scientific reports

Check for updates

OPEN

Low muscle quality index is associated with increased risk of advanced fibrosis in adult patients with nonalcoholic fatty liver disease: NHANES 2011–2014

Xinxing Tantai[1,2,3]✉, Qiuju Ran[1,2,3], Zhang Wen[1,2], Shuyue Tuo[1,2], Na Liu[1,2], Shejiao Dai[1,2], Jinhai Wang[1,2] & Chenyang Qiao[1,2]✉

Muscle quality index (MQI) is a novel indicator reflecting the quality of skeletal muscles. The association between MQI and the development of advanced fibrosis in patients with nonalcoholic fatty liver disease (NAFLD) is unknown. We investigated the association of low MQI with advanced fibrosis among adults with NAFLD using a nationally representative sample of the US population. Adults with NAFLD who participated in the National Health and Nutrition Examination Survey (NHANES) 2011–2014 were included. Sex-specific standard was used to define low and extremely low MQI. Univariate and multivariate logistic regressions were used to assess the association between MQI level and advanced fibrosis. In the study, 3758 participants with NAFLD were included. The prevalence of low and extremely low MQI was 11.7% (95% CI 10.4–13.0%) and 2.2% (95% CI 1.6–2.8%), respectively. Among these participants, 96 were assessed to have advanced fibrosis. Individuals with low [(odds ratio (OR) 2.45, 95% confidence interval (CI) 1.22–4.91)] and extremely low MQI (OR 10.48, 95% CI 3.20–34.27) were associated with advanced fibrosis in multivariable analysis. A linear trend relationship was also observed between MQI level and the risk of advanced fibrosis (P_{trend} = 0.001). Subgroup and sensitivity analyses yielded similar results to the main analyses. Decreased MQI is highly prevalent, and is associated with an increased risk of advanced fibrosis in adult US population with NAFLD.

Keywords Nonalcoholic fatty liver disease, NAFLD, Muscle quality, Liver fibrosis, NHANES

Abbreviations

NHANES	National Health and Nutrition Examination Survey
MQI	Muscle quality index
NAFLD	Nonalcoholic fatty liver disease
CI	Confidence interval
OR	Odds ratio
FLI	Fatty liver index
HIS	Hepatic steatosis index
NFS	NAFLD fibrosis score
FIB-4	Fibrosis-4
APRI	AST to platelet ratio index
HGS	Handgrip strength
DXA	Dual-energy X-ray absorptiometry
ASM	Appendicular skeletal muscle mass

[1]Department of Gastroenterology, The Second Affiliated Hospital of Xi'an Jiaotong University, No.157 Xi Wu Road, Xi'an 710004, Shaanxi Province, People's Republic of China. [2]Clinical Research Center for Gastrointestinal Diseases of Shaanxi Province, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, People's Republic of China. [3]These authors contributed equally: Xinxing Tantai and Qiuju Ran. ✉email: xinxingtantai@foxmail.com; chyqiao@xjtu.edu.cn

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ALP	Alkaline phosphatase
γ-GGT	Gamma-glutamyltransferase
PIR	Poverty-income ratio
DM	Diabetes mellitus
PA	Physical activity
BMI	Body mass index
MASLD	Metabolic dysfunction-associated steatotic liver disease

Nonalcoholic fatty liver disease (NAFLD) is a very common chronic liver disease, which has affected over 30% of the global population, with its prevalence increasing by 50.4% over the past three decades[1]. In the United States, the incidence of advanced fibrosis due to NAFLD is increasing, which can result in serious outcomes such as cirrhosis, hepatocellular carcinoma, liver transplantation, and even death[2,3]. The association between decreased muscle mass and liver fibrosis in NAFLD has been suggested, but it remains controversial[4,5]. Muscle quality index (MQI) is a measure of the quality of muscles, defined as the ratio of muscle strength to muscle mass, and MQI provides a more nuanced understanding of skeletal muscle than simply measuring muscle strength or mass alone[6]. To our knowledge, the association between MQI and the development of advanced fibrosis in patients with NAFLD has not been studied. Therefore, we investigated the association of low MQI with advanced fibrosis among adults with NAFLD using a nationally representative sample of the US population.

