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Original Article

Handgrip Strength and Body Mass Index Independently Predict All-Cause Mortality in Japanese Older Adults: An 8-Year Cohort Study

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SUMMARY

Background: This study explores the relationship between muscle strength, as measured by handgrip strength (HGS), and all-cause mortality in Japanese community-dwelling individuals, considering factors such as body mass index (BMI).
Methods: The research involved 785 males and 952 females, aged 69 ± 11 and 69 ± 9 years, respectively, who were part of the Nomura cohort study initiated in 2014 and followed up for 8 years. The Japanese Basic Resident Registry provided data on adjusted relative hazards for all-cause mortality. The data were subjected to a Cox regression analysis using a time variable of age and confounding risk factors.
Results: Among the 1,737 participants who could be followed, a total of 165 (5.5%), comprising 98 males (12.5%) and 67 females (7.0%), were confirmed deceased. When comparing mortality risks among groups based on handgrip strength (HGS) tertiles and stratified by BMI category, adjusted mortality risks were observed in individuals within the first tertile of HGS (men < 31.0 kg; women < 19.7 kg) and a BMI of < 18.5 kg/m^2 [hazard ratio, 5.77; 95% confidence interval, 3.08–10.8] and 18.5–24.9 kg/m^2 (1.88; 1.20–2.98), compared to those within the second and third HGS tertiles (men ≥ 31.0 kg; women ≥ 19.7 kg) and a BMI of ≥ 18.5–24.9 kg/m^2.
Conclusion: These findings emphasize the HGS is an important tool for prognostic of survival along with low category of BMI, irrespective of other potential confounding factors.

1. Introduction

Sarcopenia is defined as the loss of skeletal muscle mass and quality. The condition accelerates with aging and is associated with metabolic, physiological, and functional impairments.[1] Handgrip strength (HGS) is a quick, easy, and inexpensive indicator of physical frailty and sarcopenia,[2] and is used to identify phenotypes of these conditions among older people of similar age.[3] Preserving HGS could enhance health-related quality of life and contribute a crucial aspect to fostering successful aging in individuals aged 60 years and older.[4]

Body size is a crucial factor influencing muscle strength.[5] Individuals with a leaner physique tend to exhibit lower strength, increased susceptibility to illnesses, and higher mortality rates compared to those with a normal body weight.[6] Conversely, individuals with a higher body weight generally possess greater strength than those with an average body weight, but also incur a higher risk of mortality as fat accumulation progresses.[7] Consequently, understanding the impact of strength on mortality among individuals with an above-average body weight poses challenges. There is considerable variability in strength across all body weight levels. It is conceivable that individuals with lower HGS relative to their body weight may experience greater mortality, and this phenomenon could extend throughout the entire spectrum of body weight.[8] It is crucial to investigate the correlation between HGS and mortality, considering body size factors. The strength of muscles tends to decrease as people age, often accompanied by a decrease in muscle mass and a rise in body fat.[9] Research suggests that body composition might impact the lifespan of older individuals.[10] However, the extent to which it affects the connection between HGS and mortality in this demographic remains largely unexplored. Our hypothesis posits that HGS levels may serve as predictors of all-cause mortality among Japanese individuals living in communities, with this predictive ability being further enhanced by incorporating individual variations in body size into the analysis.[11]

This study aimed to investigate the prospective relationship between HGS and body size and their impact on the increased risk of all-cause mortality among individuals living in Japanese communities using data from a cohort study over 8 years.

2. Methods

2.1. Study design and participants

This research was conducted as part of the Nomura study series, which involved a community health survey of the local population.[12] Initiated in 2014, the study encompassed 1,832 individuals between the ages of 22 and 95 living in the community. Participants aged 20 and above were recruited from the Nomura Welfare Center in a rural town in Ehime Prefecture, utilizing an annual health examination

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process within the community. Detailed information regarding participants' physical activity, medical history, current health conditions, and medications was gathered through structured questionnaire interviews. The inclusion of participants followed a systematic process, as illustrated in Figure 1. Participants' living status was confirmed using Japan's Basic Resident Ledger database, which records information on Japanese citizens, was utilized to confirm their survival and mortality status (survival or deceased). For this study, data from the assessment cycle conducted in 2022 were analyzed, involving a total of 1,737 participants. The research protocol underwent a thorough evaluation and received approval from the Institutional Review Board (IRB) at Ehime University Hospital (IRB: 1903018). Before participating, all individuals furnished written informed consent.

