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RESEARCH ARTICLE

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Association of muscle mass, grip strength and fat-to-muscle ratio and metabolic dysfunction-associated steatotic liver disease in a middle-to-elderly aged population

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ABSTRACT

Objective: The association of appendicular skeletal muscle mass (ASM), grip strength and fat-to-muscle ratio (FMR) and the progression of metabolic dysfunction-associated steatotic liver disease (MASLD) are not well known.

Materials and methods: This study included participants older than 40 years who underwent bioelectrical impedance assessment in Prevalence of Metabolic Diseases and Risk Factors in Shunde (SPEED-Shunde). We measured grip strength with an electronic grip strength metre. ASM and grip strength were adjusted by dividing body mass index (BMI). FMR was calculated as total fat mass to total muscle mass. Liver steatosis and liver fibrosis were evaluated by vibration-controlled transient elastography. Multifactorial logistic regression was used to analyse the relationship between ASM, grip strength, FMR, and MASLD or MASLD-associated liver fibrosis. We performed subgroup analyses according to sex, age and BMI. Interaction tests and linear trend tests were also conducted.

Results: This study included a total of 3277 participants. FMR was positively associated with MASLD (OR: 1.89, 95% CI: 1.66–2.15) and MASLD-associated liver fibrosis (OR: 1.70, 95% CI: 1.22–2.37). While ASM/BMI (OR: 0.59, 95% CI: 0.52–0.67) or grip strength/BMI (OR: 0.72, 95% CI: 0.66–0.78) were negatively associated with MASLD. Interactions were observed between ASM/BMI and age, grip strength and sex in MASLD, as well as FMR and MASLD-associated liver fibrosis.

Conclusion: In a middle-to-elderly aged population, FMR was positively associated with the risk of MASLD and MASLD-associated liver fibrosis, and muscle mass and grip strength were negatively associated with MASLD, rather than MASLD-associated liver fibrosis.

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Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD), is characterized by hepatic steatosis, progressive steatohepatitis and fibrosis. MASLD intends to be a non-stigmatizing and affirmative term, rather than an exclusive diagnosis like NAFLD. It is estimated that 20 million people worldwide may die from fatty liver each year, as MASLD is not only a leading cause of cirrhosis and hepatocellular carcinoma [1, 2], but also a risk factor for cardiovascular disease [3] and chronic kidney disease [4]. Therefore, identifying risk factors for MASLD can help clinicians tailor their treatment regimens, which is of great clinical and public health significance.

Western diets, lack of exercise, insulin resistance and abnormal cytokine secretion all increase the risk of MASLD [5]. In addition, recent studies have suggested an association between abnormal body composition and NAFLD risk [5, 6]. While some studies with small samples have reached conclusions that increased fat-to-muscle ratio (FMR) or decreased muscle–fat ratio are associated with elevated risks of NAFLD and NAFLD-associated liver fibrosis [7–11], the association between FMR and MASLD in the middle-to-elderly general population is unknown and whether there are differences in subgroups is not well understood.

Skeletal muscle as a metabolic organ has a close relationship with glucose metabolism [5]. In a

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cross-sectional study of 3602 adults, skeletal muscle mass was negatively associated with NAFLD and NAFLD-associated liver fibrosis [12]. Similarly, data from the Korean National Health and Nutrition Examination Surveys showed that low appendicular skeletal muscle mass (ASM) divided by body mass index (BMI) was negatively associated with significant liver fibrosis assessed by NAFLD fibrosis score (NFS) or fibrosis-4 (FIB-4) [13]. However, data obtained from the National Health and Nutrition Examination Survey showed that whole-body skeletal muscle mass index was not associated with significant liver fibrosis in metabolic dysfunction-associated fatty liver disease (MAFLD) [14].

Previous studies have mainly focused on the relationship between weight-adjusted [12, 15–17] or height-adjusted muscle mass [14] and NAFLD. It is noteworthy that studies have shown that BMI-adjusted ASM predicts functional outcomes in older adults better than unadjusted ASM [18] or height-adjusted ASM [19]. Additionally, the 2019 Asian Working Group for Sarcopenia recommends that future studies use BMI-adjusted muscle mass for risk assessments since there is insufficient research evidence on these topics in Asian populations [20].

Although recent studies [21–23] indicate that low muscle strength is negatively associated with NAFLD, few studies have discussed the relationship between muscle strength and NAFLD-associated liver fibrosis. In a US population aged 18 years and older, stronger grip strength was inversely associated with fatty liver index (FLI) and NFS [24]. However, in another Korea-based population aged 20 years and older, the association between muscle strength and FIB-4 index score did not reach statistical significance after further adjusted insulin resistance [25]. And yet, the relationship between muscle strength and MASLD-associated liver fibrosis in the middle-to-elderly population remains elusive.

Thus, this study aimed to investigate the association between body composition indices, including ASM, grip strength, FMR and MASLD, as well as MASLD-associated liver fibrosis in a community-wide middle-to-elderly population.

Materials and methods

Study design and subjects

This study was based on an ongoing observational prospective cohort study (the Study on Prevalence of Metabolic Diseases and Risk Factors in Shunde, SPEED-Shunde). We included the initial part of SPEED-Shunde in this study from November 2021 to September 2022. Detailed descriptions of the SPEED-Shunde study have been published previously [26–29]. Ethical approval was obtained from the Ethics Committee of Shunde Hospital of Southern Medical University. All participants signed an informed consent.