Material and methods

Data source

We used cross-sectional data obtained from the 2011–2012 and 2013–2014 cycles of the National Health and Nutrition Examination Survey (NHANES), a nationally representative health survey of non-institutionalized US civilians. The MQI data was only available for the two 2-year cycles. The National Center for Health Statistics Research Ethics Review Board granted approval for the NHANES, and written consent was obtained from all participants. All methods were performed in accordance with the relevant guidelines and regulations. Further details about the survey can be found at http://www.cdc.gov/nchs/nhanes.

Data collection and definition

NAFLD was defined as a condition in which participants have a US Fatty Liver Index (USFLI) score of ≥ 30 or a Hepatic Steatosis Index (HSI) score of ≥ 36, in the absence of other causes of liver disease (such as positive hepatitis C antibody or positive hepatitis B surface antigen), and without significant alcohol intake (> 4 drinks/day in men and > 3 drinks/day in women)[7,8]. Advanced fibrosis was assessed using three noninvasive scoring systems: the NAFLD fibrosis score (NFS), Fibrosis-4 (FIB-4) score, and AST to platelet ratio index (APRI). Participants with NAFLD were considered to have advanced fibrosis if they met any of the following criteria: (1) NFS > 0.676, (2) FIB-4 score > 2.67, or (3) APRI > 1.5[9–11]. These scoring systems have been validated as reliable methods for diagnosing NAFLD and advanced fibrosis, and are widely used in NHANES studies[12–14].

A hand dynamometer was used to measure handgrip strength (HGS), and dual-energy X-ray absorptiometry (DXA) was utilized to evaluate appendicular skeletal muscle mass (ASM). MQI was defined as the ratio of muscle strength and muscle mass, and computed as (dominant + non-dominant HGS)/ASM (kg/kg). In addition, MQI-Arm (dominant HGS/dominant arm ASM) and MQI-appendicular (dominant HGS/ASM) were also calculated. MQI was categorized as normal, low and extremely low, with 1 SD and 2 SD sex-specific standard deviations below the mean being used as cutoffs, respectively (Supplemental Table 1)[15]. Anthropometric, sociodemographic, and laboratory data were also collected including age, sex, ethnicity, marital status, income, education, height, weight, platelet count, neutrophil count, lymphocyte count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyltransferase (γ-GGT), and uric acid.

Family income was assessed using poverty-income ratio (PIR) values, which are based on the ratio of family income to poverty. It was categorized into three groups: low (PIR ≤ 1.3), middle (1.3 < PIR < 3.5), and high income (PIR ≥ 3.5)[16]. Diabetes mellitus (DM) was defined by a fasting glucose level ≥ 126 mg/dl, random glucose level ≥ 200 mg/dl, HbA1c of ≥ 6.5%, self- reported medical history of diabetes, or treatment with anti-diabetic medication. Hypertension was defined by systolic blood pressure measure ≥ 140 mmHg, and/or diastolic blood pressure ≥ 90 mmHg, self-reported medical history of hypertension, or use of antihypertensive drugs. Hyperlipidemia was defined as an elevated triglyceride level (≥ 150 mg/dL) or cholesterol level (total cholesterol ≥ 200 mg/dL, LDL ≥ 130 mg/dL, or HDL < 40 mg/dL in men and < 50 mg/dL in women) or use of cholesterol-lowering agents[17]. Physical activity (PA) was categorized according to the 2018 PA Guidelines. PA was considered "high" level if participants engaged in ≥ 150 min per week of moderate-intensity PA, or ≥ 75 min per week of vigorous-intensity PA, or an equivalent combination. Otherwise, it was considered "low" level[18].

Statistical analysis

All results were presented using proper weighting procedures according to NHANES guidelines. Weighted mean ± standard errors and proportions (95% confidence intervals) were used for continuous and categorical variables, respectively. The chi-squared test or linear regression was used for comparing baseline characteristics when appropriate. Univariable and multivariable logistic regression were performed to evaluate the association between MQI level and advanced fibrosis. Test for linear trend was performed using MQI level as a continuous variable in the multivariable model. Subgroup analyses were performed according to the important factors, and the interaction was assessed using the likelihood ratio test. Sensitivity analyses were conducted to evaluate the

robustness of the associations between the MQI and advanced fibrosis using single definitions for NAFLD and advanced fibrosis. All analyses were performed using R software (version 4.1.2) and the 'survey' package, which accounts for the complex survey design of NHANES data. Two-sided $p < 0.05$ were considered significant.