2.2. Evaluation of risk factors

We obtained demographic details and gathered information on risk factors from clinical records. Body mass index (BMI) as body size was computed by dividing an individual's weight in kilograms by the square of their height in meters. Smoking status (pack-years) was established by multiplying the number of years a person had smoked by the average number of packs smoked per day. Participants were categorized as never smokers, former smokers, light smokers (< 20 pack-years), or heavy smokers (≥ 20 pack-years). The quantification of daily alcohol intake was conducted in terms of Japanese liquor units, with one unit equivalent to 22.9 g of ethanol. Participants were categorized into non-drinkers, occasional drinkers (< 1 unit/day), daily light drinkers (1–2 units/day), or daily heavy drinkers (2–3 units/day). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice using an automated sphygmomanometer after participants had undergone a minimum 5-minute rest period. The average of the two readings was used for analysis. Triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum uric acid (SUA), and hemoglobin A1c (HbA1c) levels were measured after an overnight fast. To estimate the glomerular filtration rate (eGFR), we utilized the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation modified with a Japanese coefficient.[13] Definitions of hypertension, hypertriglyceridemia, low HDL cholesterolemia, high LDL cholesterolemia, diabetes, chronic kidney disease (CKD), and hyperuricemia were based on previous reports.[14]

2.3. HGS test

The HGS test, aimed at assessing the isometric strength of hand and forearm muscles, was conducted using a Takei digital handgrip dynamometer. Participants were instructed to exert maximum isometric force while squeezing the dynamometer and to hold this position for approximately 5 seconds. During the test, participants were required to avoid any other body movements. To ensure comprehensive data, two measurements were taken for both left- and right-hand trajectories, and the average of the four readings was used for the analysis.

2.4. Statistical analysis

IBM SPSS Statistics Version 26 (SPSS Japan, Inc., Tokyo, Japan) was used to perform statistical analyses in this study. Continuous variables were expressed as mean ± standard deviation for normally distributed data, while non-normally distributed data, such as TG, HbA1c, and HGS, were expressed as median values (interquartile range) and log-transformed for analysis. Participants were classified into HGS tertiles, with the following criteria for men: 1st tertile, < 31.0 kg; 2nd tertile, 31.0–37.3 kg; 3rd tertile, ≥ 37.4 kg. For women, the criteria were as follows: 1st tertile, < 19.7 kg; 2nd tertile, 19.8–22.9 kg; 3rd tertile, ≥ 23.0 kg. Additionally, participants were grouped into the following BMI categories: < 18.5 kg/m^2, 18.5–24.9 kg/m^2, and ≥ 25.0 kg/m^2. Student's t-tests or ANOVAs were used to compare means and prevalence among groups for continuous data, while the χ^2 test was used for categorical data. The day survival rates were estimated by the Kaplan-Meier method and compared using the log-rank test. Time as days is plotted on the x-axis and the cumulative survival rate is plotted on the y-axis. Multiple Cox proportional hazard regressions were performed to estimate hazard ratios (HR) and 95% confidence intervals (CI). Age served as the primary time variable, with entry time defined as the subject's age in years at recruitment, and exit time defined as the subject's age in years at death or upon censure (i.e., end of the follow-up period). To verify the reliability of the Cox regression analysis, we conducted a test on the proportional hazards' assumption. This assessment involved employing graphical techniques, including log-survival plots and Schoenfeld residual plots, which displayed consistent parallelism. To assess the consistency of the relationship between HGS and BMI for all-cause mortality, subgroup analyses were conducted based on gender, age, exercise, CKD, and time to death (< 1,095 days, ≥ 1,095 days). The threshold for statistical significance was set at a level of $p < 0.05$.

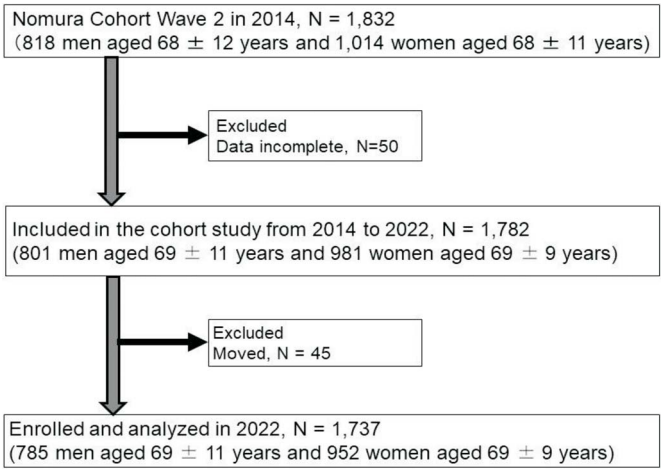

Figure 1. Flowchart of subjects who participated in the present study.