Stratified cluster sampling was used to sample the subjects. The exclusion criteria for the study were as follows: participants younger than 40 years ($n = 4367$), participants with missing information on transient elastography ($n = 2248$), alcohol consumption ($n = 69$), BMI ($n = 28$), fasting plasma glucose (FPG) testing ($n = 372$), glucose of oral glucose tolerance test (OGTT)-2h ($n = 540$), glycosylated haemoglobin (HbA1c) ($n = 6$), blood pressure ($n = 96$), triglycerides (TG) ($n = 1$), grip strength ($n = 477$), muscle mass ($n = 1910$), FMR ($n = 50$), and those diagnosis with MASLD and increased alcohol intake (MetALD) ($n = 30$), alcohol-associated liver disease (ALD) ($n = 39$), cryptogenic steatotic liver disease (SLD) ($n = 25$). Therefore, the final sample included in the current study was 3277, with 1350 individuals enrolled in the MASLD group and 1927 individuals in the non-MASLD group (as shown in Figure 1).

The definition of MASLD

The MASLD definition referenced the International Expert Consensus Statement [30]: the presence of steatosis in the liver as determined by vibration-controlled transient elastography (VCTE) and one of the following: (1) BMI ≥23 kg/m^2 or WC >94 cm for men or WC >80 cm for women; (2) FPG ≥5.6 mmol/L or glucose of OGTT-2h ≥7.8 mmol/L or HbA1c ≥5.7% or type 2 diabetes or treatment for type 2 diabetes; (3) blood pressure ≥130/85 mmHg or specific antihypertensive drug treatment; (4) plasma TG ≥1.70 mmol/L or lipid-lowering treatment; (5) plasma high-density lipoprotein (HDL) ≤1.0 mmol/L for men or HDL ≤1.3 mmol/L for women or lipid-lowering treatment. For individuals with MASLD, those who have average daily alcohol intake of 20–50 g for women or 30–60 g for men were defined as MASLD and increased alcohol intake (MetALD). To obtain the degree of hepatic steatosis and fibrosis, a trained technician performed VCTE using a FibroScan 402 Touch model (M Probe; XL Probe; Echosens, Paris, France). Hepatic steatosis was defined as controlled attenuation parameter ≥248 dB/m [28, 31, 32]. Liver fibrosis was defined as liver stiffness measurement ≥8 kPa [33].

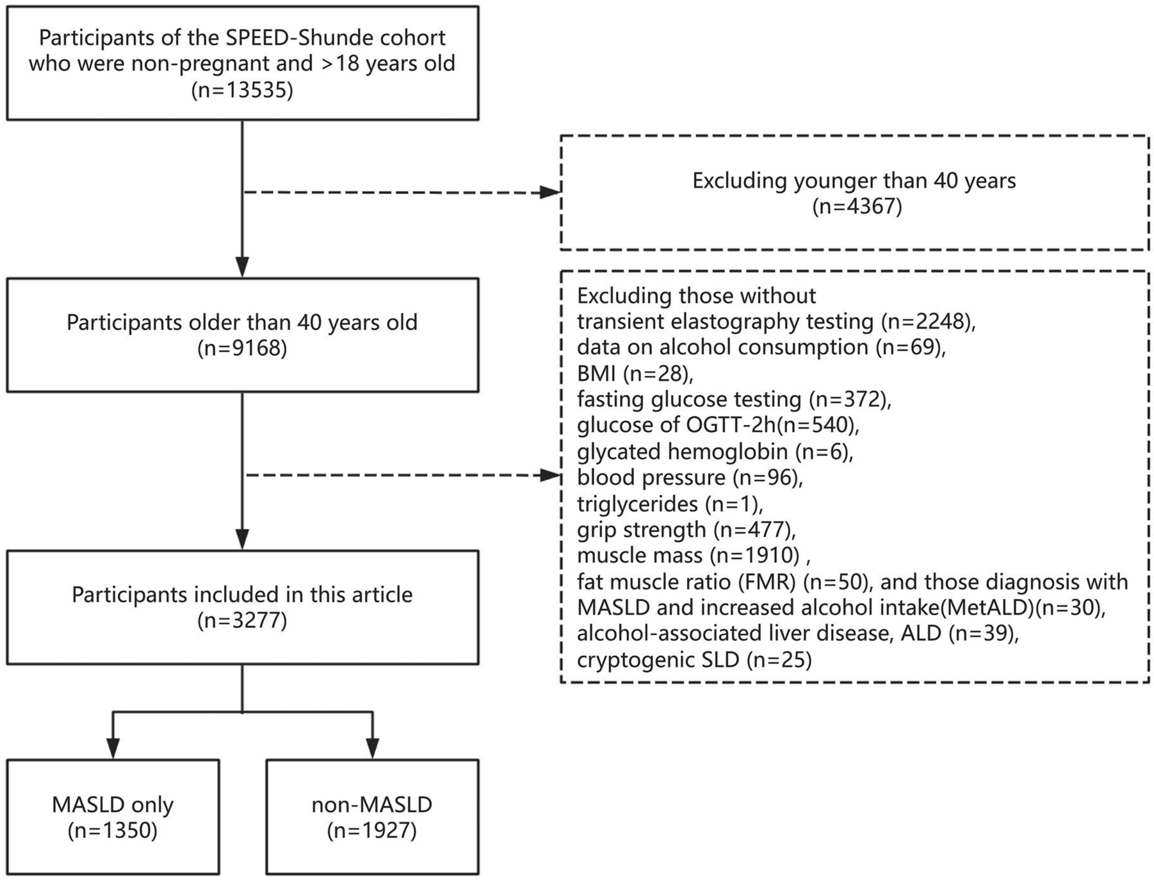

Figure 1. Flowchart of participants' inclusion and exclusion.

