Relationship of Homocysteine Levels to Quadriceps Strength, Gait Speed, and Late-Life Disability in Older Adults

Hsu-Ko Kuo,1 Kuo-Chen Liao,2 Suzanne G. Leveille,3 Jonathan F. Bean,4 Chung-Jen Yen,1 Jen-Hau Chen,1 Yau-Hua Yu,5,6 and Tong-Yuan Tai1

1Department of Internal Medicine, National Taiwan University Hospital, Taipei.
2Department of Internal Medicine, Chang Gang Memorial Hospital, Tao-Yuan, Taiwan.
3Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts.
4Department of Physical Medicine & Rehabilitation, Harvard Medical School, and Spaulding Rehabilitation Hospital, Boston, Massachusetts.
5National Yang Ming University, Taipei, Taiwan.
6Veterans General Hospital, Taipei, Taiwan.

Background. Elevated homocysteine, causing tissue injury by such mechanisms as oxidative stress, endothelial damage, and protein homocysteinylation, is associated with multiple age-related problems including cardiovascular diseases, dementia, and osteoporotic fracture. Disability is one of the most common features in older adults. However, little is known about the role of homocysteine in physical disability among older adults.

Methods. Participants (>60 years, N = 1677) were from the National Health and Nutrition Examination Survey (NHANES) 1999–2002. Nineteen questionnaires in five major domains were administered to assess the level of difficulty in performing various tasks: activities of daily living (ADL), instrumental ADL (IADL), leisure and social activities (LSA), lower extremity mobility (LEM), and general physical activities (GPA). Peak quadriceps strength was obtained by using an isokinetic dynamometer. Habitual gait speed was obtained from a 20-foot timed walk. Homocysteine levels were measured by the Abbott homocysteine assay, an automated fluorescence polarization immunoassay (FPIA).

Results. Elevated homocysteine was associated with disability in ADL, IADL, LSA, and GPA after multivariate adjustment. The odds ratios (ORs) for disability in these domains comparing participants in the highest quartile of homocysteine to those in the lowest were 2.18 (95% confidence interval [CI], 1.32–3.59) for ADL; 1.62 (95% CI, 1.02–2.57) for IADL; 2.00 (95% CI, 1.14–3.51) for LSA; and 1.52 (95% CI, 1.05–2.21) for GPA. The strength of associations weakened somewhat after additional adjustment of quadriceps strength and/or gait speed, suggesting a mediating role of quadriceps strength and gait speed in the association between homocysteine and disability. Homocysteine had an inverse relationship to quadriceps strength and gait speed. Likewise, quadriceps strength seemed to mediate the inverse association between homocysteine and gait speed.

Conclusions. Elevated homocysteine is associated with multiple domains of disability mediated in part by muscle strength and gait speed. The results suggest that homocysteine levels may be important indicators of performance status in older adults.

Homocysteine is a sulfur-containing amino acid that is derived from the metabolism of methionine, an essential amino acid. Before introduction of mandatory folic acid fortification of cereal-grain products, the prevalence of hyperhomocysteinemia had been reported to be between 5% and 10% in the general population (1) and as high as 33% in people aged 65 and older (2). In the postfortification era, elevated homocysteine levels remain a common feature among U.S. elderly adults. According the National Health and Nutrition Examination Survey (NHANES) 1999–2000, 5% of the U.S. population, 18% of elderly men, and 11% of elderly women had plasma homocysteine concentrations > 13 μmol/L (3). Elevated homocysteine, causing angiotoxicity and atherosclerosis by targeting endothelial cells, platelets, vascular smooth muscle cells, blood lipids, coagulation factors, and nitric oxide, has been demonstrated to be an important risk factor for various cardiovascular diseases (4,5). Abundant data support the notion that elevated homocysteine levels are linked to several multisystem geriatric problems (6), including dementia and Alzheimer’s disease (7), osteoporotic fracture (8,9), and decline in physical function (10). With life expectancy reaching its historic pinnacle, disability and loss of independence have become common features in an aging society (11). Although homocysteine is associated with several aging phenotypes, data examining the relationship of homocysteine to disability are very sparse and limited to acute hospitalized elderly persons (12).

