Nonlinear relationship between muscle quality index and hyperuricemia among non-elderly adults

Keywords
hyperuricemia, nonlinear relationship, muscle quality index, cross-sectional research, national health and nutrition examination survey

Abstract

Introduction
The muscle quality index (MQI) is an increasingly prominent indicator of muscle status. The objective of this research is to analyze the connection between MQI and hyperuricemia.

Material and methods
We performed a cross-sectional analysis utilizing data from the National Health and Nutrition Examination Survey (NHANES) spanning the years 2011 to 2014. Participants in this study were adults aged 20-59 years. Muscle quality index (MQI) was calculated as the ratio of handgrip strength (HGS) to appendicular skeletal muscle mass (ASM). Hyperuricemia was defined by serum uric acid concentrations exceeding 420 μmol/L (7 mg/dL) in males and 360 μmol/L (6 mg/dL) in females. Assessment of the MQI-hyperuricemia relationship involved logistic regression, analysis of subgroups, and the application of smooth curve fitting.

Results
This research included 5,283 participants, of whom 716 had hyperuricemia. The prevalence of hyperuricemia decreased with higher quartiles of MQI (P<0.001). After correcting for confounders, MQI was closely associated with hyperuricemia (OR=0.59, 95%CI□0.46-0.77, P<0.001). Smooth curve fitting indicated a nonlinear association between the variables, with a threshold identified at 2.92. Subgroup analyses demonstrated that this association was particularly evident in participants with diabetes.

Conclusions
Our findings revealed an inverse correlation between MQI and hyperuricemia, suggesting that preserving adequate muscle quality may be advantageous in reducing the risk of hyperuricemia. Further prospective research is needed.

Nonlinear relationship between muscle quality index and hyperuricemia among non-elderly adults

Menghuan Wu[1, &], Zhaoxiang Wang[2, &], Qichao Yang[3], Han Yan[3], Xuejing Shao[3, *]

[1] Department of Endocrinology, Shanghai Putuo District Liqun Hospital, Shanghai, 200000, China

[2] Department of Endocrinology, Affiliated Kunshan Hospital of Jiangsu University, Kunshan, Jiangsu, 215300, China

[3] Department of Endocrinology, Wujin Clinical College of Xuzhou Medical University, Affiliated Wujin Hospital of Jiangsu University, Changzhou, Jiangsu, 213017, China

[&] **Equal author contribution.**

* **Correspondence:**

Xuejing Shao, shaoxuejing@wjrmyy.cn

ABSTRACT

Purpose: The muscle quality index (MQI) is an increasingly prominent indicator of muscle status. The objective of this research is to analyze the connection between MQI and hyperuricemia.

Methods: We performed a cross-sectional analysis utilizing data from the National Health and Nutrition Examination Survey (NHANES) spanning the years 2011 to 2014. Participants in this study were adults aged 20-59 years. Muscle quality index (MQI) was calculated as the ratio of handgrip strength (HGS) to appendicular skeletal muscle mass (ASM). Hyperuricemia was defined by serum uric acid concentrations exceeding 420 μmol/L (7 mg/dL) in males and 360 μmol/L (6 mg/dL) in females. Assessment of

the MQI-hyperuricemia relationship involved logistic regression, analysis of subgroups, and the application of smooth curve fitting.

Results: This research included 5,283 participants, of whom 716 had hyperuricemia. The prevalence of hyperuricemia decreased with higher quartiles of MQI (***P***<0.001). After correcting for confounders, MQI was closely associated with hyperuricemia (OR=0.59, 95%CI： 0.46-0.77, ***P***<0.001). Smooth curve fitting indicated a nonlinear association between the variables, with a threshold identified at 2.92. Subgroup analyses demonstrated that this association was particularly evident in participants with diabetes.

Conclusions: Our findings revealed an inverse correlation between MQI and hyperuricemia, suggesting that preserving adequate muscle quality may be advantageous in reducing the risk of hyperuricemia. Further prospective research is needed.

Keywords: muscle quality index; hyperuricemia; cross-sectional research; nonlinear relationship; national health and nutrition examination survey

1. Introduction

Hyperuricemia, a prevalent metabolic disorder, is defined by plasma uric acid concentrations exceeding the normal range [1]. It serves as both an early warning sign of gout, while also significantly contributing to the risk of developing hypertension, diabetes, chronic kidney disease, cardiovascular diseases, and mortality [2-5]. Despite the rising global incidence of hyperuricemia and its growing health burden, effective treatment options remain limited [6].

Handgrip strength (HGS), the force produced by the muscle groups of the hand, is a common metric used to assess an individual's overall muscle strength and functional status [7]. Stronger HGS is generally correlated with a lower risk of cardiovascular diseases, reduced mortality rates, and improved quality of life [8]. However, the

association between HGS and hyperuricemia is currently controversial. Veronese et al. found that elderly patients with hyperuricemia typically exhibit reduced HGS [9]. Some studies have shown a positive correlation between uric acid levels and increased HGS, with higher uric acid levels significantly associated with greater muscle mass, HGS, and bone density [10]. Loss of muscle strength and muscle mass do not parallel each other, and simply considering muscle strength, that is, HGS, may not reflect the true condition of the muscles. Thus, the muscle quality index (MQI) is proposed as a new functional index, which is defined as the ratio of HGS and appendicular skeletal muscle mass (ASM) [11]. MQI provides a more comprehensive assessment of muscle tissue quality by considering both the mass and strength. Current research indicates that MQI is significantly associated with pulmonary function [12], cardiovascular diseases [13], trouble sleeping [14], and periodontal disease [15].

Given the uninvestigated link between MQI and hyperuricemia in non-elderly adults, we conducted a cross-sectional analysis of National Health and Nutrition Examination Survey (NHANES) data to examine this association.

2. Methods

2.1 Study population

Administered by the National Center for Health Statistics (NCHS), a branch of the Centers for Disease Control and Prevention (CDC), NHANES represents one of the most extensive population-based studies in the United States [16]. NHANES adopted a multi-stage, stratified probability sampling methodology to ensure the selection of a nationally representative cohort. Enrolled individuals participated in comprehensive health evaluations, including physical examinations, structured interviews on dietary and health behaviors, and standardized laboratory analyses. The present investigation analyzed datasets derived from the 2011-2014 NHANES survey cycles. Exclusion criteria comprised subjects under 20 or over 59 years of age, those lacking serum uric

acid (SUA) and MQI data (**Figure 1**). Ultimately, 5,283 participants (2,687 males and 2,596 females) were incorporated into the final analysis of this study.

Figure 1 Flowchart depicting the selection of participants.