Results

The study included 3758 adult individuals with NAFLD (Fig. 1), representing over 84.9 million non-institutionalized US civilians. Among these individuals, the prevalence (95% CI) of low and extremely low MQI was 11.7% (10.4–13.0%) and 2.2% (1.6–2.8%), respectively, corresponding to an estimated 9.9 million and 1.9 million individuals in the US. Of the participants with NAFLD, 96 were assessed to have advanced fibrosis. Baseline characteristics of the included participants are summarized in Table 1.

In univariable analysis, compared with normal group, the risk of advanced fibrosis was higher in low MQI group [odds ratio (OR) 6.36, 95% confidence interval (CI) 3.40–11.90], and numerically higher in participants with extremely low MQI (OR 29.84, 95% CI 15.34–58.05) (Table 2; Supplemental Table 2). After adjusting for age, ethnicity, smoking, BMI category, ALT, AST, ALP, γ-GGT, uric acid, and neu-trophil-to-lymphocyte ratio, participants with low MQI (OR 3.69, 95% CI 1.78–7.66) and extremely low MQI (OR 12.87, 95% CI 5.73–28.94) remained a significantly higher association with advanced fibrosis. In another multivariable model that further adjusted for hypertension, DM, hyperlipidemia, and PA level, the association with advanced fibrosis persisted for the low MQI group (OR 2.45, 95% CI 1.22–4.91) and extremely low MQI group (OR 10.48, 95% CI 3.20–34.27). Notably, a linear trend relationship was observed between MQI level and the risk of advanced fibrosis ($P_{trend} = 0.001$) (Table 2; Supplemental Table 2).

When stratified by sex, BMI category, hypertension, DM, hyperlipidemia, and PA level, the association of low MQI group and extremely low MQI group with advanced fibrosis remained significant in most subgroups (Supplemental Table 3). The lower rate of outcome events may account for the absence of statistical significance in some subgroups and the wide confidence intervals.

When using MQI-arm and MQI-appendicular to define MQI, similar results were found in univariable and multivariable analysis, except that no statistical difference was found for low MQI-arm in full multivariable analysis (Table 2; Supplemental Table 4; Supplemental Table 5). Sensitivity analyses indicated that the associations between MQI and advanced fibrosis remained consistent when using HSI to define NAFLD or NFS to define advanced fibrosis. Extremely low MQI, but not low MQI, was associated with a significantly higher risk of advanced fibrosis when using US FLI to define NAFLD (Supplemental Table 6).

Discussion

This is the first study that assessed the impact of MQI on the risk of advanced fibrosis in general adult population with NAFLD. We found that low MQI was associated with an increased risk of advanced fibrosis, and this association persisted even after some important confounders were taken into account including age, gender, obesity, physical activity and metabolic disorders[19]. More importantly, the association exhibited a linear trend.

Sarcopenia, defined as a loss of muscle mass and/or function, is a progressive and generalized skeletal muscle disorder associated with various adverse outcomes[20]. Originally conceptualized for elderly populations, whether its definition is applicable to individuals with NAFLD warrants further investigation. In patients with chronic liver disease, including NAFLD, sarcopenia is commonly defined by diminished muscle mass[21]. In NAFLD patients, sarcopenia may correlate with the progression of liver fibrosis through various potential mechanisms, such as insulin resistance, increased levels of inflammatory cytokines, and decreased levels of adiponectin[22]. Some cross-sectional studies have suggested that sarcopenia is significantly associated with the presence and severity of ultrasonography-graded NAFLD[23], as well as with significant or advanced fibrosis[24]. However, high-quality studies have indicated no causal relationship between sarcopenia and NAFLD or early steatohepatitis and fibrosis progression[25,26]. These inconsistent conclusions may arise from the susceptibility of cross-sectional studies to potential confounding factors. Interestingly, a study by Hsieh et al.[26], which included patients from a prospective biopsy-proven NAFLD cohort, found that myosteatosis, rather than sarcopenia, was associated with an increased risk of steatohepatitis and liver fibrosis over a median follow-up of 29 months. This highlights the critical role of muscle quality in the progression of NAFLD.