3. Results

A cohort of 785 male participants, with an average age of 69 ± 11 years (range, 24–90 years), and 952 female participants, with an average age of 69 ± 9 years (range, 26–90 years), was included in the study. Supplemental Table 1 displays the baseline characteristics of the participants, categorized based on baseline HGS tertiles within each gender.

The subsequent investigation documented 165 deaths, comprising 98 males and 67 females, resulting in mortality rates of 15.7 and 8.6 per 1,000 person-years, respectively. Kaplan-Meier survival curves were generated to illustrate survival days and cumulative survival rates, revealing discernible patterns in the associations between HGS tertiles and all-cause mortality stratified by BMI (Figure 2). The analysis revealed a significantly lower cumulative survival rate for individuals in the 1st HGS tertile compared to those in the 2nd and 3rd HGS tertiles in all three BMI categories.

Table 1 provides the HR and corresponding 95% CI for both

quantitative and categorical variables identified as significant predictors of mortality in both unadjusted and adjusted analyses. Within the adjusted model, the factors associated with all-cause mortality included gender for female subjects, age, exercise status, BMI, and HGS.

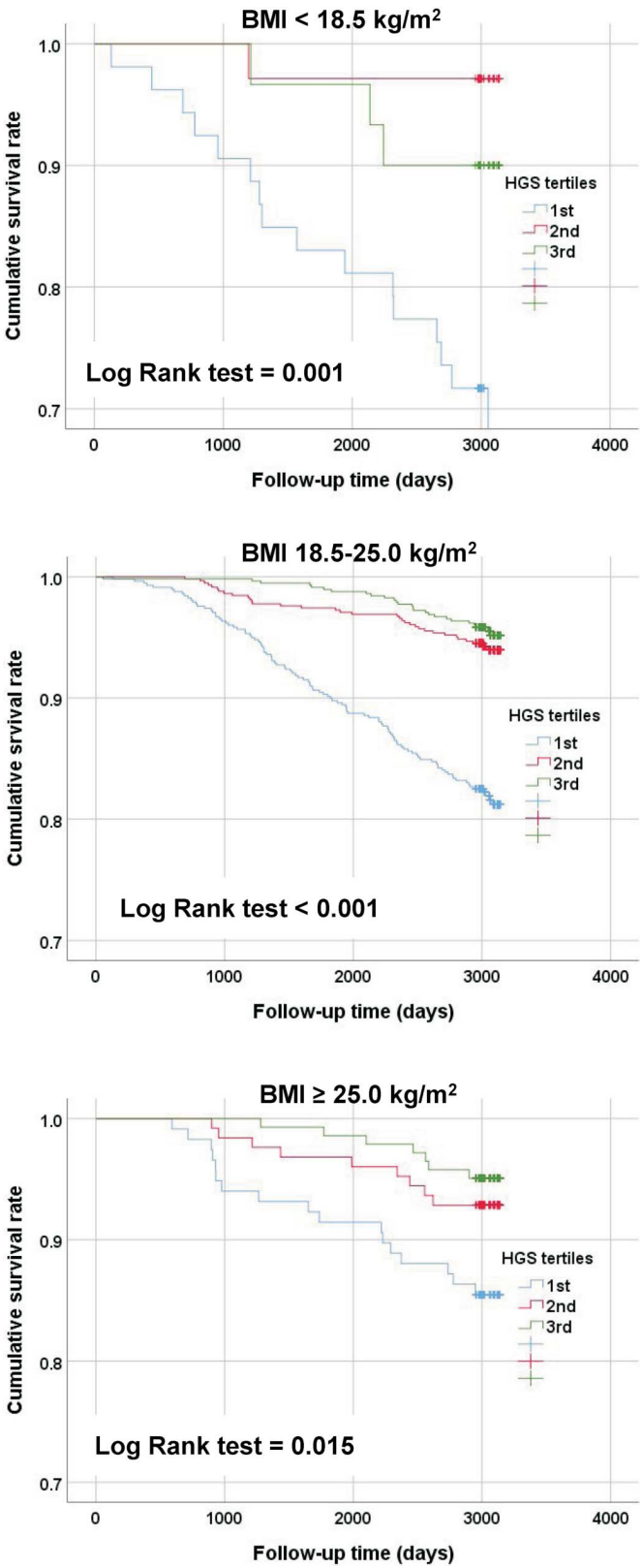

Figure 2. An association between handgrip strength categories and all-cause mortality by body mass index categories during follow-up. The cumulative survival rate was lower for the first three HGS tertiles in each body mass index group.