Physical performance measures including muscle strength and gait speed have been demonstrated to be important predictors for the development of disability in elderly people (13–17). However, there are no existing data showing the roles of muscle strength and gait speed in the association between homocysteine and late-life disability.
evaluate right quadriceps strength. The participant was asked to sit on the dynamometer chair with the back supported and to keep hands in the lap during the examination. A stabilizing strap was attached across the chest and the pelvis to help stabilize the participant in the chair. A thigh strap and shin pad were attached after the participant was positioned in the dynamometer chair. A goniometer (instrument used to measure joint angles) was used to measure the angle of the knee joint when the participant was positioned in the dynamometer chair. The start and stop angles of the isokinetic quadriiceps strength test were set at 90° and 150°, respectively. The participant was asked to push the shin pad forward through the full range of motion of the right leg. Strength of the knee extensor muscles was tested by measuring peak torque of the quadriiceps at one angular velocity speed (60°/s). Ideally, each participant would have a total of 6 trials during the strength test: 3 practice warm-ups and 3 trials for maximal voluntary effort. Highest peak force (PF) in Newtons was obtained according to the following algorithm: for examinees with > 4 trials, the highest PF was selected from Trials 4–6 (trials for maximal voluntary effort); for examinees with < 4 trials, a highest PF was selected from the completed trials (warm-up trials). Peak force velocity (PFVel) refers to the peak angular velocity (degrees [°]/s) recorded when peak quadriceps strength was measured. Most participants would have the PFVel closely approximating the chosen testing velocity (60°/s). Further details regarding this component of the NHANES assessment can be found in the NHANES Muscle Strength Procedures Manual (20).

The 20-foot timed walk test was performed at the participant’s usual pace. Participants were allowed to use a walker or cane if needed. Habitual gait speed (m/s) was calculated as walking distance (20 feet = 6.15 m) divided by time in seconds.

Measurements of Homocysteine

Blood specimens were collected at the MECs and were frozen before analysis. Plasma homocysteine was measured by the Abbott homocysteine assay, a fully automated fluorescence polarization immunoassay (FPIA). Plasma total homocysteine concentrations were calculated by the Abbott IMx Immunoassay Analyzer using a machine-stored calibration curve. The FPIA method, used by the NHANES as a primary tool to determine homocysteine levels, was fully equivalent to other frequently used methods such as high performance liquid chromatography (HPLC) (21).

Selection of Study Population

The 20-foot timed walk test along with the isokinetic quadriiceps strength test were completed in 2107 participants 60 years old or older without safety concerns (recent chest or abdominal surgery, heart attack in the past 6 weeks, brain aneurism or stroke, current neck or back pain, difficulty in bending or straightening right knee, or right knee or right hip replacement) or any administrative, communicative, or technical problems. The NHANES isokinetic muscle testing was measured at an angular velocity of 60°/s. Participants (n = 370) with PFVel that varied >5°/s from the chosen testing velocity (60°/s), i.e., greater than 65°/s or less than