Decreased muscle mass and strength are very common in patients with NAFLD[4,27]. Notably, previous research found that the rate of muscle mass and strength loss did not parallel to each other, muscle strength declined at a faster rate than muscle mass, resulting in a progressive disparity between the two; this ongoing discrepancy implies a deterioration in muscle quality that may potentially lead to impaired physical abilities[19]. MQI was defined as the muscle strength divided by muscle mass, considered the best marker of muscle quality[19], and was found to be associated with metabolic derangements, systemic inflammation, and even mortality[28–30]. Lee et al. indicated that low muscle mass was independently associated with advanced fibrosis in subjects with NAFLD[4]; however, the conclusion could not be supported by the study of Choe et al.[5]. In addition, the association between handgrip strength and advanced fibrosis also could not be proven in patients with NAFLD[27]. Relative to muscle mass or strength alone, MQI may reflect the intricate intramuscular changes[6], such as intramuscular and intermuscular fat infiltration, which is extremely common in patients with NAFLD[26].

Low MQI reflects muscle strength relative to muscle mass. Oshida et al.[31] found a significant correlation between poor muscle quality (characterized by a greater mass of non-contractile tissue, including intramuscular fat) and an increased risk of liver fibrosis. Similarly, Lee et al.[32] observed that increased low-quality muscle mass, rather than decreased normal-quality muscle mass, was associated with fibrosis progression in patients with biopsy-proven NAFLD. Interestingly, Nachit et al.[33] reported that a reduction in muscle fat mass was linked to histological improvement in non-alcoholic steatohepatitis following dietary or surgical interventions. The potential mechanisms underlying the association between muscle quality, as reflected by MQI, and advanced