2.2 Exposure and Outcome Definitions

The ratio of HGS to ASM is defined as the MQI [17]. Dynamometer is used to measure HGS. Grip strength quantification involved summation of peak values obtained from both hands, with results standardized in kilograms. Measurement of appendicular lean mass (ALM) was conducted with dual-energy X-ray absorptiometry (DXA), focusing on muscular components of upper and lower limbs (kg). DXA technology provided comprehensive body composition analysis, including bone density and soft tissue distribution across major anatomical regions (extremities, trunk, and cephalic segment). The aggregate lean tissue mass in limbs was designated as ASM. SUA values >420 μmol/L (7 mg/dL) in men and >360 μmol/L (6 mg/dL) in women are diagnostic thresholds for hyperuricemia [18-19].

2.3 Covariate definitions

To minimize potential confounding, we included the following variables as covariates in our analysis: age, gender, race, marital status, household's annual income, educational background, smoking, presence of diabetes, hypertension, and cardiovascular disease, body mass index (BMI), glycated hemoglobin (HbA1c), triglyceride levels (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), serum creatinine (SCr), and estimated glomerular filtration rate (eGFR) [20]. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [21]. BMI was classified as normal weight (<25 kg/m²), overweight (25–29.9 kg/m²), or obese (≥30 kg/m²). Information on diabetes and hypertension was obtained via self-report.

Cardiovascular disease was ascertained from participant self-reports of myocardial infarction, stroke, heart failure, coronary heart disease, or angina.

2.4 Statistical analysis

Analytical procedures accounted for the complex survey design by incorporating CDC-specified sampling weights across two survey cycles. Descriptive statistics for quantitative measures were reported as weighted mean ± standard error, while categorical measures characterized as weighted percentage (standard error). Between-group comparisons were conducted using appropriate weighted statistical tests (weighted Student's t-test and chi-squared test). Logistic and linear regression analyses were conducted to evaluate the relationships between MQI and both hyperuricemia and SUA levels. Model 1 was unadjusted and served as the reference. Model 2 adjusted for demographic variables such as age, gender, and race. Model 3 further incorporated socioeconomic and lifestyle factors, including marital status, annual household income, education level, and smokers. Model 4, extending Model 3, further adjusted for clinical and biochemical parameters: hypertension, diabetes, cardiovascular disease, BMI, TG, LDL-c, HDL-c, SCr, eGFR and HbA1c. Smoothed curve fitting and threshold effect analyses were applied to evaluate the association between MQI and hyperuricemia risk among non-elderly adults, and to determine potential inflection points in this relationship. Subgroup and interaction analyses were also conducted. All statistical procedures in this study were executed with R 4.1.1 and EmpowerStats software (http://www.empowerstats.com), with significance levels defined a priori at $P < 0.05$.

3. Results

3.1 Baseline characteristics of the study population

The cohort comprised 5,283 participants (mean age=9.38 years; 51.27%male), stratified by hyperuricemia status into two comparative groups (**Table 1**). Compared

to the non-hyperuricemia group, the proportion of men, hypertension, diabetes, overweight/obesity, TC, TG, LDL-c, SCr, HGS, ASM, and SUA were significantly higher in hyperuricemia group (***P***<0.05). Conversely, the hyperuricemia group had statistically reductions in HDL-c, eGFR, and MQI (***P***<0.05) (**Table 1**). Significant differences in racial composition were also observed between the two groups (***P***<0.05).

Table 1 Baseline characteristics of non-elderly population in NHANES from 2011 to 2014, weighted.

3.2 Clinical features of hyperuricemia participants according to MQI

Study participants were categorized into four equal groups by MQI quartile distribution (**Table 2**). Comparative analysis demonstrated that individuals in the top MQI quartile were characterized by lower mean age and higher proportion of male participants (***P***<0.01). This group also showed higher levels of education and exhibited significantly lower rates of hypertension, diabetes, cardiovascular diseases, and obesity (***P***<0.05). Moreover, their HbA1c, TG, ASM, and SUA levels were lower, while their HDL-c, SCr, and HGS levels were higher (***P***<0.05). It is noteworthy that as the levels of MQI progressively increase, the prevalence of hyperuricemia gradually decreases (17.33% vs. 14.11% vs. 12.47% vs. 8.88%, ***P***<0.001).

Table 2 Baseline characteristics of non-elderly population according to the quartiles of MQI, weighted.

3.3 Association between MQI and hyperuricemia

Table 3 shows a negative correlation between MQI and hyperuricemia with or without correction for confounding factors (***P***<0.001). Multivariable-adjusted logistic analysis found a significant inverse association between MQI and hyperuricemia risk, with each 1-unit increment corresponding to a 41% lower probability (OR=0.59, 95% CI: 0.46-0.77, ***P***<0.001). Quartile-based logistic analysis of MQI demonstrated an inverse dose-

response relationship with hyperuricemia prevalence, with progressively lower rates observed in higher quartiles after full covariate adjustment (***P*** for trend = 0.001). The linear regression model (**Table 4**), employing SUA concentrations as the outcome measure and MQI as the predictor, demonstrated a significant inverse relationship between these variables (β = -0.13, 95% CI -0.22--0.05, ***P***=0.003). Moreover, results from the smooth curve fitting analysis and threshold effect analysis confirmed that MQI is inversely associated with the risk of hyperuricemia. This relationship is nonlinear, and the threshold point is 2.92 (**Table 5, Figure 2**).

Table 3 Logistic regression analysis results of MQI and hyperuricemia.

Table 4 Linear regression analysis results of MQI and SUA levels.

Table 5 Threshold effect analysis of MQI on hyperuricemia using a two-piecewise linear regression model.

Figure 2 Smooth curve fitting results of MQI and hyperuricemia.

3.4 Subgroup analysis

Subgroup analyses were systematically used to examine potential effect modification of the MQI-hyperuricemia relationship, with results visually presented in **Figure 3**. Factors including age, gender, hypertension, cardiovascular disease, and BMI did not significantly affect these relationships (***P***>0.05). However, this association was notably stronger in participants with diabetes (OR=0.29, 95% CI: 0.14-0.64) compared to those without diabetes (OR=0.64, 95% CI: 0.49-0.84) (***P*** for interaction=0.048).

Figure 3 Subgroup analysis.

4. Discussion

The current study addresses a gap in existing literature by examining the connection between MQI and hyperuricemia risk. We identified a significant, nonlinear inverse

association between MQI and the likelihood of hyperuricemia among no-elderly adults. Moreover, subgroup analyses reveal that the inverse association between MQI and hyperuricemia is especially evident in individuals with diabetes.

