**Association between homocysteine and** **sarcopenia** **in US older adults**

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**Abstract**

**Background:** The association between homocysteine and the risk of sarcopenia remains controversial. In this study, we sought to explore the association between homocysteine and the risk of sarcopenia in US older adults.

**Methods:** We conducted a cross-sectional study consisting of 3,079 participants aged greater than 60 years from National Health and Nutrition Examination Survey (NHANES) 1999-2006. We defined sarcopenia by low muscle mass. We evaluated the association between homocysteine and the risk of sarcopenia using multivariable regression models. Subgroup and interaction analysis were also performed.

**Results:** We found a positive association between homocysteine and the risk of sarcopenia in the fully adjusted model (OR=1.023 [95% CI, 1.003, 1.043]). In addition, subgroup analysis indicated that the association between homocysteine and the risk of sarcopenia was more pronounced among participants with hypertension (OR=1.04 [95% CI, 1.01, 1.06], Pint = 0.013).

**Conclusions:**We found a positive association between homocysteine and the risk of sarcopenia in US older adults. Further studies are needed to assess our results.

**Keywords:** Homocysteine,Sarcopenia, Older adults, NHANES, Skeletal muscle index

**Introduction**

Sarcopenia is a disorder defined as the loss of muscle mass and strength with an impact on falls, disability, and high mortality [1, 2]. It has been reported that the global prevalence of sarcopenia ranged from 10% to 27% in the meta-analysis [3]. A study from US found that about 28.7 million or 15.9% of the USA population had low muscle mass during 2017–2018 [4]. Sarcopenia has gradually gradually become a global problem that brings a huge impact on economy and health. Its specific pathogenesis and molecular mechanism is multifactorial and complexity [5]. Thus, exploring the risk factors for sarcopenia and providing timely intervention may delay its progression.

 Homocysteine is a nonessential amino acid that is an intermediate in many biological processes, such as cellular antioxidant potential, and cellular methylation [6]. As a biochemical index, homocysteine is closely related to inflammation. hyperhomocysteinemia has been demonstrated as a risk factors for variety of chronic diseases, including cardiovascular and neurodegenerative diseases [7]. Previous studies reported that hyperhomocysteinemia can induce oxidative stress and chronic inflammation, leading to bone breakdown and muscle atrophy [8, 9]. Furthermore, chronic inflammation has been reported as leading to the development of sarcopenia [10, 11]. In this regard, there is ongoing research involve in detecting of the association between sarcopenia and homocysteine [12, 13]. A cross-sectional study from China reported that elevated homocysteine levels were independently associated with sarcopenia in hospitalized older and suggested that down-regulation of hyperhomocysteinemia may reduce the prevalence of sarcopenia [14]. In another study, homocysteine was positively associated with S in elderly patients with type 2 diabetes, and these biomarkers may play an important role in the pathogenesis of S [15]. In asymptomatic adults, high homocysteine elevation is independently associated with low skeletal muscle mass and may be a risk for skeletal muscle tissue decline, according to the Korean study [16]. Whether there is an association between S and homocysteine in US older adults is unclear.

To fill the aforementioned knowledge gaps, we aimed to explore the association between homocysteine and sarcopenia in older adults in the United States using data from the National Health and Nutrition Examination Survey (NHANES) database.

**Methods**

**Study population**

The present study obtained data from the NHANES database. The NHANES database is a population-based national survey focusing on nutrition and health of the US population. We collected samples from 4 NHANES cycles, ranging from 1999 to 2006. There were 7,177 participants aged over 60 years in total. We excluded participants without valid data for sarcopenia (no reliable dual-energy X-ray absorptiometry (DXA) and body mass indexes (BMI)). After further excluding individuals with missing value for arthritis status information (n = 2,876) and other covariates (n = 2,010), 3,079 participants were included for analysis (Figure 1).