The definition of ASM, grip strength and FMR

According to the manufacturer's instructions, we measured total body fat, total muscle mass and ASM by a bioelectrical impedance assessment (BIA) device (InBody770 machine, Seoul, Korea). Before measuring BIA, participants were requested to remain fast and avoid strenuous exercise. Participants were instructed to remain standing in a stationary position with the soles of their feet evenly touching the upper and lower footplate electrodes and to hold the left and right electrode handles with each hand. ASM was defined as the sum of upper and lower ASM, and ASM was adjusted by BMI, which is equal to ASM (kg)/BMI (kg/m^2) [34, 35]. FMR was defined as total fat mass (kg)/total muscle mass (kg) [36, 37]. The grip strength of the subjects was measured using an electronic grip strength metre (EH102, Guangdong Senssun Weighing Apparatus Group Ltd, China). For each participant, the dominant hand's highest value was recorded. Grip strength was adjusted by BMI, which is equal to grip strength (kg)/BMI (kg/m^2) [38, 39].

Definition of clinical and laboratory indicators

The study collected demographic information on sex, education (less than high school, completed high school and beyond high school), smoking history (current smokers were defined as having smoked at least 100 cigarettes in the past and the person was currently smoking, quitters were defined as having quit smoking for more than 6 months and non-smokers) [40]. Diabetes mellitus was defined as FPG level ≥7.0 mmol/L, HbA1c ≥6.5% and/or a history of diabetes [33]. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, and/or a history of hypertension [33]. Height, weight, waist circumference, systolic blood pressure and diastolic blood pressure were measured. BMI was calculated as weight (kg) divided by the square of height (m^2). Participants fasted overnight to measure total cholesterol (TC), TG, low-density lipoprotein (LDL), HDL, FPG, HbA1c and serum creatinine.

Statistical analysis

Participants' baseline characteristics were expressed as mean (standard deviation [SD]) for continuous variables or frequency (percentage) for categorical variables. As a result of the Kolmogorov–Smirnov test, FMR initially had a skewed distribution, which was then transformed into logarithmic distributions. We used multivariate logistic regression analysis to ascertain the association between ASM/BMI, FMR and grip strength/BMI (as continuous or categorical variables) and MASLD and MASLD-associated liver fibrosis. The lowest quartile was used as the reference group when ASM/BMI, FMR and grip strength/BMI were used as categorical variables.

To establish the association between MASLD, as well as MASLD-associated liver fibrosis, and independent variables (FMR, ASM/BMI and grip strength/BMI), we calculated bivariate correlations using point-biserial correlation coefficients [41, 42] and results were displayed with the corrplot function (corrplot package). The multivariable logistic regression models for ASM/BMI and grip strength/BMI were adjusted for age, sex, education, smoking history, serum creatinine, diabetes and hypertension. In the case of FMR, multivariate logistic regression models were further adjusted for BMI ($<24\,kg/m^2$, $\geq 24\,kg/m^2$). Inflation factors with the highest variances were less than five, suggesting no multicollinearity between variables.

The overall participants were analysed into subgroups according to sex (male, female), age (<60 years, ≥60 years). For FMR, we performed subgroup analyses additionally according to BMI ($<24\,kg/m^2$, $\geq 24\,kg/m^2$). We performed interaction tests using the 'scitb5' function in the R software. To determine the values of p for trend, the median values of grip strength/BMI, FMR and ASM/BMI of each quantile were included as continuous variables in the logistic regression model [43, 44]. A p value less than 0.05 was considered significant. Statistics were performed using R software (version 4.3.0).

To compare the term change of fatty liver disease, we also calculated the associations between ASM/BMI, FMR and grip strength/BMI and NAFLD, as well as ASM/BMI, FMR, grip strength/BMI and MAFLD (see Supplementary Materials).

Results

Characteristics of participants

This study included 3277 participants, of whom 1350 had MASLD and 117 had MASLD-related fibrosis. An overview of demographic characteristics and haematologic test indices of participants grouped by MASLD or MASLD-associated liver fibrosis are presented in Tables 1 and 2. As compared with participants without MASLD, those with MASLD had higher age, BMI, TC, LDL, HbA1c, TG, and FMR levels, lower HDL, ASM/BMI, and grip strength/BMI levels, and more individuals with diabetes and hypertension in both sexes. Participants with MASLD who had liver fibrosis had a higher BMI level and a higher prevalence of hypertension than those without liver fibrosis in the two sexes.

Association of ASM/BMI, FMR and grip strength/BMI with MASLD

MASLD correlated significantly with biomarkers of BIA (FMR, ASM/BMI and grip strength/BMI), as shown in Figure 2A. The adjusted associations of ASM/BMI, FMR and grip strength/BMI with MASLD are shown in Table 3. For the overall participants, per 1 SD elevation of FMR was positively associated with MASLD. In contrast, per 1 SD elevation of ASM/BMI, grip strength/BMI was negatively associated with MASLD. The subgroup analysis results were consistent with the overall population. Interaction was observed between ASM/BMI and age (p for interaction = 0.009), as well as grip strength/BMI and sex (p for interaction = 0.002).

As shown in Figure 3, we converted ASM/BMI, FMR and grip strength/BMI into quartiles 1 (Q1), 2 (Q2), 3 (Q3) and 4 (Q4) from lowest to highest and included them in multivariate logistic regression analyses. Among overall participants, the risk of developing MASLD was higher in the highest quartile of FMR (Q4) than in the lowest quartile (Q1). There was a significant linear trend in MASLD risk across quartiles of FMR (p for trend <0.001). According to ASM/BMI or grip strength/BMI, MASLD risk was lower in the highest quartile (Q4) than in the lowest quartile (Q1). Significant linear trends were observed for MASLD across quartiles of ASM/BMI or grip strength/BMI (both p for trend <0.001). The subgroup analysis results were consistent with those of the overall population, with only participants older than 60 years not having a statistically significant association between grip strength/BMI and MASLD.