The survival curves over an 8-year follow-up period for the community-dwelling Japanese population, stratified by HGS status and BMI group, are illustrated in Figure 3 and Table 2. When comparing mortality risks among groups based on HGS tertiles, stratified by BMI category, significantly adjusted mortality risks were observed in individuals in the 1st HGS tertile with a BMI of < 18.5 kg/m^2 and 18.5–24.9 kg/m^2, compared to those in the 2nd and 3rd HGS tertiles with a BMI of 18.5–24.9 kg/m^2.

Supplemental Table 2 shows the participants stratified by gender, age, prevalence of exercise, history of CKD, and time until death. Consistent with our previous findings, individuals in the first HGS tertile with a BMI < 18.5 kg/m^2 was associated with a higher risk of all-cause mortality in those aged of ≥ 65 years, with no history of exercise, a time until death of ≥ 1,095 days, regardless of gender and history of CKD.

4. Discussion

The key finding in the current cohort study is that HGS and BMI are significant and independent predictors of mortality among community-dwelling adults over an 8-year follow-up period, independent of demographic variables, health-related behaviors, and clinical health conditions. Those in the 1st HGS tertile with a BMI of < 25.0 kg/m^2 had a higher risk of all-cause mortality than those in the 2nd and 3rd HGS tertiles with a BMI of 18.5–24.9 kg/m^2. To our knowledge, few other prospective studies have noted an association between lower HGS values, lower BMI categories, and increased risk of all-cause mortality among the elderly in Japan.

Rantanen et al.[8] present findings indicating that HGS, as measured in mid-life among a group of healthy individuals, can be predictive of the risk of mortality from all causes over a 30-year follow-up period. Importantly, this predictive effect remains consistent regardless of the individual's BMI. Across all BMI categories, individuals in the lowest 3rd of HGS demonstrated a 20–39% higher risk of mortality compared to their counterparts in the highest 3rd of HGS. Hsu et al.[15] revealed that age, HGS, gender, history of CVD, BMI, and waist-hip ratio had significant impacts on seven-year survival. Specifically, individuals with poor HGS exhibited increased mortality, with an adjusted HR of 1.87 (95% CI, 1.52–2.30). These findings align with research conducted in Asian territories, including studies in Japan[16] and China.[17] Thus, HGS is a strong and consistent predictor of all causes of mortality in middle-aged and elderly persons.

In our study, it is noteworthy that both the elderly population segments classified as overweight or obese exhibited lower mortality rates in comparison to those within the normal weight range. Nevertheless, numerous studies have highlighted the drawbacks of using BMI as the sole indicator of obesity, commonly referred to as the obesity paradox.[18] The obesity paradox can be partially clarified by considering that BMI, as a measure of body fat, lacks precision in distinguishing between fat and lean body mass. These two components have contrasting effects on the risk of mortality; while fat mass is positively linked with mortality risk, lean mass has a negative association.[19] The commonly observed U-shaped correlation between BMI and mortality rates could be attributed to the conflicting impacts of fat mass and fat-free BMI components. Muscle strength assessment is important to determine the true relationship to mortality because the thin population consists of a mixture of those who have lost weight through exercise and those who have lost weight due to disease or smoking. Individuals who are in good health, lean, and non-smokers may not face an elevated risk of mortality.[20] Interestingly, individuals with a BMI of < 20 kg/m^2 and strong HGS in the highest tertile exhibited a slightly lower mortality risk, although the

Table 1
Hazard ratios and 95% confidence intervals of baseline characteristics for all-cause mortality.