Table 1. Self-Report Functional Status

<table>
<thead>
<tr>
<th>Domains</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activities of daily living</td>
<td>Eating difficulty: using fork and knife, and drinking from cup</td>
</tr>
<tr>
<td></td>
<td>Dressing yourself difficulty</td>
</tr>
<tr>
<td></td>
<td>Walking between rooms on same floor difficulty</td>
</tr>
<tr>
<td></td>
<td>Getting in and out of bed difficulty</td>
</tr>
<tr>
<td>Instrumental activities</td>
<td>Managing money difficulty</td>
</tr>
<tr>
<td>of daily living</td>
<td>Housework difficulty</td>
</tr>
<tr>
<td></td>
<td>Preparing meals difficulty</td>
</tr>
<tr>
<td>Leisure and social activities</td>
<td>Going out to movies and events difficulty</td>
</tr>
<tr>
<td></td>
<td>Attending social events difficulty</td>
</tr>
<tr>
<td>Lower extremity mobility</td>
<td>Walking for a quarter mile difficulty</td>
</tr>
<tr>
<td></td>
<td>Walking up 10 steps difficulty</td>
</tr>
<tr>
<td>General physical activities</td>
<td>Stooping, crouching, kneeling difficulty</td>
</tr>
<tr>
<td></td>
<td>Lifting or carrying difficulty</td>
</tr>
<tr>
<td></td>
<td>Standing up from armless chair difficulty</td>
</tr>
<tr>
<td></td>
<td>Standing for long periods difficulty</td>
</tr>
<tr>
<td></td>
<td>Sitting for long periods difficulty</td>
</tr>
<tr>
<td></td>
<td>Reaching up over head difficulty</td>
</tr>
<tr>
<td></td>
<td>Grasping/holding small objects difficulty</td>
</tr>
</tbody>
</table>

Note: Participant was asked about the abilities to perform a series of activities without using any special equipment.

We hypothesized that higher levels of homocysteine are associated with disability in community-dwelling elderly persons and that muscle strength and gait speed may mediate the association between homocysteine and disability. We sought to test the hypotheses by analyzing data from the NHANES 1999–2002.

METHODS

Data Source

The NHANES, a population-based survey, used a stratified, multistage, and cluster-sampling design to obtain a representative sample of the noninstitutionalized U.S. civilian population. NHANES consists of a detailed home interview and a health examination conducted in a mobile examination center (MEC). Data sets, survey operations manuals, consent documents, and brochures of the NHANES assessment can be found in the NHANES Web site (18,19).

Self-Reported Disability

Nineteen questions in five major domains, shown in Table 1, were administered to assess the level of difficulty in performing various tasks: activities of daily living (ADL), instrumental ADL (IADL), leisure and social activities (LSA), lower extremity mobility (LEM), and general physical activities (GPA). Response options for each disability item were “no difficulty,” “some difficulty,” “much difficulty,” or “unable to do.” Disability was defined as any difficulty in performing one or more activities in a given domain.

Measures of Isokinetic Quadriceps Strength and Habitual Gait Speed

A Kinetic Communicator (Kin Com) isokinetic dynamometer (Chattecx Corp., Chattanooga, TN) was used to...
55\%/s, might not have worked well with the isokinetic dynamometer and were thus excluded, leaving 1753 participants with reliable measures of quadriceps peak torque. Compared to participants with PFVel varied >5\%/s from 60\%/s when taking the muscle strength test (370 participants), participants with reliable measures of muscle strength (1737 participants) tended to be younger (mean age 70.2 years vs 72.3 years; \( p < .001 \)), male (64.6% vs 46.2%; \( p < .001 \)), and less disabled (\( p < .01 \)) in all disability domains. Sixty of the 1737 participants were excluded because of missing values in homocysteine (59 participants) or self-report functional status (1 participant), leaving 1677 participants in the final analytic sample.

**Covariates**

Age, gender, race/ethnicity, and educational level were obtained by self-report. Diabetes was defined by self-report of a physician’s diagnosis, the presence of a random plasma glucose level > 200 mg/dL, or use of diabetic medications (including insulin injection and/or oral hypoglycemic agents). Three and sometimes four blood pressure (BP) determinations were taken using a mercury sphygmomanometer by a NHANES physician. BP was measured in the right arm unless specific conditions prohibited the use of the right arm. Averaged systolic and diastolic BPs were obtained. The presence of hypertension was defined by self-reported doctor’s diagnosis, use of antihypertensive medications, or averaged BP > 140/90 mmHg. In addition to diabetes mellitus and hypertension, other medical comorbidities including myocardial infarction (>6 weeks), coronary heart disease, congestive heart failure, chronic bronchitis, emphysema, and arthritis were ascertained by self-report. Body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters, was categorized according to the National Institutes of Health obesity standards: <18.5 = underweight, 18.5–24.9 = normal weight, 25.0–29.9 = overweight, and >30 = obese (22). A 2-minute timed Digit Symbol Substitution test was administered to determine cognitive function. Cognitive impairment was defined as a score of 45 (median) or lower on the Digit Symbol Substitution test. Current smoker was defined by an affirmative response to the question “Do you now smoke cigarettes, pipes, or cigars?” Alcohol intake was determined by an affirmative response to the question “In any one year, have you had at least 12 drinks of any type of alcohol beverage?” and was dichotomized. Serum vitamin B\( _{12} \) and folate levels were measured by using the Bio-Rad Laboratories “Quantaphase II Folate/vitamin B\( _{12} \)” radioimmunoassay kit. Serum creatinine was measured using a standard biochemistry method.

