participants underwent VCTE. The mean CAP value for fatty liver was 268.4 dB/m. Out of 107 participants, 20 (18.7%) had no fatty liver, 26 (24.3%) had Grade-I, 34 (31.8%) had Grade-II, and 27 (25.2%) had Grade-III fatty liver. The mean LSM value was 8.9 kPa. Majority (n=73, 68.2%) had no liver fibrosis, and 21 (19.6%) had mild fibrosis, eight had moderate fibrosis, four had advanced fibrosis and

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one had cirrhosis. Out of 18 participants with high FIB-4 score, only 5 (27.8%) had VCTE-confirmed advanced fibrosis (F3-F4), out of 111 with indeterminate FIB-4 score, 12 (10.8%) had VCTE-confirmed fibrosis (F2-F4).

Multivariate analysis results are shown in Table I. The prevalence of NAFLD was 1.8 times higher among men, 1.4 times higher among Malays, and 1.7 times higher among people with T2DM. Those with elevated ALT levels were at 1.9 times more risk of developing NAFLD compared to those with normal ALT levels after adjusting for sex, ethnicity, T2DM, and triglycerides. Participants with elevated triglycerides (>150 mg/dL) had 1.3 times higher risk of NAFLD (P=0.03).

Discussion

In our study setting, the population eligible for screening was substantial given Singapore's ageing population demographic profile. The prevalence (33.4%) is consistent with previous Singaporean studies reporting approximately 40% in community settings[8,9], and aligns with the broader Southeast Asian estimate of 40.43%[22]. The slightly lower prevalence in our study may reflect the specific high-risk screening approach rather than general population screening.

The ethnic variation in NAFLD prevalence is a critical finding, with Malay participants demonstrating significantly higher rates (41.7%) compared to Chinese (31.5%). This disparity reflects Singapore's well-documented ethnic differences in metabolic disease susceptibility, with Malay ethnicity consistently showing higher rates of obesity, diabetes, and cardiovascular complications[23]. The persistence of this association after multivariable adjustment suggests genetic, epigenetic, or lifestyle factors specific to this community that warrant targeted intervention.

Our results on multivariate analysis are similar to other studies showing higher prevalence of NAFLD in men and those with T2DM[24–26]. The strong association between elevated ALT and NAFLD (aPR 1.9) supports its utility as a screening biomarker, though the low sensitivity of ALT for detecting NAFLD (present in only 15.3% of our cohort) underscores the need for composite screening tools like FLI.

Though total cholesterol is a known risk factor for NAFLD, our study did not show independent association after adjustment, likely due to collinearity with other metabolic

parameters. The significant association with elevated triglycerides (aPR 1.3) aligns with the pathophysiological role of lipotoxicity in NAFLD progression[27].

The VCTE findings provide important validation of our screening cascade. While 4.6% had high FIB-4 scores suggesting advanced fibrosis risk, only 0.9% had VCTE-confirmed cirrhosis. This discrepancy highlights FIB-4's utility as a screening tool with high negative predictive value, but also its limitation in specificity, particularly in older populations where age elevates scores independently of fibrosis.

NAFLD is associated with metabolic risk factor derangements (T2DM, hypercholesteremia, etc.). A multidisciplinary approach linking high-risk individuals and primary care physicians with specialists through referral pathways and teleconsultation is the need of the hour in Singapore's healthcare system.

The study's main strengths include the use of validated non-invasive tools with good sensitivity and specificity and robust study design. Provision of VCTE at the community level for risk stratification prevented unnecessary referral to higher centres. One of the limitations of the study is that the conclusions drawn pertaining to physical activity and dietary habits were self-reported, unlike using validated questionnaires, though the status of alcohol consumption was confirmed using GGT. Many studies reported a significant association between BMI, high waist circumference, elevated GGT and hypertriglyceridemia with NAFLD. But those variables result in collinearity due to use of fatty liver index and FIB-4 score; hence, these variables could not be used in univariate and multivariable analysis.

Use of validated non-invasive tools at the primary care level and stepwise screening cascade offers a pragmatic pathway for early NAFLD detection, risk stratification, and referral, with direct relevance for Singapore's population-based NCD control programme.

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Conflicts of Interest

None declared.

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Use of Artificial Intelligence (AI)-Assisted Technology for manuscript preparation: The authors confirm that there was no use of AI-assisted technology for assisting in the writing of the manuscript and no images were manipulated using AI.

