Muscle Strength and Body Mass Index as Long-Term Predictors of Mortality in Initially Healthy Men

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Background. Muscle weakness, low body weight, and chronic diseases are often observed in the same people; however, the association of muscle strength with mortality, independent of disease status and body weight, has not been elucidated. The aim was to assess hand grip strength as a predictor of all-cause mortality within different levels of body mass index (BMI) in initially disease-free men.

Methods. Mortality was followed prospectively over 30 years. Maximal hand grip strength tests and BMI assessments were done at baseline in 1965 to 1970. The participants were 6040 healthy men aged 45 to 68 years at baseline living on Oahu, Hawaii.

Results. The death rates per 1000 person years were 24.6 in those with BMI <20, 18.5 in the middle BMI category, and 18.0 in those with BMI ≥25. For grip strength tertiles, the mortality rates were 24.8 in the lowest, 18.5 in the middle, and 14.0 in the highest third. In Cox regression models, within each tertile of grip strength, BMI showed only minimal effect on mortality. In contrast, in each category of BMI there was a gradient of decreasing mortality risk with increasing grip strength. Among those with BMI <20, the adjusted relative risks (RRs) of mortality over 30 years were 1.36 (95% confidence interval 1.14–1.63) for those in the lowest third of strength at baseline, 1.27 (1.02–1.58) in the middle, and 0.92 (0.66–1.29) in the highest third. Correspondingly, for those with BMI 20–24.99, the RRs of death were 1.25 (1.08–1.45), 1.14 (1.00–1.32), and 1.0 (reference) in the lowest, middle, and highest third of grip strength, respectively. In those with BMI ≥25, the RRs were 1.39 (1.16–1.65) in the lowest, 1.27 (1.08–1.49) in the middle, and 1.14 (0.98–1.32) in the highest third of grip strength. Models were adjusted for age, education, occupation, smoking, physical activity, and body height.

Conclusions. In healthy middle-aged men, long-term mortality risk was associated with grip strength at baseline, independent of BMI. The possible interpretation of the finding is that early life influences on muscle strength may have long-term implications for mortality. Additionally, higher strength itself may provide greater physiologic and functional reserve that protects against mortality.

In middle-aged people, poor muscle strength has been found to be associated with lower body weight (1,2), presence of chronic diseases (3,4), physical inactivity (5), and lower education (5). All these factors are known predictors of increased mortality (6). However, muscle strength itself as a predictor of mortality has been addressed in only a few studies, with follow-up intervals of no longer than 6 years (7–10). In middle-aged men followed for 6 years, the risk of mortality was more than two times greater among those in the lower half of grip strength versus the higher half (8). In 75-year-old men and women, poor strength tested in multiple muscle groups predicted increased mortality over a follow-up of 4 to 5 years (9,10). Also, among geriatric patients, poor muscle strength was found to predict increased mortality during acute illnesses (7). These studies suggest that good strength is an important predictor of survival, but have not adequately taken into account the major correlates of strength, in particular body weight and disease status.

Body size is one of the major determinants of muscle strength (1). Thinner people more often have poorer strength and more illness and have greater mortality than those with normal body weight (2,11–14). On the other hand, heavier people are stronger than people with average body weight, but also have higher mortality, so it is difficult to understand how strength might influence mortality in this group. However, at all levels of body weight, there is wide variability in strength; it is possible that excess mortality is present in those with low strength relative to their body weight, and that this may be true across the spectrum of body weight. To fully understand how both muscle strength and body weight influence mortality risk, it is necessary to evaluate their independent and combined effects on mortality.