**Definition of sarcopenia**

Skeletal muscle mass was measured for each participant using DXA with the Hologic QDR 4500/A-Delphi (Hologic, Waltham, MA). Appendicular skeletal muscle mass (ASM (kg)) was defined as the sum of four limbs’ muscle mass. The skeletal muscle index (SMI) was calculated as the appendicular skeletal muscle mass divided by BMI. According to the National Institutes of Health (FNIH) recommendation, sarcopenia was defined as the lowest for sex- specific SMI cut- off values (SMI was < 0.789 for males and < 0.512 for females) [17].

**Assessment of homocysteine and covariates**

Homocysteine was determined by the Abbott homocysteine assay. Homocysteine concentrations were calculated through the Abbott IMx Immunoassay Analyzer using a machine-stored calibration curve [18].Covariates that could confound the association between homocysteine and sarcopenia were included. Socio-demographic covariates included age, race/ethnicity, and education. Physical activity was categorized as sedentary, low, moderate, and high. Smoking status was determined based on a questionnaire, in which the patient answers the question “Have you smoked at least 100 cigarettes in your entire life?” Medical history including hypertension and diabetes, were acquired from self-reported data. The other laboratory covariates included total protein, total cholesterol, HDL cholesterol, triglycerides, hemoglobin, serum albumin, serum calcium, C-reactive protein (CRP), and serum creatinine. All examinations were carried out by well-trained medical experts. Information on each variable and acquisition process are publicly available at [www.cdc.gov/nchs/nhanes.](http://www.cdc.gov/nchs/nhanes.)

**Statistical analysis**

Continuous variables were presented as mean ± standard deviation and categorical variables as percentages. We grouped participants on the basis of their sarcopenia status. We used the ANOVA tests for continuous variables with a normal distribution and Kruskal-Wallis test for continuous variables without a normal distribution. The chi-square tests were used for categorical variables to assess the characteristics of the participants. Multivariate logistic regression analyses were performed to evaluate the association between homocysteine and sarcopenia with odds ratio (OR) and corresponding 95% confidence interval (CI). Four models were contrasted as follows: model 1, no adjustment for covariates; model 2, adjusted for age, gender, and race/ethnicity; model 3, additionally adjusted for total protein, total cholesterol, HDL cholesterol, triglycerides, hemoglobin, serum albumin, serum calcium, C-reactive protein (CRP), and serum creatinine; model 4, additionally adjusted for education, physical activity, smoking status, hypertension, and diabetes.

In addition, subgroup analyses were also conducted stratified by different gender, education level, physical activity, hypertension, diabetes, smoking status, and BMI. A two-sided P-value < 0.05 was considered statistically significant. Statistical analyses were performed using the EmpowerStats (<http://www.empowerstats.com>, X&Y Solutions, Inc., Boston, MA) and statistical software packages R (http://www.R-project.org, The R Foundation).

**Result**

**Characteristics of Participants**

The characteristics of participants stratified by sarcopenia are presented in Table 1. Among the 3079 individuals were included in analysis, 870 (28.26%) participants were diagnosed with S. Compared with the non- sarcopenia group, the sarcopenia group tend to be older, to have higher sedentary physical activity, triglycerides, CRP, and serum creatinine, and lower serum albumin, and serum calcium. Moreover, the prevalence of diabetes was significantly higher in participants with sarcopenia compared to non-sarcopenic participants.

**Homocysteine and Sarcopenia Risk**

Table 2 showed the association between homocysteine and risk of sarcopenic. Homocysteine was significantly associated with an increased risk of sarcopenic in Model 1 (OR = 1.021 [95% CI, 1.006, 1.036]). These associations persisted after further adjusting for age, gender, and race/ethnicity in Model 2 (OR = 1.017 [95% CI, 1.001, 1.034]), additionally adjusting for total protein, total cholesterol, HDL cholesterol, triglycerides, hemoglobin, serum albumin, serum calcium, C-reactive protein (CRP), and serum creatinine in Model 3 (OR = 1.029 [95% CI, 1.009, 1.049]), and additionally adjusting for education, physical activity, smoking status, hypertension, and diabetes in Model 4 (OR = 1.023 [95% CI, 1.003, 1.043]).