Variables	Total (n = 3758)	Normal (n = 3162)	Low (n = 507)	Extremely low (n = 89)	*P* value
Age (years)	39.51 ± 0.42	39.26 ± 0.43	40.54 ± 0.84	43.57 ± 1.69	0.020
Sex (%)					0.974
Female	51.14(46.55,55.73)	86.31(84.60,88.03)	11.53(10.10,12.96)	2.15(1.31, 3.00)	
Male	48.86(43.81,53.91)	85.98(83.15,88.81)	11.81(9.69,13.94)	2.21(0.91, 3.50)	
Ethnicity (%)					< 0.001
Non-Hispanic white	63.90(53.23,74.58)	87.98(86.03,89.93)	9.97(8.48,11.46)	2.05(1.26, 2.85)	
Non-Hispanic black	12.17(9.82,14.52)	74.98(70.86,79.10)	20.64(17.54,23.73)	4.38(2.48, 6.29)	
Mexican	9.82(7.02,12.62)	85.89(82.99,88.79)	12.78(10.14,15.43)	1.33(0.33, 2.32)	
Others	14.11(12.17,16.06)	87.67(83.98,91.37)	10.87(7.54,14.21)	1.45(0.66, 2.25)	
Married (%)					< 0.001
No	46.23(43.21,49.24)	83.28(80.82,85.73)	14.05(12.05,16.05)	2.67(1.63, 3.71)	
Yes	53.77(46.54,61.01)	88.62(87.07,90.18)	9.62(8.24,11.01)	1.75(1.25, 2.26)	
Family income (%)					0.115
Low	22.47(19.59,25.36)	83.07(80.20,85.95)	14.38(11.77,16.99)	2.54(1.81, 3.28)	
Middle	31.76(27.19,36.32)	85.65(82.44,88.86)	12.40(9.57,15.24)	1.95(0.96, 2.94)	
High	40.55(34.59,46.51)	88.23(86.00,90.46)	10.02(8.10,11.94)	1.75(0.79, 2.71)	
Education (%)					0.540
Less than high school	13.65(11.31,15.98)	84.70(81.19,88.20)	13.30(10.12,16.48)	2.00(0.52, 3.48)	
High school or higher	86.33(77.30,95.36)	86.40(84.68,88.13)	11.39(10.10,12.67)	2.21(1.53, 2.89)	
Smoking (%)					0.603
Never	61.31(55.49,67.14)	86.24(84.43,88.05)	11.72(10.31,13.14)	2.04(1.25, 2.83)	
Former	18.98(15.72,22.23)	87.49(84.02,90.96)	10.75(7.66,13.84)	1.76(0.35, 3.17)	
Current	17.87(16.12,19.62)	84.49(81.81,87.17)	12.54(9.76,15.32)	2.97(1.30, 4.64)	
BMI category (kg/m^2) (%)					< 0.001
< 25	22.90(19.95,25.85)	98.89(98.30,99.48)	0.95(0.46, 1.45)	0.16(-0.06, 0.37)	
25–30	34.51(30.35,38.68)	94.01(92.54,95.49)	4.97(3.54, 6.40)	1.02(0.18, 1.86)	
≥ 30	42.59(38.43,46.74)	72.93(69.73,76.13)	22.86(20.04,25.69)	4.21(3.07, 5.35)	
ALT (IU/L)	26.21 ± 0.37	25.92 ± 0.39	28.45 ± 1.14	25.80 ± 1.25	0.080
AST (IU/L)	24.72 ± 0.23	24.59 ± 0.25	25.62 ± 0.55	25.04 ± 0.75	0.173
ALP (U/L)	64.94 ± 0.63	64.28 ± 0.66	68.85 ± 1.12	69.93 ± 5.43	0.001
γ-GGT (IU/L)	26.48 ± 0.66	26.10 ± 0.72	29.17 ± 1.17	27.09 ± 2.58	0.045
Uric acid (umol/L)	319.17 ± 1.82	314.80 ± 1.79	345.82 ± 5.08	349.62 ± 7.28	< 0.001
Neutrophil-to-lymphocyte ratio	2.15 ± 0.03	2.14 ± 0.03	2.21 ± 0.06	2.38 ± 0.14	0.176
Hypertension (%)					< 0.001
No	71.60(63.81,79.38)	89.43(88.20,90.67)	8.84(7.88, 9.80)	1.72(1.08, 2.37)	
Yes	28.40(26.11,30.69)	77.88(74.66,81.09)	18.80(15.91,21.68)	3.33(2.14, 4.52)	
Diabetes mellitus (%)					< 0.001
No	90.46(81.56,99.36)	88.17(86.80,89.54)	10.12(9.02,11.22)	1.71(1.03, 2.39)	
Yes	9.54(8.36,10.72)	67.01(62.25,71.77)	26.38(20.49,32.28)	6.60(3.26, 9.95)	
Hyperlipidemia (%)					< 0.001
No	31.69(27.79,35.59)	89.84(88.15,91.53)	9.19(7.69,10.68)	0.97(0.26, 1.69)	
Yes	68.31(61.75,74.87)	84.44(82.40,86.48)	12.82(11.14,14.50)	2.74(1.96, 3.51)	
Physical activity level (%)					< 0.001
Low	14.06(11.92,16.20)	83.55(80.35,86.75)	12.40(10.00,14.80)	4.05(2.01, 6.09)	
High	67.44(60.77,74.11)	88.64(87.08,90.19)	10.00(8.73,11.28)	1.36(0.86, 1.86)	
MQI (kg/kg)	3.33 ± 0.02	3.48 ± 0.02	2.46 ± 0.01	1.86 ± 0.06	< 0.001
MQI-arm (kg/kg)	12.57 ± 0.08	13.10 ± 0.06	9.67 ± 0.10	7.52 ± 0.13	< 0.001
MQI-appendicular (kg/kg)	1.71 ± 0.01	1.79 ± 0.01	1.27 ± 0.01	0.95 ± 0.03	< 0.001
Advanced fibrosis (%)					< 0.001
No	97.62(88.49,106.74)	87.23(85.76,88.69)	11.12(9.94,12.30)	1.65(1.05, 2.25)	
Yes	2.38(1.69, 3.08)	42.09(30.29,53.90)	34.12(23.36,44.89)	23.78(16.33,31.24)	

Table 1. Baseline characteristics of adult NAFLD patients stratified by MQI level. Data are presented as the weighted mean ± standard errors or weighted frequency (95% confidence intervals) as appropriate. The linear regressions were used for continuous variables, and the Chi-square tests were used for categorical variables in difference analyses. BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; γ-GGT, gamma-glutamyltransferase; MQI, muscle quality index.