Long-term mortality follow-up of initially disease-free people offers the opportunity to evaluate the relative contributions of strength and body weight to mortality. The aim of this study was to assess hand grip strength as a predictor of mortality within different levels of body mass index (BMI) in initially healthy men aged 45 to 68 years and followed for 30 years.
METHODS

Subjects in these analyses participated in Exams 1 and 2 of the Honolulu Heart Program which was established in 1965 (15–17). Briefly, the World War II Selective Service Registration file was used to identify 12,417 possibly eligible men of Japanese ancestry (having Japanese last name and/or listed as of Japanese origin) born between 1900 and 1919 and living on Oahu in Hawaii. These men were sent a questionnaire. Altogether, 1269 men were not located and another 1270 refused to answer the questionnaire. A further 1692 men who answered the questionnaire refused to participate in the examinations, and 180 men who responded to the questionnaire died before being scheduled for the physical examination. In 1965–68, 8006 men participated in Exam 1. Exam 2 took place approximately 3 years later, in 1968–70.

The subjects for these analyses were chosen from the 8006 Exam 1 participants as follows. To avoid potential confounding effects of prevalent diseases and early deaths, analyses were limited to a subsample of participants who were healthy at baseline and who participated in grip strength tests at both Exams 1 and 2. To accomplish this, we excluded all participants who reported diabetes, gout, stroke, cancer, heart attack, angina pectoris, or other heart disease (such as hypertensive heart disease or coronary insufficiency) on interview at Exam 1 (n = 1432) and excluded 28 men because of missing data on diseases. A total of 406 men dropped out of the study or died between Exams 1 and 2 and were excluded. Furthermore, 62 men had incident stroke, heart attack, angina pectoris, or other heart disease between Exams 1 and 2 and were also excluded. Finally, a further 20 men were excluded because at Exam 4, which took place 25 years after Exam 1, they reported that they had a disability that had lasted for more than 25 years. Altogether, 6058 men qualified for the study cohort, but another 18 men had missing data on BMI or grip strength. Thus, the final size of the study cohort was N = 6040.

Hand grip strength was measured using the Smedley Hand Dynamometer (Stoelting Co., Wood Dale, IL) at Exams 1 and 2. The width of the handle was adjusted so that when the subject held the dynamometer, the second phalanx was against the inner stirrup. Three trials with brief pauses were allowed for each hand alternately. Subjects were encouraged to exert their maximal grip. The best result was chosen for analyses. The correlation coefficient of the Exam 1 and 2 measurements done approximately 3 years apart was .797 (p < .001). The mid-life hand grip strength level was determined as the average of the best results at Exams 1 and 2.

Body weight and height were measured during Exams 1 and 2 and expressed as kilograms and centimeters, respectively. Because the correlation coefficient between body weight measurements done at Exams 1 and 2 was very high (r = .921, p < .001), we used weight and height from the first examination in the analyses. Body mass index (BMI) was calculated as follows: BMI = weight/height^2.

In Exam 1, the upper arm circumference and triceps skinfold were measured with the subject standing, arm muscles relaxed, and arms hanging vertically at the side. Recordings were done to the nearest full millimeter. Upper arm circumference was measured using a standard tape measure midway between the axilla and elbow, without applying excessive pressure. The skinfold thickness over the triceps muscle midway between the axilla and elbow was measured using a Lange Skinfold Caliper (Cambridge Scientific Industries, Cambridge, MD). A longitudinal fold of skin and subcutaneous tissue was taken between the thumb and the forefinger without applying excess pressure or traction. Caliper tips were applied 1 cm below fingertips.

Upper arm lean area and fat area were estimated from upper arm circumference and triceps skinfold thickness as follows:

\[ A_T = \frac{C^2}{4\pi} \]

where \( A_T \) is the total upper arm area and \( C \) upper arm circumference.

\[ A_L = \frac{\pi}{4} \left( \frac{C}{\pi} - S_{TR} \right)^2 \]

where \( A_L \) is upper arm lean area and \( S_{TR} \) triceps skinfold.

Thereafter upper arm fat area was calculated by subtracting the upper arm lean area from the upper arm total area (18).