Association of ASM/BMI, FMR and grip strength/BMI with MASLD-associated liver fibrosis

Although the correlation between BIA biomarkers and MASLD-associated liver fibrosis was attenuated (Figure 2B), Table 4 shows that for overall participants, per 1 SD elevation of FMR was positively associated with risk of MASLD-associated liver fibrosis, but ASM/BMI and grip strength/BMI were not associated. Interaction observed between FMR and sex (p for interaction = 0.017).

As shown in Figure 4, among the overall participants, the risk of developing MASLD-associated liver fibrosis was higher in the highest quartile of FMR (Q4) than in the lowest quartile (Q1). A significant linear

Table 1. Baseline characteristics of the study population.

	Male			Female		
	Without MASLD	With MASLD	*p* Value	Without MASLD	With MASLD	*p* Value
N	*N* = 672	*N* = 564		*N* = 1255	*N* = 786	
Age	52.7 (9.02)	51.7 (8.83)	0.045	51.4 (8.33)	53.7 (8.11)	<0.001
BMI	23.5 (2.77)	26.2 (2.91)	<0.001	22.4 (2.72)	25.2 (3.06)	<0.001
Serum creatinine	1.02 (0.23)	1.00 (0.16)	0.079	0.74 (0.19)	0.73 (0.12)	0.073
HDL	1.37 (0.31)	1.23 (0.25)	<0.001	1.62 (0.32)	1.44 (0.30)	<0.001
TC	5.25 [4.65, 5.96]	5.52 [4.90, 6.17]	<0.001	5.40 [4.78, 6.08]	5.65 [4.96, 6.41]	<0.001
LDL	3.03 [2.55, 3.49]	3.19 [2.75, 3.67]	<0.001	2.91 [2.49, 3.35]	3.13 [2.62, 3.64]	<0.001
HbA1c	5.70 [5.40, 5.90]	5.80 [5.60, 6.20]	<0.001	5.60 [5.40, 5.90]	5.80 [5.60, 6.10]	<0.001
TG	1.24 [0.92, 1.75]	1.79 [1.26, 2.67]	<0.001	1.03 [0.79, 1.43]	1.50 [1.06, 2.14]	<0.001
FMR	0.50 [0.40, 0.61]	0.64 [0.54, 0.77]	<0.001	0.80 [0.67, 0.94]	0.97 [0.85, 1.13]	<0.001
Grip strength/BMI	1.44 (0.50)	1.33 (0.45)	<0.001	0.99 (0.35)	0.86 (0.31)	<0.001
ASM/BMI	0.92 (0.13)	0.88 (0.11)	<0.001	0.67 (0.09)	0.64 (0.09)	<0.001
Education			0.082			0.012
Less than high school	266 (39.6%)	199 (35.3%)		636 (50.7%)	451 (57.4%)	
Completed high school	217 (32.3%)	174 (30.9%)		318 (25.3%)	175 (22.3%)	
Beyond high school	189 (28.1%)	191 (33.9%)		301 (24.0%)	160 (20.4%)	
Smoking			0.835			0.694
Non-smoker	426 (63.4%)	365 (64.7%)		1246 (99.3%)	781 (99.4%)	
Previous smoker	68 (10.1%)	52 (9.22%)		3 (0.24%)	3 (0.38%)	
Present smoker	178 (26.5%)	147 (26.1%)		6 (0.48%)	2 (0.25%)	
T2DM			<0.001			<0.001
No	642 (95.5%)	467 (82.8%)		1202 (95.8%)	689 (87.7%)	
Yes	30 (4.46%)	97 (17.2%)		53 (4.22%)	97 (12.3%)	
Hypertension			0.001			<0.001
No	431 (64.1%)	306 (54.3%)		973 (77.5%)	495 (63.0%)	
Yes	241 (35.9%)	258 (45.7%)		282 (22.5%)	291 (37.0%)	

MASLD: metabolic dysfunction-associated fatty liver disease; BMI: body mass index; HDL: high-density lipoprotein; TC: total cholesterol; LDL: low-density lipoprotein; HbA1c: glycosylated haemoglobin; TG: triglycerides; FMR: fat-to-muscle ratio; ASM: appendicular skeletal muscle mass; T2DM: type 2 diabetes mellitus.

Table 2. Baseline characteristics of individuals with MASLD.