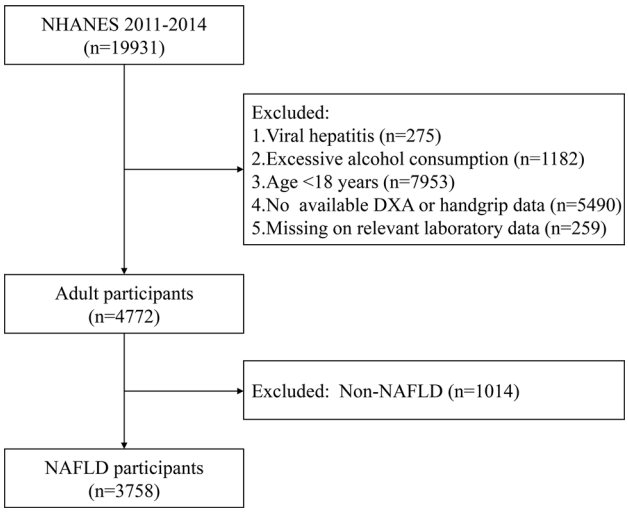

Fig. 1. Flow chart of participants selection. NHANES, National Health and Nutrition Examination Surveys; DXA, dual-energy X-ray absorptiometry; NAFLD, non-alcoholic fatty liver disease.

Variables	Univariable model		Multivariable model 1		Multivariable model 2		P_{trend}
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	
MQI							0.001
Normal	Reference		Reference		Reference		
Low	6.36(3.40, 11.90)	< 0.001	3.69(1.78, 7.66)	0.001	2.45(1.22, 4.91)	0.015	
Extremely low	29.84(15.34, 58.05)	< 0.001	12.87(5.73, 28.94)	< 0.001	10.48(3.20, 34.27)	< 0.001	
MQI-arm							0.038
Normal	Reference		Reference		Reference		
Low	5.22(2.86, 9.51)	< 0.001	2.35(1.09, 5.06)	0.031	1.47(0.68, 3.19)	0.301	
Extremely low	29.75(16.07, 55.07)	< 0.001	13.70(6.42, 29.23)	< 0.001	4.91(1.27, 19.00)	0.024	
MQI-appendicular							< 0.001
Normal	Reference		Reference		Reference		
Low	5.66(3.17, 10.13)	< 0.001	2.66(1.25, 5.65)	0.014	3.06(1.41, 6.60)	0.008	
Extremely low	28.94(14.27, 58.66)	< 0.001	13.36(5.77, 30.95)	< 0.001	7.12(1.64, 30.95)	0.012	

Table 2. Univariable and multivariable analysis of MQI, MQI-arm, MQI-appendicular for advanced fibrosis among adults with NAFLD. Survey-weight adjusted logistic regressions were used in the univariable and multivariable model. The multivariate model 1 was adjusted for age, ethnicity, smoking, BMI category, ALT, AST, ALP, γ-GGT, uric acid, and neutrophil-to-lymphocyte ratio using appropriate sampling weights. The multivariate model 2 was adjusted for hypertension, diabetes mellitus, hyperlipidemia, and physical activity level in addition to model 1 using appropriate sampling weights. OR, odds ratio; CI, confidence interval; MQI, muscle quality index; BMI, body mass index; ALP, alkaline phosphatase; γ-GGT, gamma-glutamyltransferase.

fibrosis require further investigation. Existing studies suggest that this association may relate to disrupted oxidative phosphorylation, lipotoxicity due to lipid accumulation, and systemic inflammation[34,35].

The strengths of this study included the use of a representative sample of the US population and a rigorous methodology. However, there are several limitations to our study. First, although a linear trend was found, the cross-sectional study design limits our ability to establish a causal relationship between MQI level and advanced fibrosis. Second, due to the unavailability of liver biopsy or hepatic imaging, we used multiple non-invasive formulas to define NAFLD and advanced fibrosis. Although these non-invasive formulas have been validated as reliable methods for diagnosing NAFLD and liver fibrosis in the US and other populations, and are widely used in NHANES studies, they may potentially lead to misclassification. Third, due to the small number of outcome events, sensitivity analyses evaluating the association between MQI and advanced fibrosis defined by FIB-4 or APRI could not be performed. Lastly, the nomenclature of NAFLD has recently been changed to metabolic dysfunction-associated steatotic liver disease (MASLD). Due to the unavailability of data, validating our findings under this new definition is not feasible. Although some studies indicate that findings from older NAFLD studies remain valid under the new MASLD definition[36,37], our findings still need to be validated under the MASLD definition.

In conclusion, decreased MQI is highly prevalent, and is associated with an increased risk of advanced fibrosis in adult US population with NAFLD. Resistance exercise training has been demonstrated to be an effective and feasible approach to activate underutilized muscles, thereby enhancing muscle quality[6]. This improvement in muscle quality may help prevent the progression of liver fibrosis in individuals with NAFLD.