Subgroup analysis was performed to examine whether the association between homocysteine and risk of sarcopenic were consistent among different population groups (Figure 2). Homocysteine was associated with an increased risk of sarcopenic in populations of female (OR = 1.04 [95% CI, 1.01, 1.06]), with an education level of lower than high school (OR = 1.03 [95% CI, 1.01, 1.06]), with low physical activity level (OR = 1.03 [95% CI, 1.01, 1.06]), with hypertension (OR = 1.04 [95% CI, 1.01, 1.06]), without diabetes (OR = 1.02 [95% CI, 1.01, 1.05]), smoker (OR = 1.03 [95% CI, 1.01, 1.06]), and with BMI between 24.9 and 29.9 (OR = 1.03 [95% CI, 1.01, 1.07]). The interaction with the hypertension is remarkable (Pint = 0.013), indicating that the association between homocysteine and sarcopenic was more pronounced in participants with hypertension than without hypertension. The interactions with other group are not statistically significant.

**Discussion**

In the current study, we used the data from population-based national survey to investigate whether homocysteine was associated with sarcopenia in US older adults. After fully adjusting for confounders, we found a positive association between homocysteine and the risk of sarcopenia. In addition, subgroup analysis indicated that the association between homocysteine and sarcopenia was more pronounced among participants with hypertension.

Sarcopenia is an age-related disease characterised by **a progressive decline of skeletal muscle mass, strength, and function** [19]. Currently, the pathogenesis of sarcopenia mainly including chronic inflammation, muscle mitochondrial dysfunction, redox imbalance, muscle cell autophagy, and impaired satellite cell function [20]. It is well known that homocysteine is an indicator closely related to inflammation. The pro-inflammatory properties of homocysteine may increase proteolysis of muscle and reduce its regenerative capacity, and ultimately lead to the development of sarcopenia [21]. Several previous studies have explored the association between homocysteine and sarcopenia. A cross-sectional study from Japan found that homocysteine was negatively associated with hand grip strength, but not with sarcopenia in memory clinic older outpatients [22]. Another cross-sectional study from Taiwan reported that hyperhomocysteinemia was associated with decreased muscle mass in the elderly hemodialysis patients, suggesting that lowering homocysteine levels may bring positive effect on muscle mass [23]. Results from a I-Lan longitudinal aging study showed that high levels of homocysteine were independently associated with sarcopenia in middle-aged and older community-dwelling adults [12]. In the present study, we observed a positive association between homocysteine and sarcopenia in US older adults, and the correlation remained after fully adjustment for other confounders.

The pathological mechanism for the link of homocysteine and sarcopenia were not fully understand. Until now, many studies have explored the possible molecular mechanisms for the link between homocysteine and sarcopenia. A study in mice found that hyperhomocysteinemia may inhibit satellite cell proliferation through excessive oxidative stress and p38 MAPK signaling, indicating that it is a potential risk factor for frailty in older [24]. Hyperhomocysteinemia might induce muscle atrophy in mice by reducing the PGC-1/PPARγ axis after ischemia, leading to a decrease in the anti-oxidant capacity of skeletal muscle [25]. Recent evidence suggests that hyperhomocysteinemia mediated epigenetic modification might augment mir-494 levels, diminish mtTFA amount and reduce ATP production, leading to mitochondrial dysfunction and inducing a decline in skeletal muscle function [26]. Hyperhomocysteinemia could affects muscle function by inducing multiple inflammatory factors that lead to skeletal muscle fibrosis [27]. In a mouse model, hyperhomocysteinemia mediates decreased collateral formation and angiogenesis in muscle fibers and contributes to muscle frailty [28]. In addition, increased levels of homocysteine could contribute to severe muscle atrophy via oxidative and ER-stress dependent mechanisms [29].