	Male			Female		
	Without fibrosis	With fibrosis	*p* Value	Without fibrosis	With fibrosis	*p* Value
N	*N* = 498	*N* = 66		*N* = 735	*N* = 51	
Age	51.6 (8.79)	52.4 (9.17)	0.496	53.4 (7.98)	57.9 (8.89)	0.001
BMI	26.0 (2.77)	27.8 (3.44)	<0.001	25.1 (2.99)	26.6 (3.58)	0.003
Serum creatinine	1.00 (0.15)	0.98 (0.17)	0.205	0.73 (0.12)	0.75 (0.18)	0.440
HDL	1.24 (0.25)	1.16 (0.21)	0.011	1.45 (0.30)	1.39 (0.33)	0.257
TC	5.53 [4.93, 6.21]	5.43 [4.82, 5.94]	0.363	5.69 [4.97, 6.42]	5.38 [4.64, 6.22]	0.036
LDL	3.20 [2.75, 3.68]	3.12 [2.75, 3.64]	0.593	3.14 [2.63, 3.66]	2.98 [2.43, 3.26]	0.056
HbA1c	5.80 [5.60, 6.10]	6.00 [5.70, 6.68]	0.005	5.80 [5.60, 6.10]	5.90 [5.70, 6.20]	0.117
TG	1.79 [1.25, 2.60]	1.91 [1.33, 3.07]	0.181	1.50 [1.06, 2.12]	1.60 [1.25, 2.36]	0.117
FMR	0.63 [0.53, 0.75]	0.78 [0.65, 0.90]	<0.001	0.97 [0.85, 1.13]	1.04 [0.90, 1.26]	0.052
Grip strength/BMI	1.33 (0.46)	1.26 (0.40)	0.191	0.86 (0.31)	0.85 (0.31)	0.687
ASM/BMI	0.88 (0.11)	0.85 (0.11)	0.019	0.64 (0.09)	0.61 (0.08)	0.028
Education			0.406			0.038
Less than high school	171 (34.3%)	28 (42.4%)		414 (56.3%)	37 (72.5%)	
Completed high school	157 (31.5%)	17 (25.8%)		165 (22.4%)	10 (19.6%)	
Beyond high school	170 (34.1%)	21 (31.8%)		156 (21.2%)	4 (7.84%)	
Smoking			0.329			0.006
Non-smoker	317 (63.7%)	48 (72.7%)		732 (99.6%)	49 (96.1%)	
Previous smoker	48 (9.64%)	4 (6.06%)		3 (0.41%)	0 (0.00%)	
Present smoker	133 (26.7%)	14 (21.2%)		0 (0.00%)	2 (3.92%)	
T2DM			0.005			0.158
No	421 (84.5%)	46 (69.7%)		648 (88.2%)	41 (80.4%)	
Yes	77 (15.5%)	20 (30.3%)		87 (11.8%)	10 (19.6%)	
Hypertension			0.014			0.047
No	280 (56.2%)	26 (39.4%)		470 (63.9%)	25 (49.0%)	
Yes	218 (43.8%)	40 (60.6%)		265 (36.1%)	26 (51.0%)	

MASLD: metabolic dysfunction-associated fatty liver disease; BMI: body mass index; HDL: high-density lipoprotein; TC: total cholesterol; LDL: low-density lipoprotein; HbA1c: glycosylated haemoglobin; TG: triglycerides; FMR: fat-to-muscle ratio; ASM: appendicular skeletal muscle mass; T2DM: type 2 diabetes mellitus.

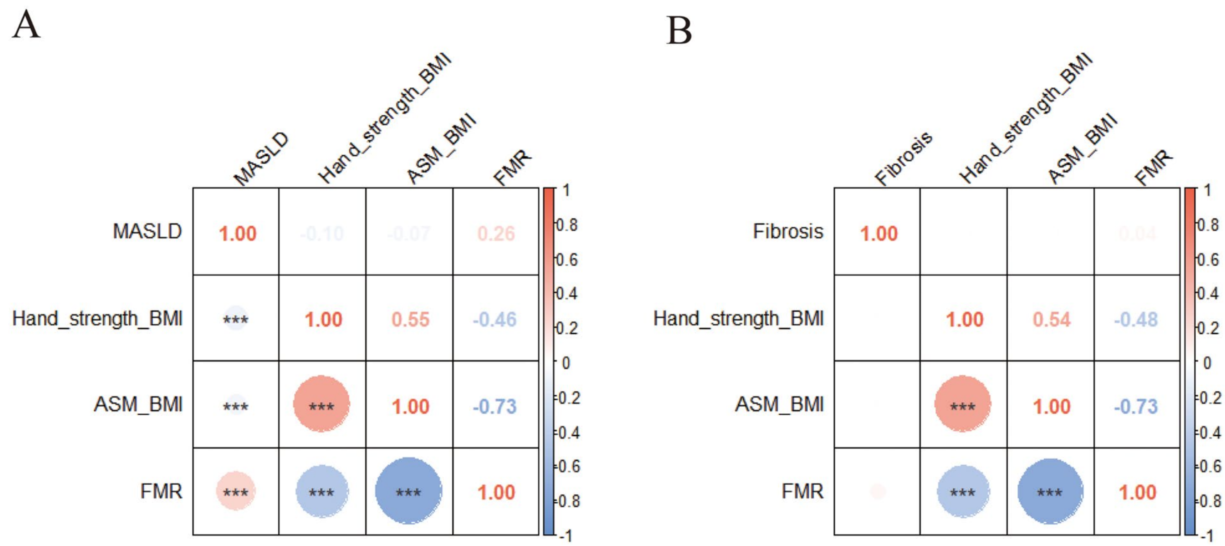

Figure 2. Correlation coefficients for MASLD (A) and independent variables, and MASLD-associated liver fibrosis (B) and independent variables.

Table 3. Association of ASM/BMI, FMR and grip strength/BMI with MASLD.

Characteristic	No. of participants	OR (95% CI)	p for interaction
FMR, per SD increase			
Overall population	3277	1.89 (1.66, 2.15)	
Subgroups			
Age			0.453
<60	2658	1.87 (1.63, 2.15)	
≥60	619	2.04 (1.63, 2.55)	
Sex			0.668
Male	1236	1.85 (1.55, 2.21)	
Female	2041	1.95 (1.65, 2.31)	
BMI			0.051
<24	1764	2.08 (1.77, 2.44)	
≥24	1513	1.73 (1.47, 2.03)	
ASM/BMI, per SD increase			
Overall population	3277	0.59 (0.52, 0.67)	
Subgroups			
Age			0.009
<60	2658	0.61 (0.54, 0.70)	
≥60	619	0.48 (0.39, 0.58)	
Sex			0.122
Male	1236	0.64 (0.54, 0.75)	
Female	2041	0.53 (0.45, 0.63)	
Grip strength/BMI, per SD increase			
Overall population	3277	0.72 (0.66, 0.78)	
Subgroups			
Age			0.286
<60	2658	0.73 (0.66, 0.80)	
≥60	619	0.65 (0.53, 0.79)	
Sex			0.002
Male	1236	0.80 (0.72, 0.90)	
Female	2041	0.61 (0.53, 0.70)	