Data availability

Data from the National Health and Nutrition Examination Survey are publicly available online at https://www.cdc.gov/nchs/nhanes/index.htm (accessed on 15 February 2023).

Received: 15 February 2024; Accepted: 23 August 2024
Published online: 27 August 2024

References

1. Younossi, Z. M. *et al.* The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): A systematic review. *Hepatology* **77**, 1335–1347 (2023).
2. Kim, D. *et al.* Race/ethnicity-based temporal changes in prevalence of NAFLD-related advanced fibrosis in the United States, 2005–2016. *Hepatol Int.* **13**, 205–213 (2019).
3. Noureddin, M. *et al.* NASH leading cause of liver transplant in women: Updated analysis of indications for liver transplant and ethnic and gender variances. *Am. J. Gastroenterol.* **113**, 1649–1659 (2018).
4. Lee, Y. H. *et al.* Sarcopenia is associated with significant liver fibrosis independently of obesity and insulin resistance in nonalcoholic fatty liver disease: Nationwide surveys (KNHANES 2008–2011). *Hepatology* **63**, 776–786 (2016).
5. Choe, H. J. *et al.* Different effects of low muscle mass on the risk of non-alcoholic fatty liver disease and hepatic fibrosis in a prospective cohort. *J. Cachexia Sarcopenia Muscle* **14**, 260–269 (2023).
6. Fragala, M. S. *et al.* Muscle quality in aging: a multi-dimensional approach to muscle functioning with applications for treatment. *Sports Med.* **45**, 641–658 (2015).
7. Ruhl, C. E. *et al.* Everhart, fatty liver indices in the multiethnic United States National Health and Nutrition Examination Survey. *Aliment Pharmacol. Ther.* **41**, 65–76 (2015).
8. Lee, J. H. *et al.* Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. *Dig. Liver Dis.* **42**, 503–508 (2010).
9. Angulo, P. *et al.* The NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology* **45**, 846–854 (2007).
10. Shah, A. G. *et al.* Comparison of noninvasive markers of fibrosis in patients with nonalcoholic fatty liver disease. *Clin. Gastroenterol. Hepatol.* **7**, 1104–1112 (2009).
11. Wai, C. T. *et al.* A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology* **38**, 518–526 (2003).
12. Henry, A. *et al.* Vigorous physical activity provides protection against all-cause deaths among adults patients with nonalcoholic fatty liver disease (NAFLD). *Aliment Pharmacol. Ther.* **57**, 709–722 (2023).
13. Kardashian, A. *et al.* Food insecurity is associated with mortality among U.S. adults with nonalcoholic fatty liver disease and advanced fibrosis. *Clin. Gastroenterol. Hepatol.* **20**, 2790-2799.e2794 (2022).
14. Kim, D., Vazquez-Montesino, L. M., Li, A. A., Cholankeril, G. & Ahmed, A. Inadequate physical activity and sedentary behavior are independent predictors of nonalcoholic fatty liver disease. *Hepatology* **72**, 1556–1568 (2020).
15. Lopes, L. C. C. *et al.* Sex and population-specific cutoff values of muscle quality index: Results from NHANES 2011–2014. *Clin. Nutr.* **41**, 1328–1334 (2022).
16. Ogden, C. L. *et al.* Prevalence of obesity among youths by household income and education level of head of household—United States 2011–2014. *MMWR Morb. Mortal Wkly. Rep.* **67**, 186–189 (2018).
17. Kammerlander, A. A. *et al.* Association of metabolic phenotypes with coronary artery disease and cardiovascular events in patients with stable chest pain. *Diabetes Care* **44**, 1038–1045 (2021).
18. Piercy, K. L. *et al.* The physical activity guidelines for Americans. *Jama* **320**, 2020–2028 (2018).
19. Barbat-Artigas, S. *et al.* Aubertin-Leheudre, How to assess functional status: A new muscle quality index. *J. Nutr. Health Aging* **16**, 67–77 (2012).
20. Kirk, B. *et al.* The conceptual definition of sarcopenia: Delphi consensus from the Global Leadership Initiative in Sarcopenia (GLIS). *Age Ageing* **53**, afae052 (2024).
21. Son, S. W. *et al.* Definition of sarcopenia in chronic liver disease. *Life (Basel)* **11**, 349 (2021).
22. Iwaki, M. *et al.* Impact of sarcopenia on non-alcoholic fatty liver disease. *Nutrients* **15**, 891 (2023).
23. Harring, M. *et al.* Sarcopenia among patients with nonalcoholic fatty liver disease (NAFLD) is associated with advanced fibrosis. *Clin. Gastroenterol. Hepatol.* **21**, 2876-2888.e2875 (2023).
24. Chung, G. E. *et al.* Sarcopenia is significantly associated with presence and severity of nonalcoholic fatty liver disease. *J. Obes. Metab. Syndr.* **28**, 129–138 (2019).
25. Zhao, Z. H. *et al.* Assessing causal relationships between sarcopenia and nonalcoholic fatty liver disease: A bidirectional Mendelian randomization study. *Front. Nutr.* **9**, 971913 (2022).
26. Hsieh, Y. C. *et al.* Myosteatosis, but not sarcopenia, predisposes NAFLD subjects to early steatohepatitis and fibrosis progression. *Clin. Gastroenterol. Hepatol.* **21**, 388-397.e310 (2023).
27. Kang, S. *et al.* Association between muscle strength and advanced fibrosis in non-alcoholic fatty liver disease: A Korean nationwide survey. *J. Cachexia Sarcopenia Muscle* **11**, 1232–1241 (2020).
28. Poggiogalle, E. *et al.* The decline in muscle strength and muscle quality in relation to metabolic derangements in adult women with obesity. *Clin. Nutr.* **38**, 2430–2435 (2019).
29. Brown, J. C. *et al.* The muscle quality index and mortality among males and females. *Ann. Epidemiol.* **26**, 648–653 (2016).
30. Lopes, L. C. C. *et al.* Low hand grip strength is associated with worse functional capacity and higher inflammation in people receiving maintenance hemodialysis. *Nutrition* **93**, 111469 (2022).
31. Oshida, N. *et al.* Muscle quality as a potential diagnostic marker of advanced liver fibrosis in patients with non-alcoholic fatty liver disease. *J. Obes. Metab. Syndr.* **33**, 143–154 (2024).
32. Lee, Y. K. *et al.* Low-quality muscle mass rather than normal-quality muscle mass determines fibrosis progression in biopsy-proven NAFLD. *Aliment Pharmacol. Ther.* **58**, 322–333 (2023).
33. Nachit, M. *et al.* Muscle fat content is strongly associated with NASH: A longitudinal study in patients with morbid obesity. *J. Hepatol.* **75**, 292–301 (2021).
34. Stretch, C. *et al.* Sarcopenia and myosteatosis are accompanied by distinct biological profiles in patients with pancreatic and periampullary adenocarcinomas. *PLoS One* **13**, e0196235 (2018).