In subgroup analysis and interaction analysis, we found that after fully adjusting for other covariates, the association of homocysteine and the risk of S was more pronounced in a population with hypertension and the interaction with hypertension status is statistically significant. Hyperhomocysteinemia can cause vascular endothelial damage and is one of the risk factors for hypertension. A meta-analysis of 40,173 individuals implementing Mendelian randomization provided evidence on causal link between homocysteine level and the risk of hypertension [30]. Another meta-analysis study conducted by Bai T et al. concluded that sarcopenia was associated with hypertension, and sarcopenia was a risk factor for the hypertension [31]. At the same time, the proportion of people with high blood pressure suffering from sarcopenia is higher than the normal population [32]. Accordingly, it is necessary for us to take more active measures to reduce homocysteine levels in hypertension population. Further prospective cohort studies are needed to assess our results.

The biggest merit of our study is the inclusion of a large and representative samples of the multi-ethnic population, which allowed us to better conduct subgroup analyses. However, several limitations need to be acknowledged. Firstly, it is hard to determine the causality between homocysteine and sarcopenia due to the nature of the cross-sectional study. Secondly, the definition of sarcopenia includes loss of muscle mass and muscle strength. However, data on muscle strength were not available in most participants and we only defined sarcopenia focuses on low muscle mass which used in previous studies [33, 34]. Thirdly, there may be other several potential confounding variables associated with homocysteine and sarcopenia were not adjusted which could alter the results.

**CONCLUSIONS**

In summary, we found a positive association between homocysteine and the risk of S in US older adults. Further studies are needed to validate our results and to assess the mechanisms underlying this association.

**Acknowledgements**

Not applicable.

**Abbreviations**

NHANES: National Health and Nutrition Examination Survey

SMI: skeletal muscle index

BMI: body mass indexes

OR: odds ratio

DXA: dual-energy X-ray absorptiometry

ASM: appendicular skeletal muscle

CRP: C-reactive protein

CI: confidence interval

SD: standard deviation

FNIH: National Institutes of Health

**Author contributions**

QQC and KW conceived the study design. KW, PP and WHF performed the statistical analysis. YXH and WHF collected the data. KW, PP and YXH drafted the manuscript. All authors read and approved the final manuscript.

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**Availability of data and materials**

Publicly available datasets were analyzed in this study. This data can be found here: www.cdc.gov/nchs/nhanes.

**Declarations**

**Ethics approval and consent to participate**

The studies involving human participants were reviewed and approved by board of the National Center for Health Statistics. All the participants provided their written informed consent to participate in this study.All methods were carried out in accordance with relevant guidelines and regulations (declaration of Helsinki).

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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**References:**

1. Sayer AA, Cruz-Jentoft A: Sarcopenia definition, diagnosis and treatment: consensus is growing. *AGE AGEING* 2022, 51(10).

 2. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, *et al*: Sarcopenia: revised European consensus on definition and diagnosis. *AGE AGEING* 2019, 48(1):16-31.

 3. Petermann Rocha F, Balntzi V, Gray SR, Lara J, Ho FK, Pell JP, *et al*: Global prevalence of sarcopenia and severe sarcopenia: a systematic review and meta‐analysis. *Journal of Cachexia, Sarcopenia and Muscle* 2022, 13(1):86-99.

 4. Murdock DJ, Wu N, Grimsby JS, Calle RA, Donahue S, Glass DJ, *et al*: The prevalence of low muscle mass associated with obesity in the USA. *SKELET MUSCLE* 2022, 12(1).

 5. Wiedmer P, Jung T, Castro JP, Pomatto LCD, Sun PY, Davies KJA, *et al*: Sarcopenia – Molecular mechanisms and open questions. *AGEING RES REV* 2021, 65:101200.

 6. Veeranki S, Tyagi S: Defective Homocysteine Metabolism: Potential Implications for Skeletal Muscle Malfunction. *INT J MOL SCI* 2013, 14(7):15074-15091.

 7. Kaplan P, Tatarkova Z, Sivonova MK, Racay P, Lehotsky J: Homocysteine and Mitochondria in Cardiovascular and Cerebrovascular Systems. *INT J MOL SCI* 2020, 21(20):7698.