Prior research has paid considerable attention to the link between muscle status and uric acid levels. A population-based study in Korea highlighted a correlation between higher HGS and elevated SUA levels in elderly individuals [22]. In kidney transplant patients, Floriano et al. also found that SUA levels were positively related to muscle mass and strength [23]. Xie et al. further demonstrated that skeletal muscle mass was positively associated with hyperuricemia in obese children and adolescents [24]. In our analysis of non-elderly adults, higher HGS and ASM were positively correlated with the prevalence of hyperuricemia. However, the MQI, represented by the HGS/ASM ratio, exhibited a negative correlation with hyperuricemia. This inconsistency may be attributed to the fact that muscle strength diminishes at a faster rate than muscle mass as individuals age [25]. Compared to traditional muscle status indicators, MQI not only considers muscle mass but also evaluates muscle strength, providing a more comprehensive reflection of overall muscle condition [26]. This approach enables earlier prediction of changes in muscle quality and function compared to relying solely on grip strength tests [26]. In this research, we also accounted for the potential confounding effects of body weight. Because both muscle quality and SUA are strongly influenced by body weight and adiposity, we adjusted for BMI in all multivariable models and conducted stratified analyses across different BMI categories. Notably, the inverse association between MQI and hyperuricemia remained robust and statistically significant after these adjustments. These findings indicate that the relationship between muscle quality and hyperuricemia is not solely attributable to the effects of body weight.

Several potential biological mechanisms help to explain these two associations. MQI might influence hyperuricemia risk through its effects on metabolic regulation,

including insulin sensitivity and systemic inflammation. Skeletal muscle is the main site of glucose uptake through glucose transporter type 4 (GLUT4), responsible for nearly 80% of total glucose clearance [27]. A decrease in muscle mass leads to altered glucose handling and increased local inflammation, promoting insulin resistance [28]. Insulin resistance is a major factor in the development of hyperuricemia, as it influences uric acid handling in the renal tubules by simultaneously enhancing uric acid reabsorption and excretion [29-30]. The enhancement of muscle strength may also indirectly reduce uric acid levels by improving insulin resistance. Our study additionally identified a more pronounced link between MQI and hyperuricemia in patients with diabetes, further highlighting the critical role of insulin resistance. Moreover, research has demonstrated that greater muscle strength is frequently linked to an elevated basal metabolic rate (BMR) [31]. An increase in BMR is generally associated with improvements in metabolic health, such as enhanced insulin sensitivity and reduced adipose tissue [32-34]. These factors help to reduce the production and accumulation of uric acid. Low levels of skeletal muscle strength and mass are significantly correlated with higher levels of circulating inflammatory markers [35-36]. Chronic inflammation accelerates hyperuricemia by inducing oxidative stress, which damages cell membranes and DNA [37]. This triggers the release and metabolism of intracellular purine nucleotides, leading to excess uric acid production [37]. While it is possible that better muscle quality may reduce the risk of hyperuricemia, the alternative hypothesis suggests that hyperuricemia itself can negatively affect muscle quality through mechanisms involving oxidative stress, lipid and carbohydrate metabolic dysfunction [38-41]. Prior research has also demonstrated that elevated SUA can induce mitochondrial dysfunction, inflammatory responses, and muscle protein degradation, resulting in impaired muscle structure and function [41-43].

Although this represents the inaugural investigation of the MQI-hyperuricemia association, several methodological constraints warrant consideration. First, the study only included participants aged 20-59, which may restrict the applicability of the

results to different age populations, such as adolescents and the elderly, potentially overlooking variations in muscle quality and hyperuricemia risk across life stages. Secondly, as discussed above, the cross-sectional nature of this study allows us to identify only an inverse association between MQI and the risk of hyperuricemia, without the ability to determine causality or the temporal sequence of events. Prospective longitudinal studies with larger and more diverse populations are warranted to further elucidate this relationship. Finally, despite adjusting for numerous confounders, unmeasured factors may still influence the results, warranting further investigation.

5. Conclusion

Our results reveal an inverse association between MQI and hyperuricemia, and maintaining an appropriate MQI level is beneficial for hyperuricemia. However, further prospective research is needed to substantiate this finding.

Declarations

Ethics approval and consent to participate

The study protocol adhered to international ethical guidelines (Declaration of Helsinki) and received formal approval from the National Center for Health Statistics (https://www.cdc.gov/nchs/nhanes/about/erb.html) Research Ethics Review Board. Prior to data collection, all subjects voluntarily provided documented informed consent following comprehensive explanation of study procedures.

Consent for publication

Not applicable

Availability of data and material

The dataset was obtained from the publicly available National Health and Nutrition Examination Survey (NHANES) repository (https://wwwn.cdc.gov/nchs/nhanes).

Funding

This study is funded by the Changzhou 11th Batch of Science and Technology Plan Projects (CJ20243003).

Competing interests

The investigators report no conflicts of interest to disclose.

Acknowledgments

Not applicable.

References

1. El Ridi R, Tallima H (2017) Physiological functions and pathogenic potential of uric acid: A review. J Adv Res 8(5): 487-493. https://doi.org/10.1016/j.jare.2017.03.003
2. Kuwabara M, Kodama T, Ae R, Kanbay M, Andres-Hernando A, Borghi C, Hisatome I, Lanaspa MA (2023) Update in uric acid, hypertension, and cardiovascular diseases. Hypertens Res 46(7): 1714-1726. https://doi.org/10.1038/s41440-023-01273-3
3. Gherghina ME, Peride I, Tiglis M, Neagu TP, Niculae A, Checherita IA (2022) Uric Acid and Oxidative Stress-Relationship with Cardiovascular, Metabolic, and Renal Impairment. Int J Mol Sci 23(6). https://doi.org/10.3390/ijms23063188
4. Crawley WT, Jungels CG, Stenmark KR, Fini MA (2022) U-shaped association of uric acid to overall-cause mortality and its impact on clinical management of hyperuricemia. Redox Biol 51102271. https://doi.org/10.1016/j.redox.2022.102271
5. Zeng F, Huang R, Lu Y, Wu Z, Wang L (2020) Association of anti-hyperuricemia treatment and prevalent cardiovascular disease in hypertensive patients. Arch Med Sci 16(3): 545-550. https://doi.org/10.5114/aoms.2019.84397
6. Dehlin M, Jacobsson L, Roddy E (2020) Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. Nat Rev Rheumatol 16(7): 380-390. https://doi.org/10.1038/s41584-020-0441-1

7. Carlos A C-M, Paul W, Donald M L, Lewis S, Fanny P, Jana A, Stamatina I, Anne S, Nicholas G, Daniel F M, Jill P P, Jason M R G, Naveed S, Stuart R G (2018) Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. BMJ 361(0). https://doi.org/10.1136/bmj.k1651

8. Rubén L-B, Lars Louis A, Ai K, Rodrigo N-C, Joaquín C, José C, Borja DPC (2022) Thresholds of handgrip strength for all-cause, cancer, and cardiovascular mortality: A systematic review with dose-response meta-analysis. Ageing Res Rev 82(0). https://doi.org/10.1016/j.arr.2022.101778

9. Nicola V, Brendon S, Caterina T, Francesco B, Marina DR, Stefania M, Leonardo S, Estella M, Sabina Z, Egle P, Marianna N, Gaetano C, Enzo M, Giuseppe S (2016) Results of an Observational Cohort Study of Hyperuricemia as a Predictor of Poor Physical Performance in the Elderly. Arthritis Care Res (Hoboken) 69(8). https://doi.org/10.1002/acr.23118