ASM: appendicular skeletal muscle mass; BMI: body mass index; FMR: fat-to-muscle ratio; MASLD: metabolic dysfunction-associated fatty liver disease; OR: odds ratio; CI: confidence interval; SD: standard deviation.

trend in MAFLD-associated liver fibrosis risk was detected between the FMR quartiles (p for trend <0.001). No correlations were observed between MASLD-associated liver fibrosis and either ASM/BMI or grip strength/BMI. Among participants under 60 years of age (p for trend = 0.002), males (p for trend <0.001), and BMI ≥24 (p for trend = 0.002), the risk of MASLD-associated liver fibrosis significantly increased with the FMR quartile.

We also examined these associations in NAFLD and MAFLD, which yielded similar results (see Supplementary figures and tables).

Discussion

This study found that high FMR and low BMI-adjusted ASM were associated with a higher risk of MASLD and MASLD-associated liver fibrosis in this community-based middle-to-elderly aged population in China. Additionally, BMI-adjusted grip strength was negatively associated with MASLD, especially in women.

Lee et al. demonstrated that in young soldiers, muscle-to-fat ratio was inversely associated with significant fibrosis [11]. In three hospital-based retrospective studies in Asia [8, 9, 45], FMR was positively associated with liver fat accumulation and liver stiffness. However, the relationship between FMR and MASLD in the middle-to-elderly general population has not been tested. According to the results of this study, FMR was positively associated with MASLD and MASLD-associated liver fibrosis in the middle-to-elderly aged population. The possible mechanisms by which FMR is positively associated with MASLD and MASLD-associated liver fibrosis are as follows: first, as a result of fat augmentation, leptin, resistin and retinol-binding proteins are elevated, adiponectin is decreased, and cytokines (tumor necrosis factor-alpha [TNF-alpha], Interleukin-6 [IL-6]) are elevated as well [46], leading to increased insulin resistance and inflammation. Cytokines entering the circulation trigger systemic inflammation in distant

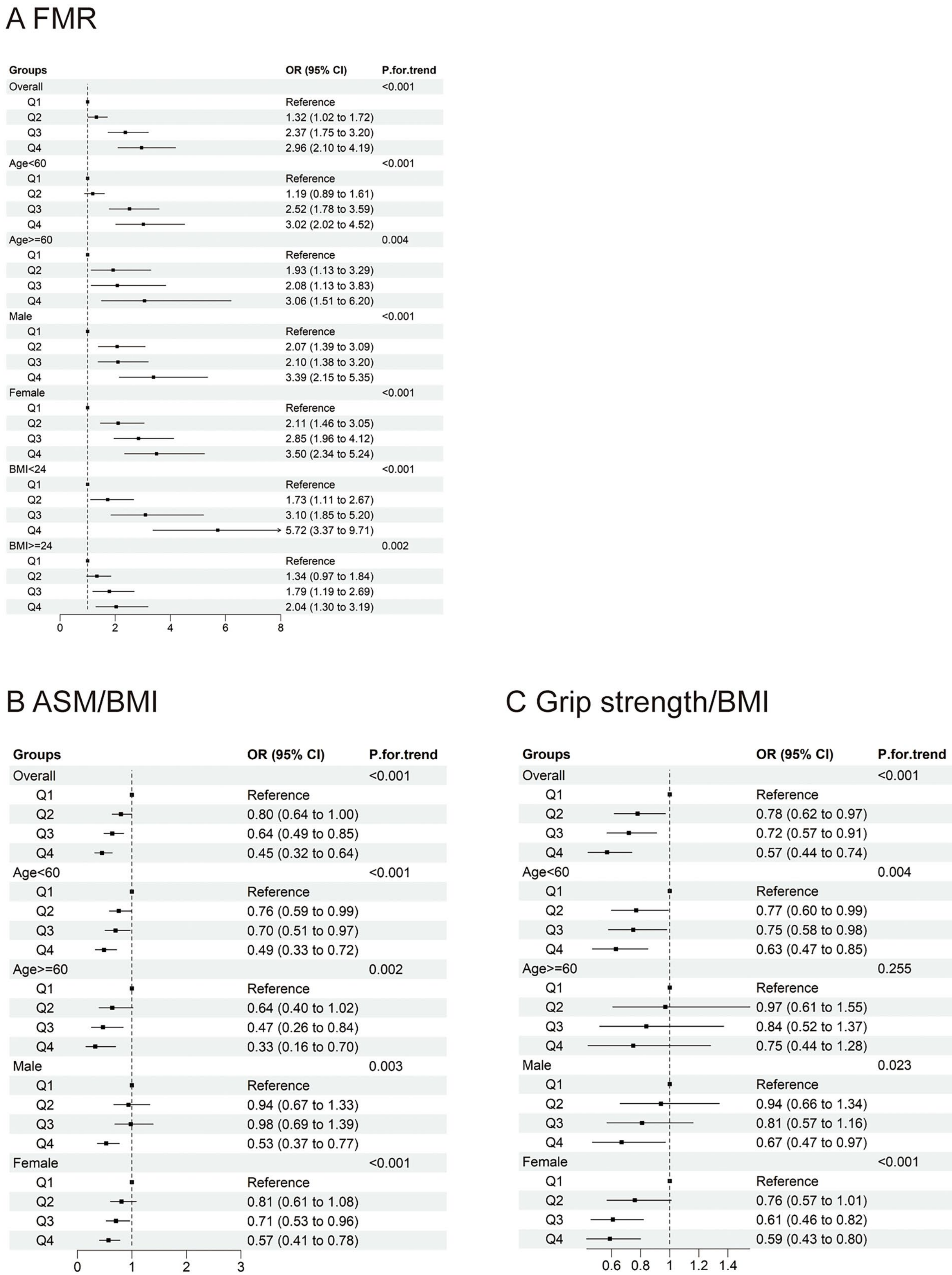

Figure 3. Risk of MASLD in each quartile of ASM/BMI, FMR or grip strength/BMI.

