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Original article

The muscle quality index and mortality among males and females

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ABSTRACT

Purpose: The muscle quality index (MQI) was proposed as a measure to quantify age-related alterations in muscle function. It is unknown if the MQI predicts mortality.
Methods: This was a population-based cohort study from the Third National Health and Nutrition Survey (NHANES III; 1988–1994). The MQI was quantified using a timed sit-to-stand test, body mass, and leg length. Vital status was obtained through the National Center for Health Statistics. We fit multivariable-adjusted regression models to estimate the hazard ratio (HR) and 95% confidence interval (CI) between the MQI and mortality.
Results: During 14.6 years of follow-up, 3299 (73.1%) of 4510 study participants died. Lower MQI was associated with a higher risk of mortality (P_{trend} <.001). The multivariable-adjusted HR for mortality was 1.50 (95% CI, 1.15–1.96) for those in the lowest quintile of MQI compared to the highest quintile. The association between MQI and mortality was stronger among males (highest vs. lowest quintile of MQI, HR = 1.37 [95% CI, 1.00–1.87]; P_{trend} = .001) compared to females (highest vs. lowest quintile of MQI, HR = 1.27 (95% CI, 0.89–1.83); P_{trend} = .044; $P_{interaction}$ = .005].
Conclusions: The MQI predicts mortality and may differ between males and females. Additional research examining the MQI is warranted.

Introduction

Two of the most important changes related to aging are the deterioration of muscle quantity and muscle quality [1]. Older adults lose approximately 1% of muscle mass, 2% of muscle strength, and 3% of muscle power annually [2]. The importance of muscle mass has been well-described among older adults [3]. However, less is known about the importance of muscle quality [1,4]. The muscle quality index (MQI) was recently proposed as a measure to quantify age-related alterations in muscle function [4]. The MQI quantifies lower extremity muscle function using anthropometric parameters and the timed sit-to-stand test [5]. The MQI may be more sensitive than other measures of muscle quality, such as relative strength (strength per unit of muscle mass [6]), because it accounts for the velocity of muscle shortening, reflecting the quality of neural innervation of muscle tissue [7]. The MQI is distinct from the sit-to-stand test by incorporating body mass and leg length [8], which modify the relationship between sit-to-stand time and lower extremity muscle strength [5]. The capacity of the MQI to predict distal health outcomes, such as mortality, has not been described.

The goal of this study was to understand the relationship between the MQI and mortality. We tested the hypothesis that the MQI would be sufficiently sensitive to distinguish risk for mortality among a nationally representative sample of community-dwelling midlife and older adults. As an exploratory aim, we tested the hypothesis that the prognostic capacity of the MQI differed between males and females.

Methods

Study design and sample

The Third National Health and Nutrition Examination Survey, 1988–1994 (NHANES III), was a stratified multistage study conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention, to provide health information on a nationally representative sample of U.S. civilians [9]. The NHANES III sample does not include persons residing in nursing homes, members of the armed forces, institutionalized persons, or U.S. nationals living abroad. Participants provided written informed consent before completing any study-related activities. Participants

The authors declare no conflicts of interest.

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in this analysis included adults of age ≥60 years with the requisite study measures necessary to calculate the MQI as described below.

Muscle quality index

The MQI was quantified using a timed sit-to-stand test, body mass, and leg length to calculate a power index that is expressed in watts (W) [5]. The MQI was calculated as follows: $[(L - 0.5) \times \text{body mass} \times g \times 5]/T_{sit-to-stand}$, where 0.5 (m), L (m), g (m/s^2), and T represent the height of the chair, leg length, acceleration of gravity (9.8 m/s^2), and time required to complete the sit-to-stand test, respectively. Using a stopwatch, sit-to-stand time was calculated as the time to stand from a seated position and return to sitting consecutively five times. The use of arms was not allowed during the sit-to-stand test. Body mass was measured using a digital scale with the participant dressed in an examination gown without shoes. Leg length was taken as the sum of upper leg length and knee height. Upper leg length was measured from the inguinal crease to the patella along the midline of the thigh. Knee height was measured with the participant sitting on an examination table with the legs hanging, using a sliding caliper placed under the heel of the leg to the anterior surface of the thigh, above the condyles of the femur. The MQI is correlated with knee-extensor cross-sectional area, measured using magnetic resonance imaging ($r = 0.801$; $P < .001$) and knee-extensor strength, measured using isometric dynamometry ($r = 0.730$; $P < .001$) [5].

