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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:

$$A_T = C^2/4\pi$$

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

$$A_L = \pi/4 \cdot (C/\pi - S_{TR})^2$$

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.

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

		Age (years)		Weight (kg)		Height (cm)		BMI		Arm Lean Area (cm^2)		Arm Fat Area (cm^2)	
	n	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*
BMI <20													
Lowest grip strength tertile	383	57.3	5.8	50.1	4.7	157.8	5.2	18.6	1.1	40.3	7.5	5.7	2.5
Middle grip strength tertile	205	54.2	5.4	53.7	4.3	162.1	5.3	18.9	0.87	43.8	7.4	5.8	2.3
Highest grip strength tertile	105	51.9	3.9	56.2	5.3	165.5	5.3	19.1	0.83	45.9	7.8	6.4	3.0
p value		<.001		<.001		<.001		<.001		<.001		.063	
BMI 20–24.99													
Lowest grip strength tertile	1174	56.6	5.7	58.1	5.4	157.2	5.3	22.6	1.4	47.2	7.8	9.5	3.6
Middle grip strength tertile	1201	53.7	5.1	61.0	5.2	160.5	4.8	22.8	1.4	50.2	8.0	9.7	3.6
Highest grip strength tertile	956	51.6	4.0	64.0	5.7	163.7	5.0	23.0	1.3	54.1	8.8	9.9	3.8
p value		<.001		<.001		<.001		<.001		<.001		.017	
BMI ≥25													
Lowest grip strength tertile	498	56.2	5.7	67.4	6.4	156.6	5.3	27.0	1.7	53.3	8.9	13.6	5.0
Middle grip strength tertile	625	53.6	5.3	70.6	6.5	160.1	4.9	27.1	2.0	57.9	9.2	14.0	5.3
Highest grip strength tertile	893	51.3	4.1	73.2	6.8	163.0	5.1	27.1	1.8	60.5	10.1	13.6	5.0
p value		<.001		<.001		<.001		.266		<.001		.468	

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, 18.5 in the middle BMI category, and 18.0 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 category as reference group were 1.11 (95% confidence interval [CI] 0.99–1.24) in the lowest and 1.09 (1.00–1.19) in the highest BMI category. For grip strength tertiles, the death rates per 1000 person years were 24.8 in the lowest, 18.5 in the middle, and 14.0 in the highest third. The fully adjusted relative risks of death over 30 years were 1.24 (1.11–1.39) in the lowest and 1.14 (1.03–1.26) in middle grip strength tertiles with the highest tertile as the reference group.

In the lowest and middle third of grip strength, the adjusted mortality risk was lowest among those with BMI 20–24.99, whereas for those in the highest third of grip strength, the mortality risk was lowest among those with BMI ≤20 (Table 2). However, the differences in risks among groups were not statistically significant. When mortality risks were compared in groups according to grip strength tertiles in data stratified on the basis of BMI category, greatest mortality risks were seen among those in the lowest third of grip strength and intermediate risks 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 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

	Grip Strength Tertiles					
	Lowest		Middle		Highest	
BMI	RR	95% CI	RR	95% CI	RR	95% CI
<20	1.09	0.93–1.27	1.12	0.91–1.39	0.95	0.67–1.32
20–24.99*	1		1		1	
≥25	1.11	0.96–1.29	1.11	0.95–1.28	1.14	0.98–1.33
	BMI Categories					
	<20		20–24.99		≥25	
Grip Strength Tertiles	RR	95% CI	RR	95% CI	RR	95% CI
Lowest	1.44	0.96–2.07	1.21	1.03–1.41	1.34	1.10–1.63
Middle	1.38	0.95–2.02	1.13	0.98–1.31	1.17	0.98–1.38
Highest*	1		1		1	

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.

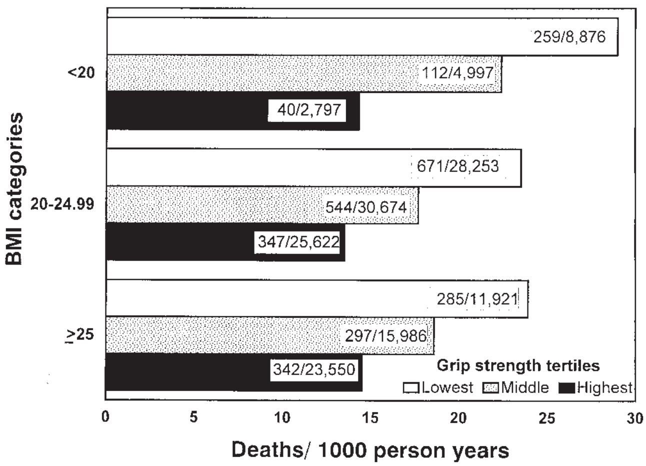

Figure 1. Mortality rates in groups based on BMI and hand grip strength.

Table 3. The Relative Risks of Death Over 30 Years' Follow-Up in Groups According to Baseline Body Mass Index and Hand Grip Strength Tertiles

	Grip Strength Tertiles					
	Lowest		Middle		Highest	
BMI	RR	95% CI	RR	95% CI	RR	95% CI
<20	1.36	1.14–1.63	1.27	1.02–1.58	0.92	0.66–1.29
20–24.99	1.25	1.08–1.45	1.14	1.00–1.32	1*	
≥25	1.39	1.16–1.65	1.27	1.08–1.49	1.14	0.98–1.32

Notes: The model is adjusted for age, education, occupation, smoking, leisure time physical activity and body height. RR, relative risk; CI, confidence interval. *Reference level.