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Tables and Legends

Table 1. Association between clinical and biochemical factors with NAFLD among the study participants

Variable	Total (N=392)	NAFLD present n (%)	Univariate Analysis PR (95% CI)	P value	Multivariable Analysis aPR (95% CI)	P value
Sex						
Male	164	68 (41.2)	2.1 (1.5-2.9)	<0.01	1.8 (1.3-2.5)	<0.01*
Female	228	63 (27.6)	Ref		Ref	
Ethnicity						
Chinese	267	84 (31.5)	Ref		Ref	
Malay	72	30 (41.7)	1.6 (1.1-2.3)	0.01	1.4 (1.0-2.0)	0.04*
Indian	42	16 (38.1)	1.4 (0.9-2.1)	0.12	1.2 (0.8-1.9)	0.38
Others	11	3 (27.3)	0.9 (0.3-2.4)	0.81	0.8 (0.3-2.2)	0.68
Physical activity						
Yes	50	12 (24.0)	Ref			
No	342	119 (34.8)	1.8 (1.1-2.9)	0.02	-	-
Type 2 Diabetes Mellitus						

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Variable	Total (N=392)	NAFLD present n (%)	Univariate Analysis PR (95% CI)	P value	Multivariable Analysis aPR (95% CI)	P value
Yes	136	62 (45.6)	2.0 (1.5-2.7)	<0.01	1.7 (1.3-2.3)	<0.01*
No	256	69 (26.9)	Ref		Ref	
Central obesity						
Yes	280	108 (38.6)	2.4 (1.6-3.6)	<0.01	-	-
No	112	23 (20.5)	Ref			
Elevated ALT						
Yes	60	38 (63.3)	2.5 (1.8-3.5)	<0.01	1.9 (1.3-2.7)	<0.01*
No	332	93 (28.0)	Ref		Ref	
Elevated triglycerides (>150 mg/dL)						
Yes	148	62 (41.9)	1.7 (1.2-2.3)	<0.01	1.3 (1.0-1.8)	0.03*
No	244	69 (28.3)	Ref		Ref	
Low HDL cholesterol						
Yes	142	54 (38.0)	1.4 (1.0-1.9)	0.03	-	-

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Variable	Total (N=392)	NAFLD present n (%)	Univariate Analysis PR (95% CI)	P value	Multivariable Analysis aPR (95% CI)	P value
No	250	77 (30.8)	Ref			

*Chi-square test, P<0.05 is statistically significant. $Prevalence ratio (PR); adjusted prevalence ratio (aPR) after adjusting for confounders – sex, ethnicity, T2DM, ALT, and triglycerides using logistic regression analysis. Only variables with P <0.2 in univariate analysis and biological relevance were included in multivariable analysis. Regression model with least BIC (Bayesian information criterion) was considered robust model. We have used step wise selection model for including variables in regression model. HDL, high density lipoprotein; ALT, alanine transaminase.

Table 2. Prevalence of NAFLD by demographic and metabolic characteristics among study participants

Characteristic	NAFLD Prevalence (%)	95% CI
Overall	33.4	28.9-38.2
Sex		
Male	41.2	33.8-49.0
Female	27.6	22.1-33.8
Ethnicity		
Chinese	31.5	26.2-37.2
Malay	41.7	30.8-53.4

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Characteristic	NAFLD Prevalence (%)	95% CI
Indian	38.1	24.2-54.0
Others	27.3	7.1-61.0
Age group (years)		
35-44	24.3	16.8-33.6
45-54	32.8	24.8-41.9
55-64	38.9	29.8-48.9
≥65	41.7	30.8-53.4
Diabetes status		
T2DM	45.6	37.4-54.0
No T2DM	26.9	21.9-32.6
BMI category (Asian cut-offs)		
Normal (<23 kg/m²)	18.4	11.2-28.2
Overweight (23-24.9 kg/m²)	28.6	20.0-39.0
Obese (≥25 kg/m²)	42.1	35.8-48.7

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Figures and Legends

Figure 1. Distribution of fatty liver index and FIB-4 scores among study participants (N=392)