10. Zhe-Rong X, Qin Z, Lu-Fang C, Ke-Ying X, Jia-Ying X, Shu-Min L, Yun-Mei Y (2018) Characteristics of hyperuricemia in older adults in China and possible associations with sarcopenia. Aging Med (Milton) 1(1). https://doi.org/10.1002/agm2.12004

11. Lorena Cristina Curado L, Larissa V-G, Raquel Machado S, Maria Cristina G, Carla M P, Erick P dO, João Felipe M (2022) Sex and population-specific cutoff values of muscle quality index: Results from NHANES 2011-2014. Clin Nutr 41(6). https://doi.org/10.1016/j.clnu.2022.04.026

12. Luoqi W, Zhixiao X, Yuhan C, Chengshui C (2023) Associations between the muscle quality index and adult lung functions from NHANES 2011-2012. Front Public Health 11(0). https://doi.org/10.3389/fpubh.2023.1146456

13. Yanlin C, Weidong L, Lu F, Huiyi L, Shuyu J, Xingdong Y, Sijia P, Yumei X (2023) Muscle quality index and cardiovascular disease among US population-findings from NHANES 2011-2014. BMC Public Health 23(1). https://doi.org/10.1186/s12889-023-17303-1

14. Yanwei Y, Yuquan C, Qi Z, Ning Y, Yi N, Qiang C (2023) Muscle quality index is associated with trouble sleeping: a cross-sectional population based study. BMC Public Health 23(1). https://doi.org/10.1186/s12889-023-15411-6

15. Jukun S, Yadong W, Hong M, Junmei Z (2023) Association between muscle quality index and periodontal disease among American adults aged ≥ 30 years: a cross-sectional study and mediation analysis. BMC Oral Health 23(1). https://doi.org/10.1186/s12903-023-03520-y

16. Wang Z, Zhao G, Cao Y, Gu T, Yang Q (2024) Association between monocyte to high-density lipoprotein cholesterol ratio and kidney stone: insights from

NHANES. Front Endocrinol (Lausanne) 151374376. https://doi.org/10.3389/fendo.2024.1374376

17. Dulce G-I, Robinson R-H, Laura F-C, Arturo O-T, Susana G-A, Nadia H-L, Mariana I V-M, Rocío S-S, Juan Carlos G-H, Armando C-M (2023) Association between muscle quality index and pulmonary function in post-COVID-19 subjects. BMC Pulm Med 23(1). https://doi.org/10.1186/s12890-023-02745-5

18. Abdul-Quddus M, Fuad A A, Lu L, Wen Z, Guoqing Y, Yawei X, Wenliang C (2021) Hyperuricemia Predicts Adverse Outcomes After Myocardial Infarction With Non-obstructive Coronary Arteries. Front Med (Lausanne) 8(0). https://doi.org/10.3389/fmed.2021.716840

19. Han Y, Cao Y, Han X, Di H, Yin Y, Wu J, Zhang Y, Zeng X (2023) Hyperuricemia and gout increased the risk of long-term mortality in patients with heart failure: insights from the National Health and Nutrition Examination Survey. J Transl Med 21(1): 463. https://doi.org/10.1186/s12967-023-04307-z

20. Wang Z, Tang F, Zhao B, Yan H, Shao X, Yang Q (2024) Composite dietary antioxidant index and abdominal aortic calcification: a national cross-sectional study. Nutrition Journal 23(1): 130. https://doi.org/10.1186/s12937-024-01029-w

21. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J (2009) A new equation to estimate glomerular filtration rate. Ann Intern Med 150(9): 604-12. https://doi.org/10.7326/0003-4819-150-9-200905050-00006

22. Lee J, Hong YS, Park SH, Kang KY (2019) High serum uric acid level is associated with greater handgrip strength in the aged population. Arthritis Res Ther 21(1): 73. https://doi.org/10.1186/s13075-019-1858-2

23. Floriano JP, Nahas PC, de Branco FMS, Dos Reis AS, Rossato LT, Santos HO, Limirio LS, Ferreira-Filho SR, de Oliveira EP (2020) Serum Uric Acid Is Positively Associated with Muscle Mass and Strength, but Not with Functional Capacity, in Kidney Transplant Patients. Nutrients 12(8). https://doi.org/10.3390/nu12082390

24. Xie L, Mo PKH, Tang Q, Zhao X, Zhao X, Cai W, Feng Y, Niu Y (2022) Skeletal Muscle Mass Has Stronger Association With the Risk of Hyperuricemia Than Body Fat Mass in Obese Children and Adolescents. Front Nutr 9792234. https://doi.org/10.3389/fnut.2022.792234

25. Scott D, Hayes A, Sanders KM, Aitken D, Ebeling PR, Jones G (2014) Operational definitions of sarcopenia and their associations with 5-year changes in falls risk in community-dwelling middle-aged and older adults. Osteoporos Int 25(1): 187-93. https://doi.org/10.1007/s00198-013-2431-5

26. Daniel J-M, Pedro D-F, Leonardo I, Christian C-J, Leonidas A-P, Juan G-V, Amador G-R, Luis Javier C (2020) Behavior of the muscle quality index and isometric strength in elderly women. Physiol Behav 227(0). https://doi.org/10.1016/j.physbeh.2020.113145

27. Hiroki N, Akira A, Shinya F, Shuhei N, Kazuhide H (2021) Metabolic Syndrome and Sarcopenia. Nutrients 13(10). https://doi.org/10.3390/nu13103519

28. Jakub M, Ayse Z, Barbora DC, Peter R E, David S (2019) Sarcopenia and type 2 diabetes mellitus: a bidirectional relationship. Diabetes Metab Syndr Obes 12(0). https://doi.org/10.2147/dmso.S186600

29. Asma Sakalli A, Küçükerdem HS, Aygün O (2023) What is the relationship between serum uric acid level and insulin resistance?: A case-control study. Medicine (Baltimore) 102(52): e36732. https://doi.org/10.1097/md.0000000000036732

30. Toyoki D, Shibata S, Kuribayashi-Okuma E, Xu N, Ishizawa K, Hosoyamada M, Uchida S (2017) Insulin stimulates uric acid reabsorption via regulating urate transporter 1 and ATP-binding cassette subfamily G member 2. Am J Physiol Renal Physiol 313(3): F826-f834. https://doi.org/10.1152/ajprenal.00012.2017

31. Sung-Kwan O, Da-Hye S, Yu-Jin K, Hye Sun L, Ji-Won L (2019) Association between Basal Metabolic Rate and Handgrip Strength in Older Koreans. Int J Environ Res Public Health 16(22). https://doi.org/10.3390/ijerph16224377

32. Stanhope KL (2016) Sugar consumption, metabolic disease and obesity: The state of the controversy. Crit Rev Clin Lab Sci 53(1): 52-67. https://doi.org/10.3109/10408363.2015.1084990