 8. Kirk B, Feehan J, Lombardi G, Duque G: Muscle, Bone, and Fat Crosstalk: the Biological Role of Myokines, Osteokines, and Adipokines. *CURR OSTEOPOROS REP* 2020, 18(4):388-400.

 9. Kositsawat J, Duque G, Kirk B: Nutrients with anabolic/anticatabolic, antioxidant, and anti-inflammatory properties: Targeting the biological mechanisms of aging to support musculoskeletal health. *EXP GERONTOL* 2021, 154:111521.

10. Xie WQ, He M, Yu DJ, Wu YX, Wang XH, Lv S, *et al*: Mouse models of sarcopenia: classification and evaluation. *Journal of Cachexia, Sarcopenia and Muscle* 2021, 12(3):538-554.

11. Bano G, Trevisan C, Carraro S, Solmi M, Luchini C, Stubbs B, *et al*: Inflammation and sarcopenia: A systematic review and meta-analysis. *MATURITAS* 2017, 96:10-15.

12. Lee W, Peng L, Loh C, Chen L: Sex-different associations between serum homocysteine, high-sensitivity C-reactive protein and sarcopenia: Results from I-Lan Longitudinal Aging Study. *EXP GERONTOL* 2020, 132:110832.

13. Kositsawat J, Vogrin S, French C, Gebauer M, Candow DG, Duque G, *et al*: Relationship Between Plasma Homocysteine and Bone Density, Lean Mass, Muscle Strength and Physical Function in 1480 Middle-Aged and Older Adults: Data from NHANES. *CALCIFIED TISSUE INT* 2023, 112(1):45-54.

14. Lu B, Shen L, Zhu H, Xi L, Wang W, Ouyang X: Association between serum homocysteine and sarcopenia among hospitalized older Chinese adults: a cross-sectional study. *BMC GERIATR* 2022, 22(1).

15. Mu Z, Fu J, Sun L, Chan P, Xiu S: Associations between homocysteine, inflammatory cytokines and sarcopenia in Chinese older adults with type 2 diabetes. *BMC GERIATR* 2021, 21(1).

16. Choi J, Seo J, Lee M, Lee Y, Yoon KJ, Park C: Association between Elevated Plasma Homocysteine and Low Skeletal Muscle Mass in Asymptomatic Adults. *Endocrinology and Metabolism* 2022, 37(2):333-343.

17. Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB, *et al*: The FNIH Sarcopenia Project: Rationale, Study Description, Conference Recommendations, and Final Estimates. *The Journals of Gerontology: Series A* 2014, 69(5):547-558.

18. Huang J, Yang X, Zhang J, Wang F, Tang X: The Correlation between Helicobacter pylori Immunoglobulin G Seropositivity and Plasma Homocysteine Levels in Adults. *MEDIAT INFLAMM* 2023, 2023:1-6.

19. Dennison EM, Sayer AA, Cooper C: Epidemiology of sarcopenia and insight into possible therapeutic targets. *NAT REV RHEUMATOL* 2017, 13(6):340-347.

20. Picca A, Calvani R: Molecular Mechanism and Pathogenesis of Sarcopenia: An Overview. *INT J MOL SCI* 2021, 22(6):3032.

21. Ostrakhovitch EA, Tabibzadeh S: Homocysteine and age-associated disorders. *AGEING RES REV* 2019, 49:144-164.

22. Yamada Y, Umegaki H, Kinoshita F, Huang CH, Sugimoto T, Fujisawa C,*et al*: Cross-Sectional Examination of Homocysteine Levels with Sarcopenia and Its Components in Memory Clinic Outpatients. *Journal of Alzheimer's Disease* 2021, 82(3):975-984.

23. Wang C, Wong T, Duong TV, Su C, Chen H, Chen T, *et al*: Hyperhomocysteinemia Associated with Low Muscle Mass, Muscle Function in Elderly Hemodialysis Patients: An Analysis of Multiple Dialysis Centers. *BIOMED RES INT* 2019, 2019:1-8.