Mortality outcome

Vital status was identified using the National Death Index database through December 31, 2006. Participants were linked to the National Death Index database using probabilistic matching that included 12 identifiers such as social security number, sex, and date of birth [10]. The National Center for Health Statistics found that 96.1% of deceased participants and 99.4% of living participants were correctly classified using the probabilistic matching algorithm [11]. The National Center for Health Statistics removed select subject characteristics in the file to prevent re-identification of study participants. The publically released survival data are nearly identical to the restricted-use NHANES III mortality-linked file [12].

Covariates

Demographic information including age, sex, and race were reported using a standardized questionnaire [13]. Behavioral and clinical information including smoking status, self-rated health, hospitalization, and falls were reported using a standardized questionnaire [13]. Cognitive function was quantified using the short-portable version of the mini mental status examination to form a score that ranges from 0 to 17, with higher scores indicating better cognition [14]. The presence of comorbid health conditions was reported by asking participants if a healthcare provider had ever told them that they had any of the following: hypertension, diabetes, hyperlipidemia, chronic obstructive pulmonary disease (COPD), cancer, arthritis, myocardial infarction, stroke, congestive heart failure, or kidney disease. Hemoglobin, albumin, c-reactive protein, glycated hemoglobin, insulin, glucose, and creatinine were quantified using standardized laboratory assay procedures that have been described in detail [15,16]. Poor balance was defined as the inability to maintain a full tandem stand for 10 seconds [17]. Gait speed was assessed using a 4-meter walk with a stopwatch.

Statistical analysis

Continuous variables are presented as means (standard error [SE]), and categorical variables are presented as percentages (%). Multivariable linear regression was used to identify baseline correlates of the MQI. Cox proportional hazards regression models were used to estimate the hazard ratio (HR) and 95% confidence interval (95% CI) to quantify the association of MQI quintiles and mortality. The assumption of proportional hazards was confirmed using log-log plots. Five regression models were specified to systematically understand the relationship between the MQI and mortality after incrementally accounting for important covariates. Covariates were selected and included in regression models on the basis of biologic plausibility, statistical evidence of confounding, and previously established prognostic importance among adults. To determine if the relationship between MQI and mortality differed between subgroups of males and females, we included a statistical interaction term between the MQI and sex in the Cox proportional hazards regression models. Male and female subgroup-stratified analyses are presented to facilitate interpretation. The C-statistic using receiver operating characteristic analysis was conducted to determine if the MQI provided incremental discriminative capacity beyond that of the sit-to-stand test to predict mortality [18]. In a post hoc power analysis, our study sample had sufficient statistical power to detect a hazard ratio ≥1.1 between extreme quintiles of the MQI. The threshold for statistical significance for all analyses was $P < .05$. All statistical analyses incorporated sample weights to account for nonresponse bias, multistage sampling probabilities, and the subpopulation of participants included in this analytic sample [19]. Stata/SE v.13.1 statistical software was used for all analyses.

Results

Baseline characteristics associated with mortality

Participant characteristics stratified by vital status (Table 1) demonstrate that various demographic (e.g., age, sex, race), clinical (e.g., smoking status, cognitive function, comorbid health conditions, self-rated health, hospitalization, falls), biochemical (e.g., albumin, c-reactive protein, glycated hemoglobin, insulin, glucose, creatinine), and physical (e.g., poor balance, gait speed) characteristics associated with mortality.

MQI characteristics

Among all participants, the median MQI was 110.1 W (interquartile range [IQR], 80.6–148.5). The mean MQI was 117.5 W (SE, 1.37) among those who died compared to 126.2 W (SE, 2.16) among those who were alive at the end of follow-up ($P < .001$). The MQI correlated with gait speed ($r = 0.39$; $P < .0001$).

Baseline correlates of the MQI

Several demographic, clinical, biochemical, and physical function characteristics associated with MQI in univariable and multivariable regression analyses (Table 2). Select variables of interest that associated with MQI in the multivariable linear regression model included age, sex, smoking status, history of COPD or myocardial infarction, self-reported health, hemoglobin, and gait speed (all $P < .05$). The multivariable regression model accounted for 38.8% of the variability in the MQI.