33. Maciak S, Sawicka D, Sadowska A, Prokopiuk S, Buczyńska S, Bartoszewicz M, Niklińska G, Konarzewski M, Car H (2020) Low basal metabolic rate as a risk factor for development of insulin resistance and type 2 diabetes. BMJ Open Diabetes Res Care 8(1). https://doi.org/10.1136/bmjdrc-2020-001381

34. Petrie JL, Patman GL, Sinha I, Alexander TD, Reeves HL, Agius L (2013) The rate of production of uric acid by hepatocytes is a sensitive index of compromised cell ATP homeostasis. Am J Physiol Endocrinol Metab 305(10): E1255-65. https://doi.org/10.1152/ajpendo.00214.2013

35. Camilla S L T, Lachlan A N T, Andrea B M (2020) Markers of inflammation and their association with muscle strength and mass: A systematic review and meta-analysis. Ageing Res Rev 64(0). https://doi.org/10.1016/j.arr.2020.101185

36. Ertek S, Cicero A (2012) Impact of physical activity on inflammation: effects on cardiovascular disease risk and other inflammatory conditions. Arch Med Sci 8(5): 794-804. https://doi.org/10.5114/aoms.2012.31614

37. Du L, Zong Y, Li H, Wang Q, Xie L, Yang B, Pang Y, Zhang C, Zhong Z, Gao J (2024) Hyperuricemia and its related diseases: mechanisms and advances in therapy. Signal Transduct Target Ther 9(1): 212. https://doi.org/10.1038/s41392-024-01916-y

38. Oncel Yoruk E, Dost FS, Ontan MS, Ates Bulut E, Aydin AE, Isik AT (2023) Hyperuricemia may be associated with muscle wellness in older adults. Int Urol Nephrol 55(11): 2981-2988. https://doi.org/10.1007/s11255-023-03588-z

39. Chen L, Wu L, Li Q, Hu Y, Ma H, Lin H, Gao X (2022) Hyperuricemia Associated with Low Skeletal Muscle in the Middle-Aged and Elderly Population in China. Exp Clin Endocrinol Diabetes 130(8): 546-553. https://doi.org/10.1055/a-1785-3729

40. Shao Y, Wang Y, Jiang X, Shao M, Liu B, Li L, Zhong H (2025) Muscle quality index and hyperuricemia: adipose tissue as a mediator. Front Endocrinol (Lausanne) 161562837. https://doi.org/10.3389/fendo.2025.1562837

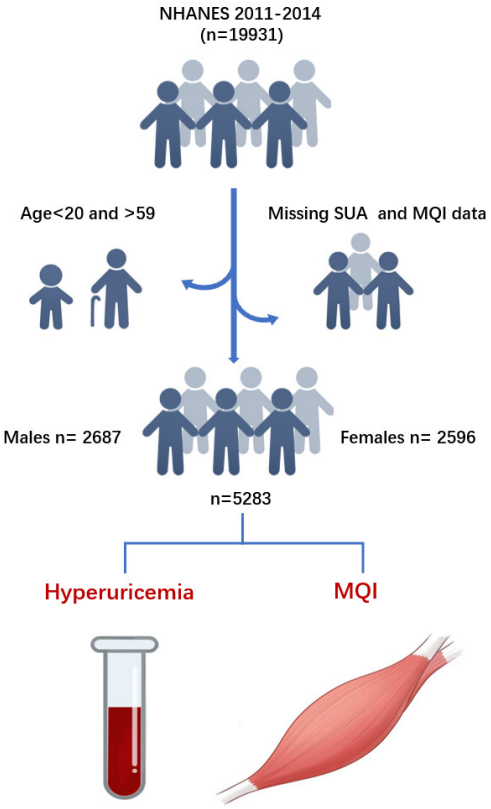
41. Wang F, Wen L, Guo X, Wang W, Cao Y, Zhou G, Wang J, Zheng C (2025) Association of Serum Uric Acid With Relative Muscle Loss: A US Population-Based Cross-Sectional Study. J Cachexia Sarcopenia Muscle 16(3): e13867. https://doi.org/10.1002/jcsm.13867

42. Chao HH, Liu JC, Lin JW, Chen CH, Wu CH, Cheng TH (2008) Uric acid stimulates endothelin-1 gene expression associated with NADPH oxidase in human aortic smooth muscle cells. Acta Pharmacol Sin 29(11): 1301-12. https://doi.org/10.1111/j.1745-7254.2008.00877.x

43. Roumeliotis S, Roumeliotis A, Dounousi E, Eleftheriadis T, Liakopoulos V (2019) Dietary Antioxidant Supplements and Uric Acid in Chronic Kidney Disease: A Review. Nutrients 11(8). https://doi.org/10.3390/nu11081911

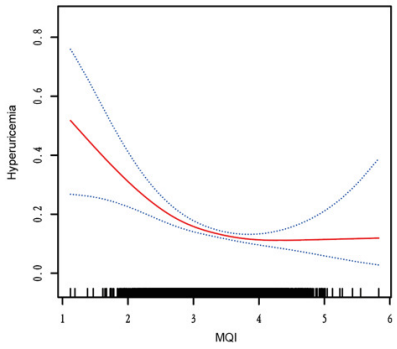
Nonlinear relationship between muscle quality index and hyperuricemia among non-elderly adults

Population



Key Findings

MQI inversely linked to hyperuricemia with threshold at 2.92



Stronger MQI protection against hyperuricemia in diabetics

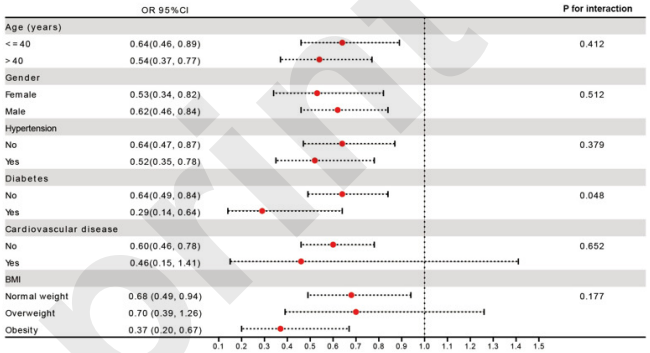


Table 1 Baseline characteristics of non-elderly population in NHANES from 2011 to 2014, weighted.