organs as well. Second, when adipose tissue expands beyond its ability to compensate, ectopic fat deposition occurs [47]. Lastly, lower protein intake leads to lower muscle mass among the middle-to-elderly population [5], which is linked to insulin resistance since muscle is one of the organs that regulate insulin

Table 4. Association of ASM/BMI, FMR and grip strength/BMI with MASLD-associated liver fibrosis.

Characteristic	No. of participants	OR (95% CI)	*p* for interaction
FMR, per SD increase			
Overall population	1350	1.70 (1.22, 2.37)	
Subgroups			
Age			0.071
<60	1077	1.50 (1.05, 2.14)	
≥60	273	2.50 (1.46, 4.30)	
Sex			0.017
Male	564	2.32 (1.52, 3.54)	
Female	786	1.11 (0.71, 1.74)	
BMI			0.544
<24	417	1.51 (0.90, 2.54)	
≥24	933	1.79 (1.24, 2.59)	
ASM/BMI, per SD increase			
Overall population	1350	0.74 (0.54, 1.01)	
Subgroups			
Age			0.124
<60	1077	0.80 (0.57, 1.12)	
≥60	273	0.55 (0.34, 0.89)	
Sex			0.879
Male	564	0.74 (0.51, 1.07)	
Female	786	0.70 (0.41, 1.21)	
Grip strength/BMI, per SD increase			
Overall population	1350	0.98 (0.78, 1.24)	
Subgroups			
Age			0.123
<60	1077	1.03 (0.81, 1.33)	
≥60	273	0.69 (0.41, 1.14)	
Sex			0.508
Male	564	0.92 (0.70, 1.20)	
Female	786	1.09 (0.71, 1.68)	

ASM: appendicular skeletal muscle mass; BMI: body mass index; FMR: fat-to-muscle ratio; MASLD: metabolic dysfunction-associated fatty liver disease; OR: odds ratio; CI: confidence interval; SD: standard deviation.

sensitivity. All of the above changes contribute to the progression of MASLD [46]. We also found that higher FMR was associated with MASLD-associated liver fibrosis, especially in men. A possible explanation for the gender difference is that higher FMR is associated with a higher degree of insulin resistance in men compared to women [48], which is a risk factor for the progression of MASLD [5].

Although previous studies [21, 49] suggest that elevated weight-adjusted ASM is associated with a lower risk of NAFLD, we added evidence that BMI-adjusted ASM was negatively associated with MASLD, but not associated with MASLD-associated liver fibrosis. As the BMI-adjusted ASM corrects for height and weight simultaneously, the effect of body composition differences is minimized [19]. In addition, studies have also demonstrated that sarcopenic obesity leads to decreased activity [50], cognitive dysfunction [51] and cardiovascular disease [35], suggesting that BMI-adjusted ASM, which takes obesity into account, may be a more accurate evaluation tool. In a retrospective single-center study, although individuals with decreased ASM had increased hepatic steatosis index and FLI scores, the association was not found with NFS [52]. Furthermore, in a biopsy-proved NAFLD study including 401 Chinese males, low ASM was associated with severe steatosis and non-alcoholic steatohepatitis (NASH), but not with the presence of fibrosis [16]. In this study, we found that BMI-adjusted ASM was inversely associated with MASLD, especially in individuals older than 60 years old. Coincidentally, Kim et al. [53] demonstrated that the risk of NAFLD according to decreased skeletal muscle index was significantly higher in men older than 45 years. Although the specific mechanism is still unclear, the potential benefits of exercise for middle-to-elderly people appear clinically meaningful.

Sarcopenia, defined by BMI-adjusted grip strength rather than unadjusted grip strength, is closely associated with composite outcomes, including falls, hospitalizations and emergency room visits [19]. In addition, BMI-adjusted grip strength was negatively associated with the risk of all-cause mortality, as well as cardiovascular-related mortality in the individuals with NAFLD [54]. Therefore, we used BMI-adjusted grip strength to assess MASLD risk in the present study. According to Kang et al. [25], low grip strength was associated with NAFLD and progressive liver fibrosis (>F2). One possible explanation for the inconsistent results may be explained by the different methods of detection and definition of liver fibrosis, where FIB-4 index scores were used in the previous study [25], while VCTE was used in the present study. We also found that there was a stronger negative association between BMI-adjusted grip strength and MASLD in women. Similarly, in a nationwide study including 31,649 participants, the ORs of lower muscle strength for MAFLD were higher in women than men [55]. One possible explanation is that in women oestrogen may play a role in the association between grip strength and MASLD.

This study has some advantages. First, this study simultaneously analysed the correlation between FMR, muscle mass, muscle strength and MASLD in a Chinese population, which is helpful for identifying people at high risk for MASLD and MASLD-associated liver fibrosis in the community. Second, the present study provides a research basis for the associations of BMI-adjusted muscle mass and muscle strength with adverse outcomes.