Baseline characteristics (N = 1,737)	Non-adjusted HR (95% CI)	Adjusted HR (95% CI)
Gender (male = 0, female = 1)	**0.55 (0.40–0.75)**	**0.53 (0.31–0.92)**
Age (per 1 year)	**1.11 (1.09–1.14)**	**1.08 (1.05–1.11)**
Body height (per 1 cm)	0.98 (0.96–1.00)	0.99 (0.96–1.02)
Smoking habits (never = 0/past = 1/light = 2/heavy = 3)	1.08 (0.91–1.28)	1.14 (0.92–1.42)
Drinking habits (never = 0/occasional =1/light = 2/heavy = 3)	1.03 (0.90–1.17)	1.09 (0.92–1.29)
Exercise habits (no = 0, yes = 1)	0.75 (0.54–1.04)	**0.68 (0.49–0.95)**
History of cardiovascular disease (no = 0, yes = 1)	**1.81 (1.11–2.95)**	1.11 (0.67–1.84)
Hypertension (no = 0, yes = 1)	**1.60 (1.14–2.62)**	1.08 (0.75–1.56)
Hypertriglyceridemia (no = 0, yes = 1)	1.01 (0.65–1.55)	1.05 (0.65–1.69)
Low-HDL cholesterolemia (no = 0, yes = 1)	1.10 (0.68–1.80)	0.98 (0.58–1.66)
High-LDL cholesterolemia (no = 0, yes = 1)	0.91 (0.67–1.24)	1.33 (0.94–1.87)
Diabetes (no = 0, yes = 1)	1.19 (0.77–1.85)	1.02 (0.64–1.61)
Chronic kidney disease (no = 0, yes = 1)	**2.35 (1.71–3.23)**	1.39 (0.99–1.95)
Hyperuricemia (no = 0, yes = 1)	1.15 (0.78–1.70)	1.05 (0.70–1.58)
Body mass index (< 18.5 kg/m^2 = 0, 18.5–24.9 kg/m^2 = 1)	**0.47 (0.30–0.75)**	**0.36 (0.22–0.59)**
Body mass index (< 18.5 kg/m^2 = 0, ≥ 25.0 kg/m^2 = 1)	**0.45 (0.26–0.78)**	**0.36 (0.20–0.64)**
Handgrip strength (1st tertiles = 0, 2nd & 3rd tertiles = 1)	**0.26 (0.19–0.36)**	**0.54 (0.37–0.79)**

CI, confidence interval; HR, hazard ratio.
Significant values (p < 0.05) are presented in bold.

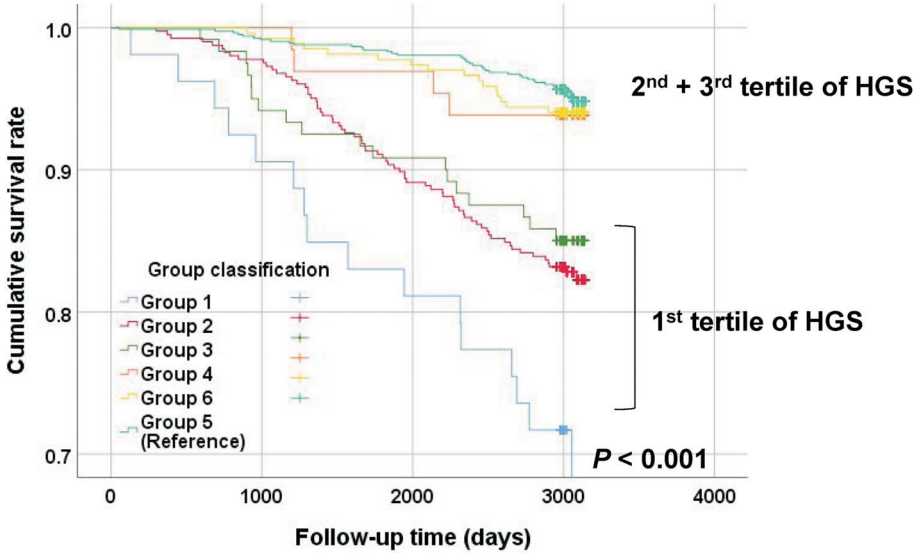

Figure 3. Cumulative survival curves of 6 groups stratified by handgrip strength categories and body mass index categories. HGS, handgrip strength; BMI, body mass index. Group 1: 1st tertile of HGS & BMI < 18.5 kg/m^2; Group 2: 1st tertile of HGS & BMI 18.5–24.9 kg/m^2; Group 3; 1st tertile of HGS & BMI ≥ 25.0 kg/m^2; Group 4: 2nd + 3rd tertiles of HGS & BMI < 18.5 kg/m^2; Group 5: 2nd + 3rd tertiles of HGS & BMI 18.5–24.9 kg/m^2 (Reference); Group 6: 2nd + 3rd tertiles of HGS & BMI ≥ 25.0 kg/m^2.