**Analysis**

We divided homocysteine levels into quartiles, and participants in the lowest quartile were the reference group. Multiple logistic regression was used to examine the relationship between homocysteine and disability in ADL, IADL, LSA, LEM, or GPA. We used an extended-model approach for covariate adjustment: Model 1 = age, sex, race, BMI category, educational level, smoking status, alcohol intake, presence of comorbidities (diabetes, hypertension, myocardial infarction, congestive heart failure, coronary heart disease, chronic bronchitis, emphysema, arthritis, and cognitive impairment), as well as levels of folate, vitamin B\( _{12} \), and serum creatinine; Model 2 = Model 1 + peak quadriceps strength; Model 3 = Model 1 + habitual gait speed; Model 4 = Model 1 + peak quadriceps strength + habitual gait speed.

We also assessed the relationship of homocysteine levels and performance-based physical measures, specifically quadriceps strength and habitual gait speed, by using multiple linear regression while adjusting for covariates in Model 1. Given the fact that muscle strength is a proximal pathway component in the impairment–disability pathway, we additionally adjusted for quadriceps strength in the association between homocysteine and habitual gait speed to observe possible change of association. Effect modification of sex was examined by testing the Sex \( \times \) Homocysteine interaction.

Because the NHANES population weights are only applicable to analyses that use the entire population and we limited our analyses to a special subset of participants, we did not use the NHANES 1999–2002 population weights for the purposes of this study. Data management and analysis were performed using STATA 8.0 software (STATA Corporation, College Station, TX).

**RESULTS**

**Characteristics of Study Population**

Selected baseline characteristics of the study participants as a whole (\( N = 1677 \), mean age 70.2 years) and by quartiles of homocysteine levels are summarized in Table 2. The quartile-based homocysteine levels among the study population were: <7.42 \( \mu \)mol/L, 7.42–9.06 \( \mu \)mol/L, 9.07–11.25 \( \mu \)mol/L, and >11.25 \( \mu \)mol/L, respectively. Participants in the upper quartile of homocysteine seemed more likely to be male and hypertensive. They tended to have higher levels of creatinine and lower levels of vitamin B\( _{12} \) and folate. Participants with higher levels of homocysteine tended to walk slower and had a higher prevalence of disability.

**Homocysteine and Self-Reported Disability**

We observed positive associations between homocysteine levels and multiple domains of disability. In Model 1, the odds ratios (ORs) for disability in ADL, IADL, LSA, and GPA comparing participants in the highest quartile of homocysteine to the lowest were 2.18 (95% confidence interval [CI], 1.32–3.59), 1.62 (95% CI, 1.02–2.57), 2.00 (95% CI, 1.14–3.51), and 1.52 (95% CI, 1.05–2.21), respectively (Table 3). The trends of disability in these domains were all statistically significant across homocysteine quartiles. When quadriceps strength, habitual gait speed, or both were additionally introduced in the homocysteine–disability models, the magnitude of the association was attenuated (Model 2 to Model 4). However, the association between homocysteine and ADL disability remained statistically significant even after full adjustment (Model 4). There
Homocysteine and Performance-Based Physical Measures

Homocysteine levels were inversely associated with quadriceps strength and habitual gait speed. Participants in the highest quartile of homocysteine had lower peak quadriceps strength ($\beta = -26.52, p < .001$) and slower gait speed ($\beta = -0.036, p = .039$) compared to those in the lowest quartile (Model 1). Moreover, the decreasing trends of quadriceps strength and habitual gait speed across increasing quartiles of homocysteine levels were significant ($p < .001$ and $p = .013$, respectively) (Table 4). Additional adjustment was no effect modification of sex in the association between homocysteine and disability.