	Overall (N= 5,283)	Non-hyperuricemia (N= 4,567)	Hyperuricemia (N= 716)	***P*** value
Age (years)	39.38±0.38	39.33±0.41	39.75±0.45	0.399
Male gender, % (SE)	51.27 (0.77)	47.16 (0.89)	78.56 (1.49)	<0.001
Race, % (SE)				0.017
Mexican American	11.00 (1.42)	10.22 (1.46)	7.83 (1.42)	
Non-Hispanic Black	64.19 (1.30)	10.86 (1.28)	11.92 (1.73)	
Non-Hispanic White	6.45 (2.69)	63.83 (2.74)	66.58 (2.85)	
Other Hispanic	8.45 (0.98)	6.72 (1.03)	4.71 (0.99)	
Other Races	11.00 (0.73)	8.37 (0.69)	8.96 (1.37)	
Annual household income (under $20,000), % (SE)	13.25 (1.27)	13.34 (0.53)	12.71 (0.87)	0.653
Education level (above high school), % (SE)	65.45 (2.06)	65.61 (2.13)	64.37 (2.77)	0.623
Married, % (SE)	52.01 (1.55)	51.55 (1.65)	55.07 (2.39)	0.160
Smokers, % (SE)	41.79 (1.27)	41.39 (1.45)	44.43 (2.47)	0.304
Hypertension, % (SE)	22.82 (0.91)	20.47 (0.90)	38.43 (2.69)	<0.001
Diabetes, % (SE)	5.22 (0.41)	5.22 (0.44)	7.18 (0.94)	0.040
Cardiovascular disease, % (SE)	3.20 (0.38)	3.13 (0.41)	3.68 (0.95)	0.570
BMI (kg/m2), % (SE)				<0.001
Normal weight	32.34 (1.10)	35.52 (1.25)	11.32 (1.27)	
Overweight	33.61 (0.91)	33.19 (0.95)	36.45 (2.30)	
Obesity	34.04 (1.00)	31.29 (1.21)	52.23 (2.02)	
HbA1c (%)	5.50±0.02	5.49±0.02	5.56±0.04	0.109
TC (mmol/L)	4.97±0.02	4.93±0.02	5.24±0.06	<0.001
TG (mmol/L)	1.43±0.05	1.36±0.05	1.87±0.09	<0.001
HDL-c (mmol/L)	1.35±0.01	1.37±0.01	1.18±0.02	<0.001
LDL-c (mmol/L)	2.97±0.02	2.93±0.03	3.18±0.06	<0.001
SCr (μmol/L)	76.52±0.44	74.74±0.43	88.28±0.98	<0.001
eGFR (ml/min/1.73 m^2)	101.12±0.46	102.17±0.47	94.19±1.00	<0.001
HGS (kg)	77.23±0.40	75.66±0.41	87.64±0.78	<0.001
ASM (kg)	23.03±0.14	22.39±0.14	27.29±0.29	<0.001
SUA (mg/dl)	5.34±0.03	4.99±0.02	7.65±0.04	<0.001
MQI	3.40±0.02	3.43±0.02	3.25±0.02	<0.001

Note: Values for categorical variables are given as weighted percentage (standard error); for continuous variables, as weighted mean ± standard error. Weighted Student's t-test and chi-squared test were used.

Abbreviations: BMI, body mass index; HbA1c, glycated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; SCr, serum creatinine; eGFR, estimated glomerular filtration rate; HGS, combined handgrip strength; ASM, arm and appendicular skeletal muscle; MQI, muscle quality index.

Table 2 Baseline characteristics of non-elderly population according to the quartiles of MQI, weighted.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	***P*** value
Age (year)	41.15±0.64	40±0.56	38.9±0.54	37.66±0.44	0.001
Male gender, % (SE)	41.60 (2.36)	50.71 (1.52)	53.29 (1.81)	58.56 (1.67)	<0.001
Race, % (SE)					<0.001
Mexican American	9.83 (1.73)	9.9 (1.55)	9.04 (1.15)	10.93 (1.90)	
Non-Hispanic Black	18.87 (2.21)	10.87 (1.49)	8.21 (1.14)	6.9 (0.95)	
Non-Hispanic White	58.96 (3.22)	64.62 (3.25)	67.67 (2.62)	64.82 (3.23)	
Other Hispanic	6.04 (1.17)	7.73 (1.01)	6.13 (1.35)	5.88 (1.02)	
Other Races	6.3 (1.07)	6.87 (0.74)	8.96 (0.75)	11.47 (1.22)	
Annual household income (under $20,000), % (SE)	15.4 (1.66)	12.87 (1.43)	12.55 (1.33)	12.43 (1.95)	0.236
Education level (above high school), % (SE)	62.65 (2.71)	68.54 (2.05)	69.16 (2.20)	60.89 (2.71)	<0.001
Married, % (SE)	48.15 (2.06)	53.51 (2.49)	54.12 (2.07)	51.78 (2.13)	0.098
Smokers, % (SE)	40.11 (2.20)	41.06 (2.17)	41.16 (1.87)	44.76 (2.18)	0.355
Hypertension, % (SE)	31.7 (1.75)	24.73 (1.50)	19.29 (1.34)	16.51 (1.42)	<0.001
Diabetes, % (SE)	11.8 (0.96)	5.95 (0.91)	3.16 (0.57)	1.66 (0.33)	<0.001
Cardiovascular disease, % (SE)	5.31 (0.79)	2.8 (0.60)	2.87 (0.73)	2.03 (0.38)	<0.001
BMI (kg/m^2), % (SE)					<0.001
Normal weight	9.69 (1.16)	21.98 (1.76)	37.89 (1.57)	57.78 (1.78)	
Overweight	22.14 (1.50)	36.60 (1.32)	40.62 (1.56)	33.64 (1.98)	
Obesity	68.18 (1.48)	41.41 (1.65)	21.49 (1.54)	8.57 (1.14)	
HbA1c (%)	5.83±0.04	5.52±0.02	5.37±0.02	5.33±0.02	<0.001
TC (mmol/L)	4.95±0.04	4.99±0.04	4.97±0.04	4.96±0.04	0.869
TG (mmol/L)	1.56±0.11	1.44±0.09	1.44±0.09	1.47±0.07	0.017
HDL-c (mmol/L)	1.26±0.01	1.33±0.01	1.36±0.02	1.42±0.02	<0.001
LDL-c (mmol/L)	3.01±0.04	2.96±0.05	3.00±0.04	2.90±0.04	0.169
SCr (μmol/L)	76.56±1.37	75.42±0.47	76.88±0.60	77.20±0.62	0.029
eGFR (ml/min/1.73 m^2)	100.49±0.68	101.21±0.64	100.72±0.78	102.05±0.69	0.410
HGS (kg)	65.93±0.79	75.55±0.69	80.00±0.85	86.33±0.79	<0.001
ASM (kg)	25.57±0.33	23.78±0.21	22.26±0.23	20.76±0.20	<0.001
SUA (mg/dl)	5.51±0.06	5.42±0.04	5.29±0.05	5.16±0.05	<0.001
Hyperuricemia, % (SE)	17.33 (1.75)	14.11 (1.50)	12.47 (1.34)	8.88 (1.42)	<0.001

Table 3 Logistic regression analysis results of MQI and hyperuricemia

Hyperuricemia	OR (95%CI), ***P*** value			
	Model 1	Model 2	Model 3	Model 4
Continuous				
MQI	0.60 (0.53, 0.68) <0.001	0.48 (0.42, 0.55) <0.001	0.46 (0.40, 0.53) <0.001	0.59 (0.46, 0.77) <0.001
Categories				
Quartile 1	Ref.	Ref.	Ref.	Ref.
Quartile 2	0.70 (0.57, 0.86) <0.001	0.60 (0.48, 0.75) <0.001	0.58 (0.47, 0.73) <0.001	0.72 (0.50, 1.03) 0.072
Quartile 3	0.59 (0.48, 0.74) <0.001	0.46 (0.37, 0.58) <0.001	0.44 (0.35, 0.56) <0.001	0.56 (0.38, 0.83) 0.004
Quartile 4	0.44 (0.35, 0.55) <0.001	0.32 (0.25, 0.40) <0.001	0.30 (0.23, 0.38) <0.001	0.51 (0.32, 0.80) 0.003
P for trend	<0.001	<0.001	<0.001	0.001

OR: odds ratio.