Table 2
Hazard ratios and 95% confidence intervals of groups according to baseline handgrip strength and body mass index categories for all-cause mortality.

Baseline characteristics (N = 1,737)		Total	Death	Non-adjusted and adjusted HR (95% CI)			
Handgrip strength	Body mass index	N	N (%)	Model 1	Model 2	Model 3	Model 4
1st tertile	< 18.5 kg/m^2	53	17 (32.1)	**7.98 (4.52–14.1)**	**4.87 (2.68–8.86)**	**5.11 (2.76–9.44)**	**5.77 (3.08–10.8)**
(men < 31.0 kg;	18.5–24.9 kg/m^2	404	70 (17.3)	**3.87 (2.62–5.71)**	**1.94 (1.27–2.98)**	**1.86 (1.20–2.90)**	**1.88 (1.20–2.93)**
women < 19.7 kg)	≥ 25.0 kg/m^2	120	18 (15.0)	**3.34 (1.92–5.83)**	**1.93 (1.09–3.43)**	**1.86 (1.02–3.39)**	1.71 (0.93–3.13)
2nd + 3rd tertiles	< 18.5 kg/m^2	65	4 (6.2)	1.31 (0.47–3.65)	1.69 (0.60–4.73)	1.74 (0.62–4.87)	1.96 (0.69–5.53)
(men ≥ 31.0 kg;	18.5–24.9 kg/m^2	827	40 (4.8)	Reference	Reference	Reference	Reference
women ≥ 19.7 kg)	≥ 25.0 kg/m^2	268	16 (6.0)	1.25 (0.70–-2.23)	1.23 (0.69–2.20)	1.21 (0.68–2.17)	1.16 (0.64–2.07)

Model 1 was non-adjusted; Model 2 was adjusted for age and gender; Model 3 was adjusted for body height, smoking status, drinking habits, exercise habits, and history of cardiovascular disease in addition to covariates in model 2; Model 4 was adjusted for hypertension, hypertriglyceridemia, low-HDL cholesterolemia, high-LDL cholesterolemia, diabetes, chronic kidney disease, and hyperuricemia in addition to covariates in model 3. Significant values (p < 0.05) are presented in bold.

difference was not statistically significant, compared to those with a normal weight and HGS in the highest tertile.[8]

The mechanisms linking HGS, BMI, and mortality are not fully understood. Malnutrition and sarcopenia can significantly affect HGS.[21] Higher skeletal muscle is an endocrine organ and is associated with the release of several cytokines and peptides (i.e., myo-

kines) into the circulation, which reduce inflammatory actions.[22] Several proposed mechanisms contribute to the age-related loss of muscle mass, including alterations in neurons and hormones, being underweight, insufficient nutrition with low protein intake, lack of physical activity, metabolic impairment, cardiovascular risk factors, and inflammation.[23] Furthermore, there's a connection between HGS and physical activity,[24] which is known to correlate with improved chances of survival.[25] We did make adjustments for initial levels of physical activity (i.e., exercise habits), but the measurement used was rather basic and might not have fully accounted for its variability. Thus, low HGS, a measure of muscle strength, is associated with increased mortality in this context and is further spurred by the decline in BMI, which indicates poor nutritional status.

Our study has several limitations that should be acknowledged. Firstly, we utilized a cross-sectional methodology, assessing baseline characteristics including BMI and HGS levels at the initial examination. However, it is important to acknowledge that HGS levels and some covariates may fluctuate over time, possibly altering during the prolonged follow-up duration. Secondly, the sample of participants from a Japanese rural community mainly comprised middle-aged and elderly individuals, limiting its representativeness of the broader population. Thirdly, our focus on individuals registered as deceased in the basic resident register may not have captured all deaths, potentially introducing bias. Lastly, the potential influence of medications and other factors such as underlying diseases or lifestyle modifications on our findings could not be completely ruled out.

5. Conclusions

These findings contribute further evidence to the conclusion that the functionality of muscles might play a more pivotal role in determining survival than does BMI alone.

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Competing interests

The authors declare that they have no competing interests.

Supplementary materials

Supplementary materials for this article can be found at http://www.sgecm.org.tw/ijge/journal/view.asp?id=31.

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