Table 3. Logistic Regression Models Testing the Association Between Quartiles of Homocysteine and Functional Status

<table>
<thead>
<tr>
<th>Model</th>
<th>Quartile Comparison</th>
<th>ADL Disability</th>
<th>IADL Disability</th>
<th>LSA Disability</th>
<th>LEM Disability</th>
<th>GPA Disability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Q2 vs Q1</td>
<td>1.24 (0.78–1.95)</td>
<td>0.86 (0.57–1.31)</td>
<td>1.07 (0.65–1.77)</td>
<td>0.89 (0.62–1.27)</td>
<td>1.11 (0.82–1.51)</td>
</tr>
<tr>
<td></td>
<td>Q3 vs Q1</td>
<td>1.59 (1.00–2.51)</td>
<td>1.06 (0.70–1.61)</td>
<td>1.21 (0.73–2.00)</td>
<td>0.99 (0.69–1.42)</td>
<td>1.35 (0.97–1.86)</td>
</tr>
<tr>
<td></td>
<td>Q4 vs Q1</td>
<td>2.18 (1.32–3.59)</td>
<td>1.62 (1.02–2.57)</td>
<td>2.00 (1.43–3.51)</td>
<td>1.46 (0.97–2.18)</td>
<td>1.52 (1.05–2.19)</td>
</tr>
<tr>
<td>2</td>
<td>Q2 vs Q1</td>
<td>1.26 (0.80–2.00)</td>
<td>0.88 (0.58–1.33)</td>
<td>1.10 (0.66–1.82)</td>
<td>0.90 (0.63–1.29)</td>
<td>1.11 (0.82–1.52)</td>
</tr>
<tr>
<td></td>
<td>Q3 vs Q1</td>
<td>1.57 (0.99–2.49)</td>
<td>1.05 (0.69–1.59)</td>
<td>1.19 (0.72–1.98)</td>
<td>0.94 (0.65–1.37)</td>
<td>1.30 (0.94–1.81)</td>
</tr>
<tr>
<td></td>
<td>Q4 vs Q1</td>
<td>2.01 (1.21–3.32)</td>
<td>1.45 (0.91–2.32)</td>
<td>1.74 (1.08–3.08)</td>
<td>1.27 (0.84–1.91)</td>
<td>1.39 (0.96–2.02)</td>
</tr>
<tr>
<td>3</td>
<td>Q2 vs Q1</td>
<td>1.27 (0.80–2.02)</td>
<td>0.89 (0.58–1.36)</td>
<td>1.12 (0.67–1.87)</td>
<td>0.89 (0.62–1.28)</td>
<td>0.24 (0.13–1.34)</td>
</tr>
<tr>
<td></td>
<td>Q3 vs Q1</td>
<td>1.55 (0.98–2.46)</td>
<td>1.02 (0.67–1.57)</td>
<td>1.17 (0.70–1.96)</td>
<td>0.92 (0.64–1.34)</td>
<td>1.30 (0.90–1.83)</td>
</tr>
<tr>
<td></td>
<td>Q4 vs Q1</td>
<td>2.07 (1.25–3.43)</td>
<td>1.50 (0.93–2.41)</td>
<td>1.84 (1.03–3.30)</td>
<td>1.31 (0.87–1.99)</td>
<td>1.44 (0.99–2.10)</td>
</tr>
<tr>
<td>4</td>
<td>Q2 vs Q1</td>
<td>1.29 (0.81–2.05)</td>
<td>0.90 (0.59–1.37)</td>
<td>1.13 (0.68–1.89)</td>
<td>0.90 (0.62–1.30)</td>
<td>0.11 (0.83–1.55)</td>
</tr>
<tr>
<td></td>
<td>Q3 vs Q1</td>
<td>1.53 (0.97–2.44)</td>
<td>1.01 (0.66–1.55)</td>
<td>1.15 (0.69–1.93)</td>
<td>0.89 (0.62–1.31)</td>
<td>0.17 (0.91–1.76)</td>
</tr>
<tr>
<td></td>
<td>Q4 vs Q1</td>
<td>1.94 (1.17–3.23)</td>
<td>1.40 (0.87–2.25)</td>
<td>1.68 (0.94–3.02)</td>
<td>1.19 (0.78–1.81)</td>
<td>1.35 (0.93–1.98)</td>
</tr>
</tbody>
</table>