95% CI: 95% confidence interval.

Model 1: non-adjusted.

Model 2: adjusted for age, gender, and race.

Model 3 adjusted for age, gender, and race, marital status, annual household income, education level, and smokers.

Model 4: adjusted for age, gender, and race, marital status, annual household income, education level, smokers, hypertension, diabetes, cardiovascular disease, BMI, TG, LDL-c, HDL-c, SCr, eGFR and HbA1c.

Table 4 Linear regression analysis results of MQI and SUA levels

SUA (mg/dL)	β (95%CI), ***P*** value			
	Model 1	Model 2	Model 3	Model 4
Continuous				
MQI	-0.25 (-0.30, -0.19) <0.001	-0.41 (-0.46, -0.36) <0.001	-0.43 (-0.49, -0.38) <0.001	-0.13 (-0.22, -0.05) 0.003
Categories				
Quartile 1	Ref.	Ref.	Ref.	Ref.
Quartile 2	-0.14 (-0.24, -0.04) 0.008	-0.26 (-0.35, -0.17) <0.001	-0.27 (-0.36, -0.18) <0.001	-0.05 (-0.17, 0.08) 0.455
Quartile 3	-0.27 (-0.37, -0.17) <0.001	-0.46 (-0.55, -0.37) <0.001	-0.48 (-0.58, -0.39) <0.001	-0.17 (-0.31, -0.04) 0.012
Quartile 4	-0.40 (-0.50, -0.29) <0.001	-0.65 (-0.75, -0.56) <0.001	-0.68 (-0.78, -0.59) <0.001	-0.15 (-0.29, -0.00) 0.050
P for trend	<0.001	<0.001	<0.001	0.017

95% CI: 95% confidence interval.

Model 1: non-adjusted.

Model 2: adjusted for age, gender, and race.

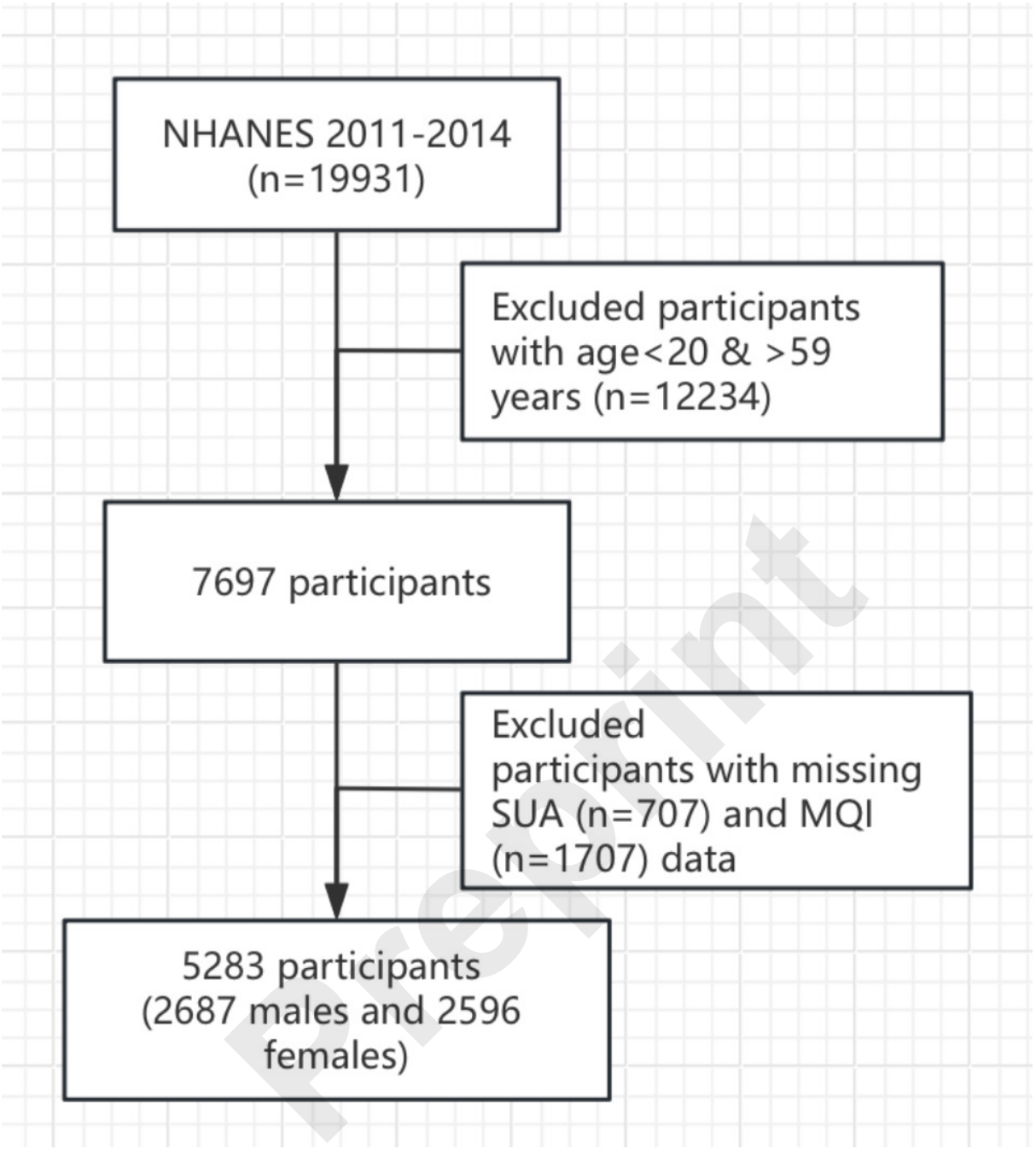
Model 3 adjusted for age, gender, and race, marital status, annual household income, education level, and smokers.

Model 4: adjusted for age, gender, and race, marital status, annual household income, education level, smokers, hypertension, diabetes, cardiovascular disease, BMI, TG, LDL-c, HDL-c, SCr, eGFR and HbA1c.