35. Correa-de-Araujo, R. *et al.* Myosteatosis in the context of skeletal muscle function deficit: An interdisciplinary workshop at the National Institute on Aging. *Front. Physiol.* **11**, 963 (2020).
36. Song, S. J. *et al.* Can we use old NAFLD data under the new MASLD definition?. *J. Hepatol.* **80**, e54–e56 (2024).
37. Perazzo, H. *et al.* Changing from NAFLD through MAFLD to MASLD: Similar prevalence and risk factors in a large Brazilian cohort. *J. Hepatol.* **80**, e72–e74 (2024).

Author contributions

X.T. and C.Q.: study concept and design; X.T., Q.R., Z.W., and S.T.: acquisition of data; X.T. and N.L.: analysis and interpretation of data; X.T. and Q.R.: drafting of the manuscript and preparing all Tables or Figures; X.T., S.D., J.W., and C.Q.: critical revision of the manuscript for important intellectual content.

Funding

This study was supported by grants from Xi'an Science and Technology Plan Project(22YXYJ0122).

Competing interests

The authors declare no competing interests.

Ethical approval

This study protocol was reviewed and approved by NCHS Ethics Review Board, approval number (Protocol #2011-17). Written informed consent was collected from all participants enrolled in the National Health and Nutrition Examination Survey. Further details can be found at https://www.cdc.gov/nchs/nhanes/irba98.htm.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-71096-w.

Correspondence and requests for materials should be addressed to X.T. or C.Q.