Baseline variables that were studied as potential confounders included age, socioeconomic status, physical activity, and smoking. Information about these variables was collected by interviewing the subject. Socioeconomic status at Exam 1 was described on the basis of level of education (1 = primary school or less; 2 = junior or senior high school; 3 = technical school or university) and usual occupation (1 = physical work, unskilled or semiskilled; 2 = physical work, skilled or farming; 3 = light work, sales or clerical; 4 = light work, managerial, professional). Leisure time physical activity was studied separately from occupational activity. The participants were asked to choose one of the following categories that best described their activity level at home or during recreation: 1 = mostly sitting; 2 = moderate activity; 3 = much activity. Smoking status at Exam 1 was categorized as follows: 1 = never smoked; 2 = former smoker; 3 = current smoker.

Mortality records were collected from the beginning of the study. Death ascertainment was based upon perusal of newspaper obituaries and listings of death certificates filed with the Hawaii State Department of Health. At Exam 4 (1991–1993), a computer linkage to National Death Index was established. In addition, when recruiting the participants to later examinations (Exam 5 that took place 1994–1996), family or other contacts were called to find out when the participants had died.

Statistical Methods

Participants were divided into groups based on baseline hand grip strength tertiles and BMI categories using the recent National Institutes of Health (NIH) guidelines as cutoff point criteria for overweight (19). One-way analysis of variance was used to compare age, weight, height, BMI, arm lean area, and arm fat area between groups, based on BMI categories. Cox proportional hazard regression models with adjustments for potential confounders were used to estimate the relative risks of mortality. Survival was expressed in days until death after Exam 1. Participants who died during the first 3 years after Exam 1 were excluded from the analyses.
Results

The average age at Exam 1 was 54 years (range 45–68 years). The average grip strength at baseline was 39.2 kg, and the cutoff points for grip strength tertiles were 37.0 kg and 42.0 kg. The average BMI at Exam 1 was 23.7. The age-adjusted partial correlation coefficient between body weight and BMI was strong ($r = .801$, $p < .001$), whereas height was not associated with BMI ($r = -.009$, $p = .478$). Participants were categorized into three groups: BMI <20 (underweight), BMI 20–24.99 (normal weight), and BMI ≥25 (overweight). Nine groups based on combined distributions of BMI and grip strength were formed. In each BMI category, strong positive gradients according to grip strength tertiles were seen for weight, height, and upper arm lean area, whereas the association of upper arm fat area and grip strength within BMI categories was weak or not significant (Table 1).

Thirty years after baseline, 2900 men (47.9% of the study population) had died. The unadjusted death rates per 1000 person years were 24.6 in those with BMI <20, 18.0 in the middle BMI category, and 14.0 in those with BMI ≥25. However, the relative risks of mortality adjusted for age, education, occupation, smoking, leisure time physical activity, and body height differed only slightly between BMI categories. The relative risks of death over 30 years with the middle BMI category as reference group were 1.11 (95% confidence interval [CI] 0.99–1.24) in the lowest and 1.14 (1.03–1.26) in the middle BMI category, and 1.15 (1.04–1.28) in the highest third of grip strength and 1.15 (1.04–1.28) in the middle third, with the highest third as the reference group (Table 2). Grip strength remained a significant predictor of death also after entering BMI in the same model. The relative risks of death over thirty years were 1.26 (95% CI 1.13–1.42) in the lowest third of grip strength and 1.15 (1.04–1.28) in the middle third with the highest third as the reference group. In this model, the adjusted relative risk of death for those with BMI

Table 1. The Characteristics of the Population in Groups Based on Their Body Mass Index (BMI) and Hand Grip Strength Tertiles at Baseline