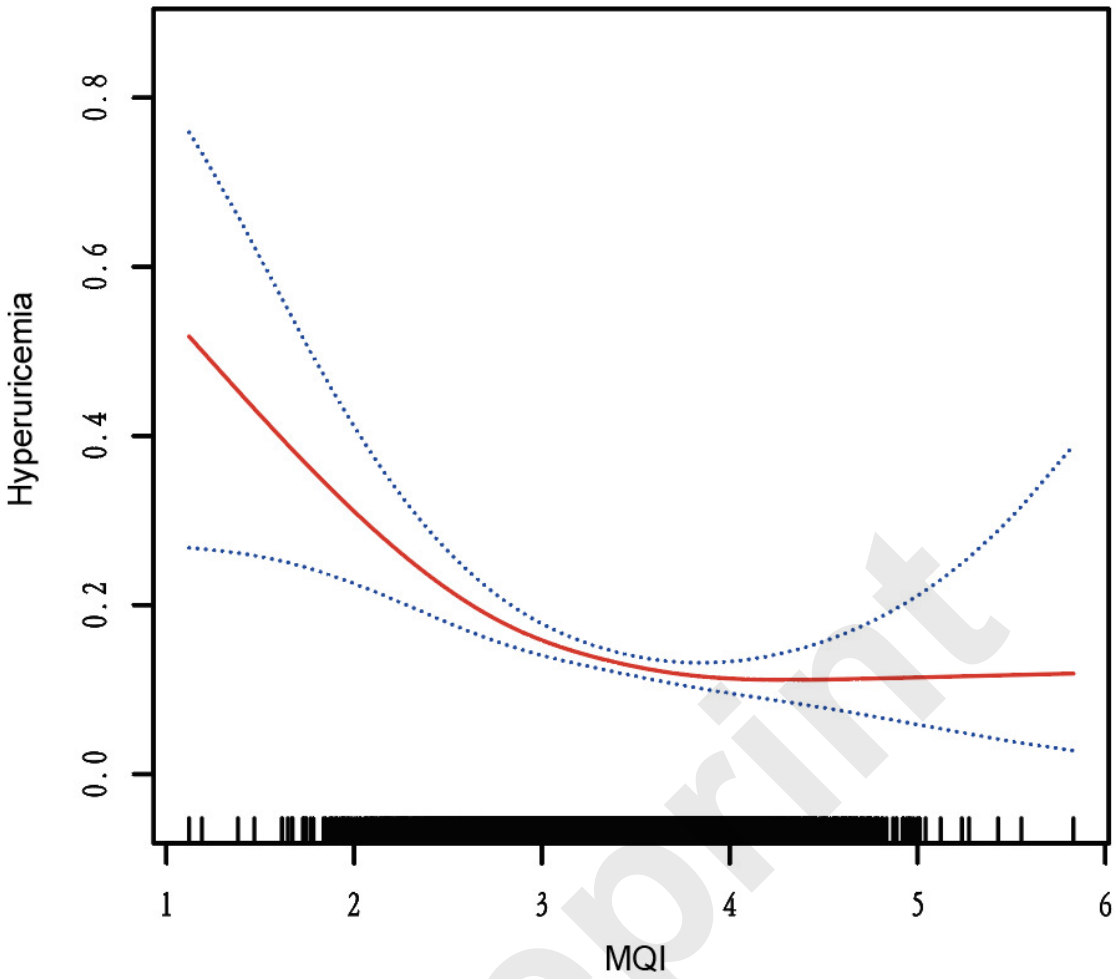
Table 5 Threshold effect analysis of MQI on hyperuricemia using a two-piecewise linear regression model

Model	OR (95% CI), ***P*** value
Fitting by standard linear model	
	0.59 (0.46, 0.77), <0.001
Fitting by two-piecewise linear model	
Breakpoint (K)	2.92
OR1 (<2.92)	0.28 (0.16, 0.51) <0.001
OR2 (>2.92)	0.83 (0.58, 1.18) 0.292
OR2/OR1	2.92 (1.35, 6.31) 0.006
P for logarithmic likelihood ratio	0.007

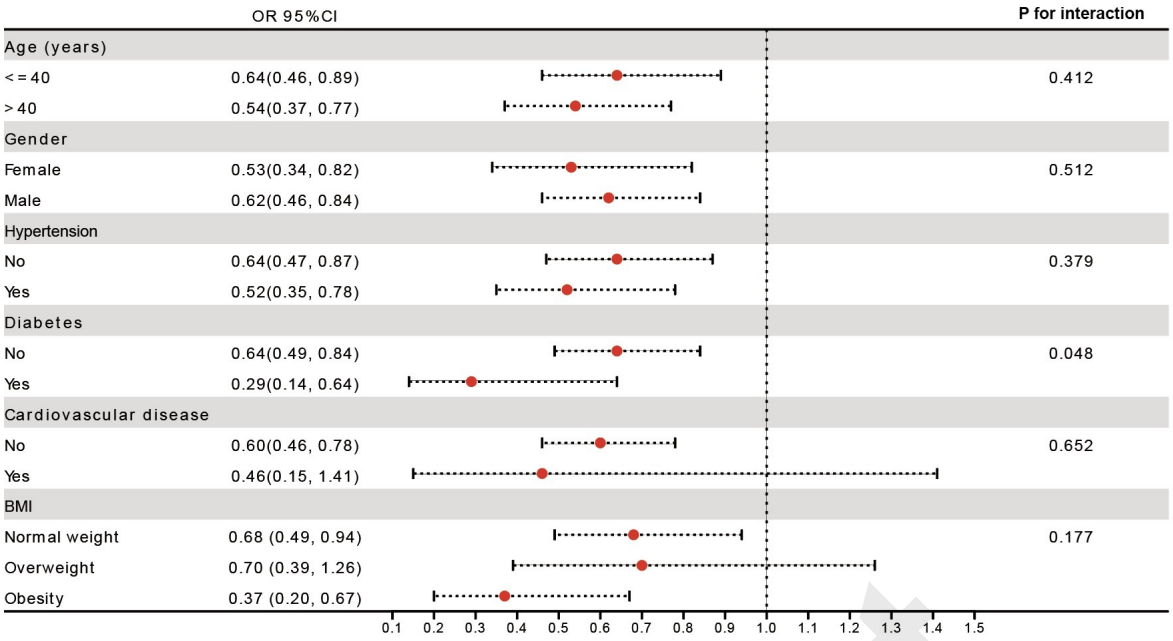
adjusted for age, gender, and race, marital status, annual household income, education level, smokers, hypertension, diabetes, cardiovascular disease, BMI, TG, LDL-c, HDL-c, SCr, eGFR and HbA1c.



Flowchart depicting the selection of participants.



Smooth curve fitting results of MQI and hyperuricemia.



Subgroup analysis.