24. Veeranki S, Lominadze D, Tyagi SC: Hyperhomocysteinemia inhibits satellite cell regenerative capacity through p38 alpha/beta MAPK signaling. *AM J PHYSIOL-HEART C* 2015, 309(2):H325-H334.

25. Veeranki S, Tyagi S: Mechanisms of Hyperhomocysteinemia Induced Skeletal Muscle Myopathy after Ischemia in the CBS−/+ Mouse Model. *INT J MOL SCI* 2015, 16(1):1252-1265.

26. Veeranki S, Winchester LJ, Tyagi SC: Hyperhomocysteinemia associated skeletal muscle weakness involves mitochondrial dysfunction and epigenetic modifications. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease* 2015, 1852(5):732-741.

27. Winchester LJ, Veeranki S, Pushpakumar S, Tyagi SC: Exercise mitigates the effects of hyperhomocysteinemia on adverse muscle remodeling. *Physiol Rep* 2018, 6(6):e13637.

28. Veeranki S, Givvimani S, Pushpakumar S, Tyagi SC: Hyperhomocysteinemia attenuates angiogenesis through reduction of HIF-1α and PGC-1α levels in muscle fibers during hindlimb ischemia. *AM J PHYSIOL-HEART C* 2014, 306(8):H1116-H1127.

29. Majumder A, Singh M, Behera J, Theilen NT, George AK, Tyagi N, *et al*: Hydrogen sulfide alleviates hyperhomocysteinemia-mediated skeletal muscle atrophy via mitigation of oxidative and endoplasmic reticulum stress injury. *Am J Physiol Cell Physiol* 2018, 315(5):C609-C622.

30. Fu L, Li YN, Luo D, Deng S, Wu B, Hu YQ: Evidence on the causal link between homocysteine and hypertension from a meta‐analysis of 40 173 individuals implementing Mendelian randomization. *The Journal of Clinical Hypertension* 2019, 21(12):1879-1894.

31. Bai T, Fang F, Li F, Ren Y, Hu J, Cao J: Sarcopenia is associated with hypertension in older adults: a systematic review and meta-analysis. *BMC GERIATR* 2020, 20(1).

32. Ata AM, Kara M, Ekiz T, Kara Ö, Culha MA, Ricci V, *et al*: Reassessing Sarcopenia in Hypertension: STAR and ACE Inhibitors Excel. *INT J CLIN PRACT* 2021, 75(3):e13800.

33. Chen W, Shi S, Jiang Y, Chen K, Liao Y, Huang R, *et al*: Association of sarcopenia with ideal cardiovascular health metrics among US adults: a cross-sectional study of NHANES data from 2011 to 2018. *BMJ OPEN* 2022, 12(9):e61789.

34. Huang Y, Zeng M, Zhang L, Shi J, Yang Y, Liu F, *et al*: Dietary Inflammatory Potential Is Associated With Sarcopenia Among Chronic Kidney Disease Population. *Frontiers in Nutrition* 2022, 9.

**Figure Legends**

**Figure 1** Flowchart of the participants selection.

**Figure 2** Association between homocysteine and risk of sarcopenia in different subgroups. Age, gender, race/ethnicity, total protein, total cholesterol, HDL cholesterol, triglycerides, hemoglobin, serum albumin, serum calcium, C-reactive protein (CRP), serum creatinine, education, physical activity, smoking status, hypertension, and diabetes were adjusted (the stratified variable was omitted from the model).