<table>
<thead>
<tr>
<th>BMI Categories</th>
<th>Lowest</th>
<th>Middle</th>
<th>Highest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean</td>
<td>57.3</td>
<td>54.2</td>
<td>51.9</td>
</tr>
<tr>
<td>Weight (kg) Mean</td>
<td>50.1</td>
<td>53.7</td>
<td>56.2</td>
</tr>
<tr>
<td>Height (cm) Mean</td>
<td>157.8</td>
<td>162.1</td>
<td>165.5</td>
</tr>
<tr>
<td>BMI Mean</td>
<td>20.1</td>
<td>20.2</td>
<td>20.2</td>
</tr>
<tr>
<td>Arm Lean Area (cm²) Mean</td>
<td>40.3</td>
<td>43.8</td>
<td>45.9</td>
</tr>
<tr>
<td>Arm Fat Area (cm²) Mean</td>
<td>5.7</td>
<td>5.8</td>
<td>6.4</td>
</tr>
</tbody>
</table>

Table 2. The Relative Risks of Death Over 30 Years’ Follow-Up According to BMI Categories in Grip Strength Strata, and According to Grip Strength Tertiles in BMI Strata

<table>
<thead>
<tr>
<th>BMI Categories</th>
<th>Lowest</th>
<th>Middle</th>
<th>Highest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grip Strength Tertiles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>1.09</td>
<td>1.12</td>
<td>0.95</td>
</tr>
<tr>
<td>20–24.99*</td>
<td>0.93–1.27</td>
<td>0.91–1.39</td>
<td>0.67–1.32</td>
</tr>
<tr>
<td>≥25</td>
<td>1.1</td>
<td>1.11</td>
<td>1.14</td>
</tr>
<tr>
<td>0.96–1.29</td>
<td>0.95–1.28</td>
<td>0.98–1.33</td>
<td></td>
</tr>
</tbody>
</table>

Notes: The models are adjusted for age, education, occupation, smoking, leisure time physical activity and body height. RR, relative risk; CI, confidence interval. *Reference level.
be reported in people with chronic conditions (2–4). Some evidence exists that poor strength precedes the development of insulin resistance and predicts diabetes (21). Poor muscle strength may be an etiologic factor in osteoarthritis (22). Osteoarthritis causes pain and disability (23), and disability is known to be a risk factor for mortality (24,25). Disability and poor muscle strength are often found in the same people (26), and good muscle strength has been found to protect older people from disability, independent of chronic diseases (27).

Thirdly, grip strength was associated with upper arm lean area and may indicate a reserve of muscle mass which is important in cases of trauma. After trauma, uninjured muscle goes into negative amino acid balance, which facilitates gluconeogenesis in the liver to provide glucose to damaged tissues. In addition, synthesis of antibodies and cellular components is critical for survival in severe injury. If muscle has been severely depleted by wasting, for example, due to inactivity or aging, the amino acid reserve is low and the healing may be compromised (13). For example, Griffith and colleagues found that those who suffered postsurgery complication or died after the operation had lower preoperative grip strength than those who showed no complications (10,26), which in itself predicts better survival (30,31). We did adjust for baseline physical activity, but the measure available was fairly crude and may have not captured all of the variance in it.

Fourthly, strength is associated with physical activity (10,26), which in itself predicts better survival (30,31). We did adjust for baseline physical activity, but the measure available was fairly crude and may have not captured all of the variance in it.

It is worth noting that maximal voluntary muscle strength is determined both by neural drive from motor cortex to muscles and muscle mass (32–35). Maximal voluntary strength is thus, in fact, an indicator of the functioning of both the neural and the muscular systems, and may be an overall indicator of a person’s vigor. Greater strength may mark some general intrinsic mid-life vitality or stamina that tracks into survival into old age, and it may be a true characteristic of the long-lived phenotype. There is a substantial
Analyses. In addition, only 2.5% had BMI could also be partly explained by the fact that we re-
moved all people with cardiovascular diseases from the
BMI could also be partly explained by the fact that we re-
significantly, lower mortality risk than those with normal weight
in the highest tertile had a somewhat, though not signifi-
cantly, lower mortality risk than those with normal weight.

In conclusion, we found that poor muscle strength mea-
sured in mid-life predicts increased risk of all-cause mortal-
ity. Consequently, increasing muscle strength by physical
activity and strengthening exercises in middle age may thus
have a favorable impact on old age morbidity and mortality.

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