<20 was 1.07 (0.96–1.21), and for those with BMI ≥25, it was 1.12 (1.12–1.42), with the middle BMI group as referent.

Finally, the mortality risks were compared among the nine groups based on the joint distribution of grip strength and BMI. Figure 1 shows a gradient of decreased mortality rate with increasing grip strength tertiles within all three BMI categories. In the fully adjusted Cox proportional hazard model for mortality over 30 years (Table 3), the greatest risks of death were found among those who were either underweight or overweight and whose grip strength was in the lowest third, using those in the middle BMI category and highest grip strength tertile as the reference group. However, those whose grip strength was in the highest third had similar mortality risks regardless of their BMI.

Discussion

Our study provides evidence that in a healthy population hand grip strength measured during mid-life predicts risk of mortality from all causes over a follow-up of 30 years, and its effect is independent of BMI. Within all BMI categories, those in the lowest third of grip strength had 20–39% greater risk than those in the highest third of grip strength, as shown in Table 3. Within individual grip strength tertiles, BMI had much smaller and nonsignificant relationships with mortality.

There are several potential mechanisms that may explain why mid-life grip strength predicts long-term mortality. One explanation could be earlier life influences that affect mid-life muscle strength. Good strength could be an indicator of better childhood and early life nutrition as those with better strength were taller. In addition, mid-life strength may be modified by earlier life-style characteristics, such as exercise habits; other factors such as type of work; or early life diseases that have been cured but have had a negative effect on strength (5,20).

Secondly, poor muscle strength could be a risk factor for diseases or an indicator of a subclinical disease. However, there is very little information on whether strength predicts incident diseases, even though poor muscle strength has been 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 after the surgery (28). However, the number of subjects in that study was small ($N = 55$), and consequently the differences did not yield statistical significance; also, the health status before the surgery was not adjusted for. The importance of protein reserve is also supported by a finding that moderately overweight people more frequently survive hospitalization (29).

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 genetic component explaining the variability in muscle strength, with heritability estimates varying between 30% and 79% (36,37). Genes that determine muscle strength are therefore possible candidate genes for longevity.

The advantages of these analyses are that we had a healthy population at baseline and a very long follow-up period. However, the limitation of this study is that the Japanese-American male population studied here is not representative of all older people. For example, differences in muscle strength and body composition are known to exist between men and women and between ethnic groups. From early adulthood on, women have on average 30 to 40% less muscle strength than men (38), yet they have longer average life expectancy than men. People of Asian origin have lower BMI than Caucasian people, indicating lower muscle mass (2). In addition, African Americans have been found to have greater muscle strength (26), lean body mass, and muscle mass than U.S. whites of the same weight and height (39,40). It is obvious that different populations or ethnic groups have strength distributions that are shifted either lower (women) or higher (blacks) than the distribution of the subjects of the current study. However, it is unlikely that major racial or gender differences in the strength-mortality relationship would be found. Nevertheless, these analyses should be repeated in women and in populations consisting of diverse racial groups.

Concluding that muscle strength is a more powerful predictor of mortality than BMI may not be warranted on the basis of current data. In this study, BMI alone showed only moderate effects on mortality. About 10% greater mortality risk was observed in underweight and 11% in overweight people as compared to persons with normal weight. The moderate effect of BMI on mortality may partly be explained by the fact that we removed from the analyses all subjects with documented diseases at Exam 1, as well as all deaths that happened during the first 3 years after Exam 1. Previously, in older populations, thin people have been found to have greater mortality risk than normal weight persons (11). However, it has been suggested that thin people comprise a mix of those who are lean because they are physically active, and those who are at greater mortality risk because they have lost weight due to a sickness or who are thin because they smoke tobacco (13,41,42). Healthy, thin, nonsmoking people may not be at increased mortality risk (41). In fact, people whose BMI was <20 and grip strength in the highest tertile had a somewhat, though not significantly, lower mortality risk than those with normal weight and grip strength in the highest tertile.

The unexpectedly flat mortality curve in the upper end of BMI could also be partly explained by the fact that we removed all people with cardiovascular diseases from the analyses. In addition, only 2.5% had BMI ≥ 30, indicating that this population had very few obese people who might contribute to increased mortality in the high BMI group. In a previous analysis on these data using the total population ($N = 8006$) without the exclusions done here, the relative risk of death over 22 years of follow-up adjusted for age, smoking, and alcohol consumption was 1.29 for the fifth quintile of BMI (BMI >26.30), with the third quintile (BMI 23.01–24.60) as the reference group (43). In our subsample of healthy people, overweight was not a strong predictor of mortality. However, the same exclusions of high-risk men were true for grip strength analyses, and yet a gradient of risk was evident in the population included. When the analyses were carried out in the total population, grip strength was even a stronger predictor of mortality, because those who were sick at baseline had poorer strength and were at increased risk of death.

In conclusion, we found that poor muscle strength measured in mid-life predicts increased risk of all-cause mortality. 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.

Acknowledgment

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