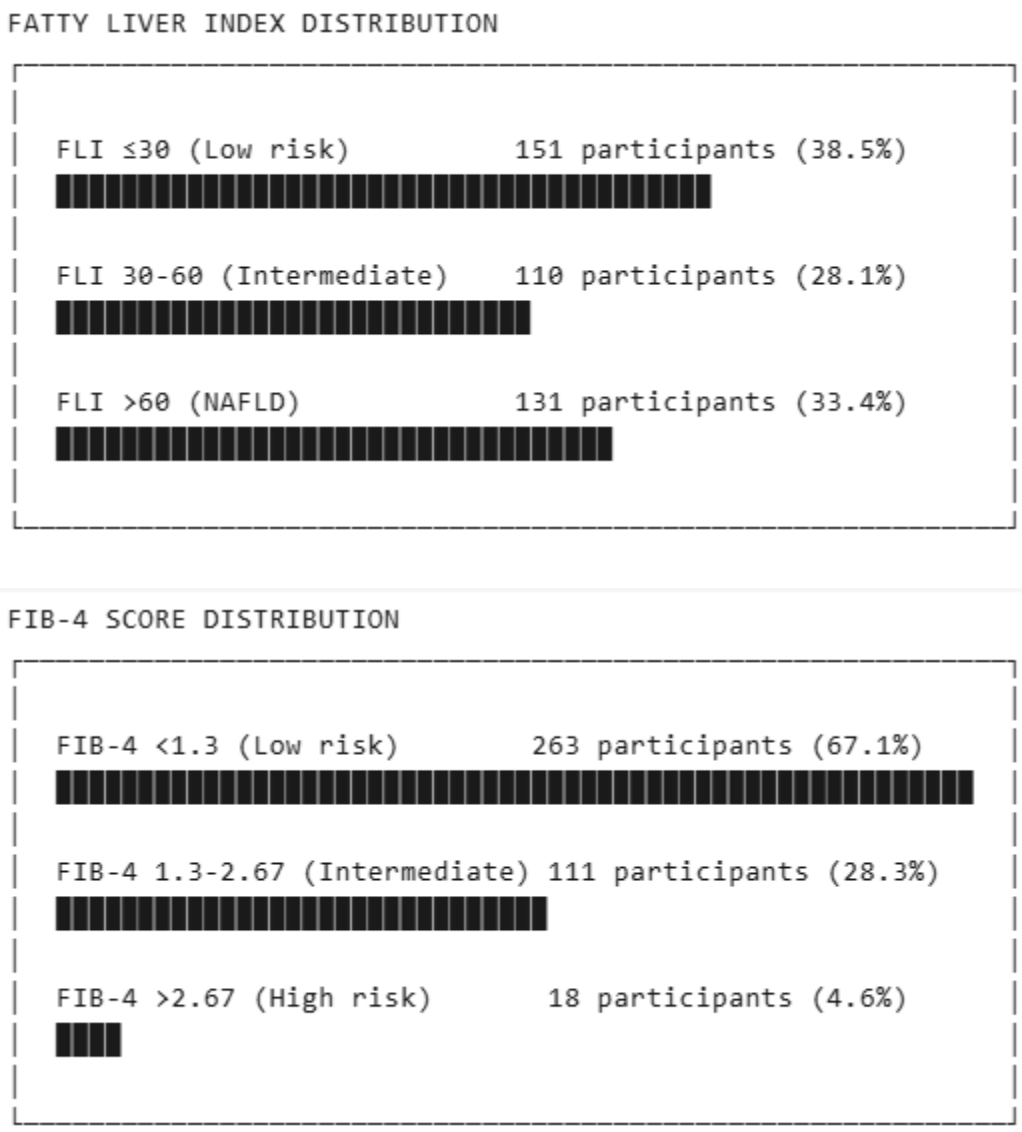

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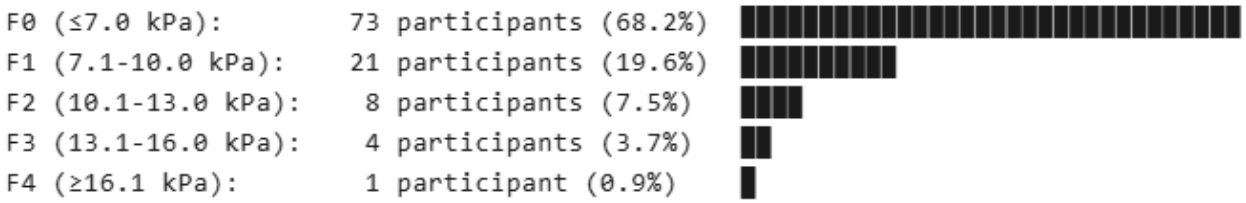
Figure 2. VCTE liver stiffness measurement and controlled attenuation parameter results (n=107)

A. Liver Stiffness Measurement (Fibrosis Staging):



B. Controlled Attenuation Parameter (Steatosis Grading):