Notes: *Adjusted covariates: Model 1 = age, sex, race, body mass index category, educational level, smoking status, alcohol intake, presence of comorbidities (diabetes, hypertension, myocardial infarction, congestive heart failure, coronary heart disease, chronic bronchitis, emphysema, arthritis, and cognitive impairment), as well as levels of folate, vitamin B12, and serum creatinine. Model 2 = Model 1 + peak quadriceps strength. Model 3 = Model 1 + habitual gait speed. Model 4 = Model 1 + peak quadriceps strength + habitual gait speed.

ORs were for disability in a specific domain comparing participants in the 2nd, 3rd, or 4th quartiles of homocysteine to those in the lowest quartile.

ADL = activities of daily living; IADL = instrumental activities of daily living; LSA = leisure and social activities; LEM = lower extremity mobility; GPA = general physical activities; OR = odds ratio; CI = confidence interval.
levels to those in the lowest quartile. Model 2
independent of age, sex, race, BMI category, educational
gap, smoking status, alcohol intake, presence of comor-
bidities, as well as levels of folate, vitamin B₁₂, and serum creatinine. Moreover, the association between homocysteine and disability in ADL, IADL, LSA, and
strength and habitual gait speed. There was no
impact from sex and homocysteine on quadriceps strength and habitual gait speed.

**DISCUSSION**

Among older adults in the United States, homocysteine was associated with disability in ADL, IADL, LSA, and GPA. These homocysteine–disability associations were independent of age, sex, race, BMI category, educational level, smoking status, alcohol intake, presence of comor-
bidities, as well as levels of folate, vitamin B₁₂, and serum creatinine. Moreover, the association between homocysteine and disability was partially mediated by quadriceps strength and habitual gait speed.

Our study supports and extends previous investigations examining the relationship between homocysteine and functional status. Kado and colleagues from the MacArthur Studies of Successful Aging followed 499 highly functioning older adults for an average of 28 months. They suggested that elevated plasma homocysteine levels were predictive of decline in summary measure of physical performance which included balance, gait, lower body strength and coordination, and manual dexterity (10). Marengoni and colleagues (12) cross-sectionally examined 214 acutely hospitalized geriatric patients and demonstrated that homocysteine levels were inversely related to both ADL and IADL (12). However, both studies had limitations in terms of external validity because Kado and colleagues studied only high functioning community-dwelling elderly people, and Marengoni and colleagues investigated hospitalized geriatric patients. To the best of our knowledge, this is the first report to present the relationship of homocysteine to self-reported disability while considering the roles of performance-based physical measures by using a national population–based sample of elderly persons living in the United States.

Our results suggest an explanation for the association of homocysteine and disability. We found that the magnitude of the association diminished after additional adjustment of quadriceps strength, gait speed, or both, meaning that both measures, to a large extent, may mediate the association between homocysteine and disability. Likewise, quadriceps strength seemed to mediate the association between homocysteine and gait speed. Homocysteine is metabolized to homocysteine thiolactone by methionyl-transfer RNA (tRNA) synthetase. Homocysteine thiolactone acylates lysine residues of cellular and extracellular proteins, a process called protein homocysteinylatonation (23). The protein homocysteinyla-
tion is a possible mechanism of homocysteine-related protein damage (23) and may thus affect muscle strength, resulting in slow gait speed and subsequent functional dependence. Moreover, as an independent risk factor for vascular diseases (4,5), elevated homocysteine predicts stroke (24), silent brain infarction (25,26), and cerebral white matter lesions (leukoaraiosis) (26). These cerebrovascular changes may disrupt the descending motor fibers arising from the medial cortical area which is important for lower extremity motor control and may debilitate the frontal–subcortical circuit responsible for normal gait and balance (27). Impairment or limitation in balance, gait, or muscle strength has been linked to incident disability among older adults (13). Our study sheds new light on possible consequences of homocysteine-related tissue injury.