There are also limitations to this study. First, as a cross-sectional study, the present study was unable to conclude a causal relationship between body composition and MASLD, and prospective studies are needed to confirm this. Second, BIA was obtained by indirect imputation rather than direct measurement, making it less accurate than computed tomography (CT) and dual-energy X-ray absorptiometry (DXA) [56]. However, BIA devices are more suitable for primary care due to

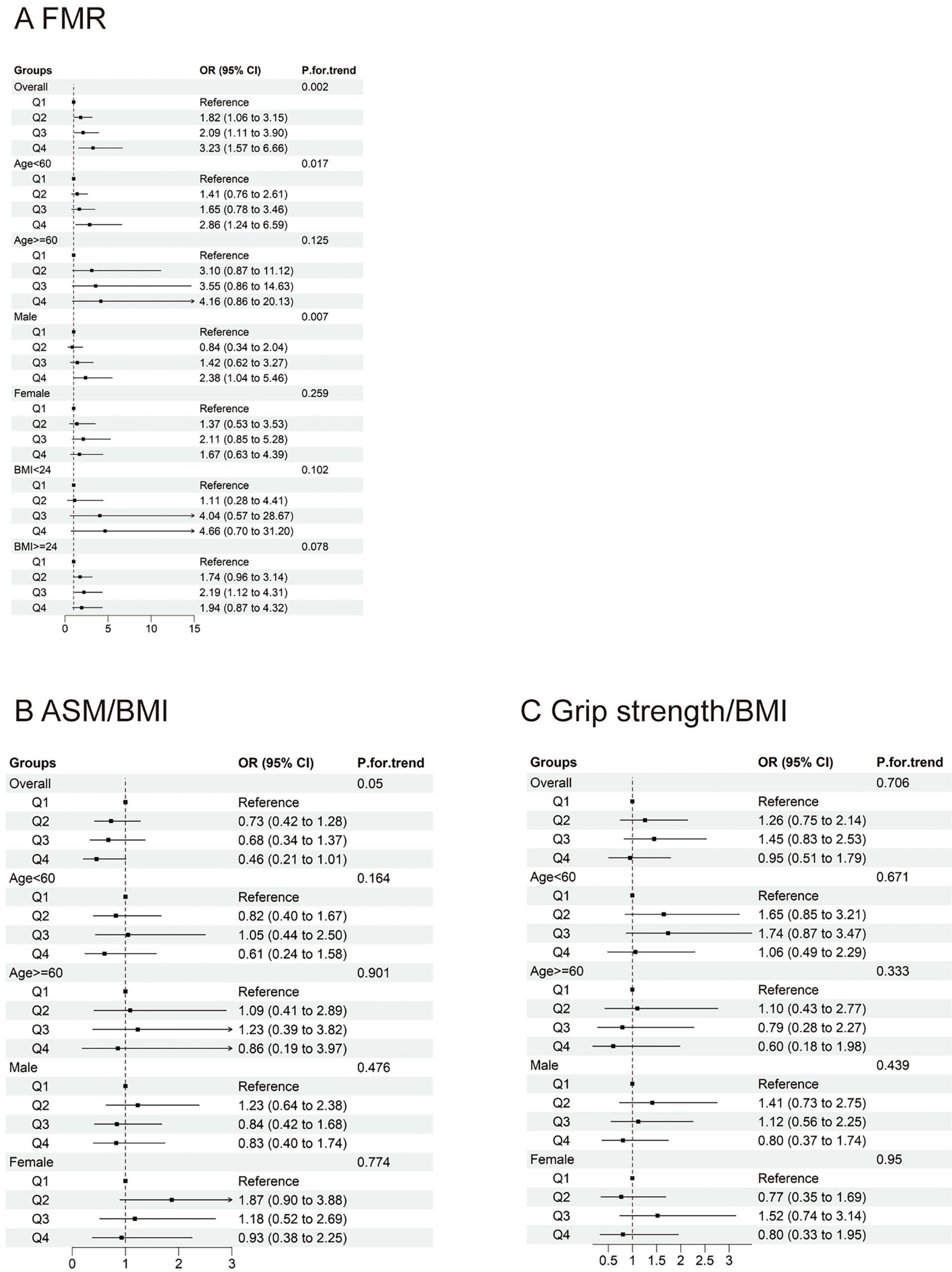

Figure 4. Risk of MASLD-associated liver fibrosis in each quartile of ASM/BMI, FMR or grip strength/BMI.

their lower cost, portability and feasibility [5]. Third, this study lacks information on steroid medication, which may affect fat metabolism. Moreover, previous literature has demonstrated the validity of BIA [8, 36]. This study does not examine myosteatosis, which has been linked to MASLD progression [57] and warrants further analysis.

In addition, region-specific associations of muscle mass and MASLD merit further exploration.

In conclusion, the study showed that MASLD risk increases with higher FMR, lower ASM and lower grip strength. Furthermore, FMR was associated with MASLD-associated liver fibrosis. Longitudinal studies will be necessary to determine the causal relationship between MASLD and abnormal body composition.

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Authors contributions

SYL, YJH, GFY, CS, DMW, LL, HL, HW and JS contributed to the conception and design of the study, analysis and interpretation of data, critical review, and final approval of the manuscript for publication. SYL, YJH, LL, HL, HW and JS acquired the data. Drafting of the manuscript was primarily led by SYL, YJH, HW and JS. Each author affirms their dedication to maintaining the accuracy and integrity of all aspects of the study.

Ethical approval and consent to participate

Ethical approval was obtained from the Ethics Committee of Shunde Hospital of Southern Medical University (ethical approval number 20211103). All participants signed an informed consent.

Disclosure statement

No potential conflicts of interest relevant to this article were reported.

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Data availability statement

The findings of this study are supported by data that may be obtained upon request from the corresponding author. The data are not publicly accessible due to ethical or privacy constraints.

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