Table 1 Baseline characteristics of participants according to sarcopenia status

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Total(n = 3079) | No Sarcopenia (n = 2209) | Sarcopenia (n = 870) | *P*-value |
| Age (y) | 70.44 ± 7.86 | 69.72 ± 7.67 | 72.29 ± 8.05 | <0.001 |
| Gender (%) |  |  |  | 0.796 |
| Male | 50.60 | 50.75 | 50.23 |  |
| Female | 49.40 | 49.25 | 49.77 |  |
| Race (%) |  |  |  | <0.001 |
| Non- Hispanic White | 58.14 | 59.48 | 54.71 |  |
| Non- Hispanic Black | 14.29 | 18.92 | 2.53 |  |
| Mexican American | 21.50 | 15.98 | 35.52 |  |
| Other Hispanic | 2.89 | 2.49 | 3.91 |  |
| Other ethnicity | 3.18 | 3.12 | 3.33 |  |
| Education (%) |  |  |  | <0.001 |
| Lower than high school | 37.12 | 33.06 | 47.41 |  |
| High school | 23.46 | 23.90 | 22.33 |  |
| More than high school | 39.43 | 43.04 | 30.27 |  |
| Physical activity (%) |  |  |  | <0.001 |
| Sedentary | 30.37 | 27.80 | 36.90 |  |
| Low | 25.24 | 24.58 | 26.90 |  |
| Moderate | 16.82 | 17.61 | 14.83 |  |
| High | 27.57 | 30.01 | 21.38 |  |
| Hypertension (%) |  |  |  | 0.195 |
| Yes | 53.20 | 52.47 | 55.06 |  |
| No | 46.80 | 47.53 | 44.94 |  |
| Diabetes (%) |  |  |  | 0.005 |
| Yes | 21.18 | 19.87 | 24.48 |  |
| No | 78.82 | 80.13 | 75.52 |  |
| Smoking status (%) |  |  |  | 0.218 |
| Non-smoker | 46.28 | 45.59 | 48.05 |  |
| Smoker | 53.72 | 54.41 | 51.95 |  |
| Total protein (g/dL) | 7.31 ± 0.51 | 7.32 ± 0.51 | 7.29 ± 0.50 | 0.283 |
| Total cholesterol (mg/dl) | 210.25 ± 43.00 | 210.30 ± 42.89 | 210.12 ± 43.33 | 0.427 |
| HDL cholesterol (mg/dl)  | 54.03 ± 16.68 | 54.28 ± 16.77 | 53.42 ± 16.43 | 0.163 |
| Triglycerides (mg/dl) | 153.41 ± 113.89 | 149.89 ± 110.36 | 162.34 ± 122.02 | <0.001 |
| Hemoglobin (g/dL) | 14.27 ± 1.41 | 14.26 ± 1.40 | 14.27 ± 1.45 | 0.664 |
| Serum albumin (g/dL) | 4.23 ± 0.31 | 4.24 ± 0.31 | 4.19 ± 0.32 | <0.001 |
| Serum calcium (mg/dl) | 9.49 ± 0.41 | 9.50 ± 0.42 | 9.46 ± 0.40 | 0.027 |
| CRP (mg/dl) | 0.50 ± 0.97 | 0.46 ± 0.78 | 0.62 ± 1.34 | <0.001 |
| Serum creatinine (mg/dl) | 1.17 ± 0.37 | 1.15 ± 0.35 | 1.21 ± 0.40 | <0.001 |

Mean ± SD for continuous variables and P value was calculated by Kruskal-Wallis test. % for Categorical variables and P value was calculated by weighted chi-square test.

Abbreviations: CRP: C-reactive protein.

Table 2 Association between homocysteine and risk of sarcopenia.

|  |  |  |
| --- | --- | --- |
|  | OR (95% CI) | P value |
| Model 1 | 1.021 (1.006, 1.036) | 0.005 |
| Model 2 | 1.017 (1.001, 1.034) | 0.035 |
| Model 3 | 1.029 (1.009, 1.049) | 0.018 |
| Model 4 | 1.023 (1.003, 1.043) | 0.021 |

Model 1: no covariate was adjusted.

Model 2: age, gender, race/ethnicity were adjusted.

Model 3: additionally adjusted for total protein, total cholesterol, HDL cholesterol, triglycerides, hemoglobin, serum albumin, serum calcium, C-reactive protein (CRP), and serum creatinine.

Model 4: additionally adjusted for education, physical activity, smoking status, hypertension, and diabetes.

Abbreviations: CI, confidence interval; OR, odds ratio.