The study findings have several implications. In addition to being a marker for poor nutritional status and high cardiovascular risk, high homocysteine may be useful in screening elderly individuals for physical disability. Second, pharmacological therapies such as B vitamins have been shown to lower homocysteine levels (28). Although homocysteine-lowering therapy with B vitamins has not been shown to have cardiovascular benefits (29,30), clinical

Table 4. Associations Between Quartiles of Homocysteine and Performance-Based Physical Measures

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Model*</th>
<th>Quartile</th>
<th>β (SE)¹</th>
<th>p Value</th>
<th>Adjusted Means</th>
<th>p for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak quadriceps strength</td>
<td>1</td>
<td>Q1</td>
<td>Reference</td>
<td>0.98 (0.019)</td>
<td>.362</td>
<td>343.57</td>
</tr>
<tr>
<td></td>
<td>Q2</td>
<td>0.03 (0.015)</td>
<td>.712</td>
<td>0.996</td>
<td>.013</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Q3</td>
<td>0.006 (0.015)</td>
<td>.672</td>
<td>0.996</td>
<td>.013</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Q4</td>
<td>0.009 (0.015)</td>
<td>.716</td>
<td>0.996</td>
<td>.013</td>
<td></td>
</tr>
<tr>
<td>Habitual gait speed 1</td>
<td>Reference</td>
<td>0.006 (0.015)</td>
<td>.672</td>
<td>0.996</td>
<td>.013</td>
<td></td>
</tr>
<tr>
<td>Habitual gait speed 2</td>
<td>Reference</td>
<td>0.006 (0.015)</td>
<td>.672</td>
<td>0.996</td>
<td>.013</td>
<td></td>
</tr>
</tbody>
</table>

Notes: Units of measure: quadriceps strength (Newtons) and habitual gait speed (m/s).

*Adjusted covariates: Model 1 = age, sex, race, body mass index category, educational level, smoking status, alcohol intake, presence of comorbidities (diabetes, hypertension, myocardial infarction, congestive heart failure, coronary heart disease, chronic bronchitis, emphysema, arthritis, and cognitive impairment), as well as levels of folate, vitamin B₁₂, and serum creatinine. Model 2 = Model 1 + peak quadriceps strength.

¹Coefficients (β) can be interpreted as differences in mean quadriceps strength or gait speed comparing subjects in the 2nd, 3rd, or 4th quartiles of homocysteine levels to those in the lowest quartile.

SE = standard error.
trials of B vitamins with physical function and disability as outcomes are needed.

Our study has potential limitations deserving comment. First, a causal relationship between homocysteine, physical performance, and late-life disability cannot be established based on the cross-sectional design. The relationship should be confirmed prospectively. Second, although late-life disability was evaluated beyond the traditional scope of ADL, IADL, or mobility, measures of physical performance were confined to quadriceps strength and gait speed. Other suitable physical performance measures, such as maximal gait speed or transfer ability, were not available in the NHANES and may mediate the homocysteine–disability association in a different way. Finally, although the data were drawn from a national population–based sample, we limited the sample to participants 60 years old or older who had reliable measures of isokinetic quadriceps strength without technical, physical, administrative, or safety reasons. Therefore, our results were not generalizable to the entire U.S. elderly population.

Conclusion

Homocysteine levels were associated with multiple domains of physical disability. The association between homocysteine and disability was mediated somewhat by quadriceps strength and usual gait speed. We provide new information about the association of homocysteine on physical functioning in older adults living in the community. Further research in this important area is needed to determine whether clinical or public health interventions are warranted.

REFERENCES


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