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## APPENDIX

Physical-strength test (translation from Japanese into English from reference 5).

### *Grip strength*

Grip strength is measured using a hand dynamometer. The handle of the dynamometer is modulated to bend the second joint of the first finger to an angle of 90 degrees. When the grip-strength test is given in a standing position, the subject opens his legs to shoulder width. The subject's arm is positioned naturally. The subject performs the maximum contraction by the right and left arms twice. The higher values of the right and left arms are recorded in kilograms.

### *Side step*

A center line is drawn on the floor. Two side lines are drawn at a distance of 100 cm from the center line. The subject stands straddling the center line. At the signal, the subject steps to the side and touches or steps over the right (or left) side line. Then the subject steps back to the center line. Then the subject steps to the opposite side line and again steps back to the center line. This side-stepping is performed for 20 seconds as rapidly as possible. Points are scored according to the number of times the subject steps over the line. This procedure is repeated twice and the higher point is recorded.

### *Vertical jump*

The subject stands against a wall, stretches his arm and marks with a fingertip the highest attained position. Then

the subject jumps as high as possible and marks with a fingertip the highest position he can reach. The jumping height is the distance between the two heights. This procedure is repeated twice and the higher jump is recorded in centimeters.

### *Standing trunk flexion*

Standing trunk flexion is measured using a 30-cm height stand and a rule. The subject stands with his feet together on the stand. The subject bends his body and lowers both hands and fingers along the rule. The subject does not bend his knees. The subject is stationary at the lowest

point for a few seconds. The distance from the base line is recorded in centimeters.

### *Sit-ups*

The subject lies on his back with his knees bent, folding his arms at the back of his head. The subject opens his legs to a width of 30 cm. An assistant holds the subject's ankles with both hands and places both knees on the subject's insteps. At the signal, the subject sits up and touches his elbows to his knees and then lays down. This procedure is repeated as rapidly as possible for 30 seconds. The number of repetitions is recorded.

論文名	Physical-strength tests and mortality among visitors to health-promotion centers in Japan.						
著者	Fujita Y, Nakamura Y, Hiraoka J, Kobayashi K, Sakata K, Nagai M, Yanagawa H.						
雑誌名	J Clin Epidemiol.						
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発行年	1995						
PubMedリンク	<a href="http://www.ncbi.nlm.nih.gov/pubmed/7490598">http://www.ncbi.nlm.nih.gov/pubmed/7490598</a>						
対象の内訳		ヒト	動物	地域	アジア	研究の種類	縦断研究
	対象	一般健常者	空白		( )		コホート研究
	性別	男女混合	( )		( )		( )
	年齢	男:40-84歳、 女:40-85歳			( )		前向き研究
	対象数	5000~10000	空白		( )		( )
調査の方法	実測	( )					
アウトカム	予 防	心疾患予防	なし	なし	なし	(皮脂厚)	(血糖、血清コレステロール)
	維持・改善	なし	なし	なし	なし	(%肺活量)	(血圧)
図 表							
図表掲載箇所							
概 要 (800字まで)	<p>本追跡調査は、すべての死亡原因およびガンと心血管疾患などから、体力水準と死亡リスクとの関係を明らかにするために実施されたものである。1982~1987年の間で、日本の7つの健康増進センターに参加する7286人を用いて追跡調査した。1992年1月までに、質問紙調査で6259人(85.9%)の回答が得られた。それらは、3117人の男性(対象者の49.8%)(ベースラインの平均年齢53.6±9.0歳:年齢範囲40-84歳)、および3142人の女性(対象者の50.2%)(ベースラインの平均年齢54.5±8.5歳:年齢範囲40-85歳)を含んだ。各々の平均追跡期間は、年間38253人で6.1年であった。この期間、155の死亡が報告された。ベースラインにおいては、5つの体力テスト(握力、反復横跳び、垂直跳び、立位体前屈、および腹筋)を実施した。また、5つの臨床検査項目(皮脂厚、血糖、血清コレステロール、%肺活量、血圧)が測定された。参加者は、喫煙状態(現在の喫煙、非喫煙、喫煙の既往歴)について質問された。皮脂厚の高い(厚い)男性(相対リスク=2.11)および高血糖(相対リスク=1.89)をもっている人では、すべての原因における死亡リスクが高かった。血清コレステロール値の高い男性(相対リスク=5.08)、皮脂厚の高い(厚い)男性(相対リスク=4.54)、および高血圧の男性(相対リスク=2.33)では、心血管疾患による死亡リスクが高かった。女性では、臨床検査値と死亡リスクの間でいかなる関連性もみられなかった。また、反復横跳び(相対リスク=2.43)、垂直跳び(相対リスク=2.37)、腹筋(相対リスク=1.93)、および握力(相対リスク=1.92)で低値を示す男性において、すべての原因における死亡リスクが高かった。さらに、垂直跳び(相対リスク=5.51)で低値を示した男性では、心血管疾患による死亡リスクが高かった。皮脂厚、血糖、血清コレステロール、血圧、%肺活量、および喫煙状態補正後において、反復横跳び、垂直跳び、および握力で低値を示した男性では、すべての原因における死亡リスクが高かった。女性においては、体力水準と死亡リスクとの間にそのような関係はみられなかった。男性においては、低体力状態がその後の健康結果(状態)に関連する可能性が高いことが結論づけられた。</p>						
結 論 (200字まで)	低い筋力レベルは、男性の場合の死亡リスクを高める。						
エキスパートによるコメント (200字まで)	本邦において、体力、特に筋力と総死亡リスクとの関連について検討した国際的に価値ある研究。介護の予防のみならず健康作りの現場において活用できるエビデンス。						

担当者 宮地 劉

## Handgrip strength and mortality in the oldest old population: the Leiden 85-plus study

Carolina H.Y. Ling MD, Diana Taekema MD, Anton J.M. de Craen PhD,  
Jacobijn Gussekloo MD PhD, Rudi G.J. Westendorp MD PhD, Andrea B. Maier MD PhD

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∞ See related commentary by Huang, page 423

### ABSTRACT

**Background:** Poor muscular strength has been shown to be associated with increased morbidity and mortality in diverse samples of middle-aged and elderly people. However, the oldest old population (i.e., over 85 years) is underrepresented in such studies. Our objective was to assess the association between muscular strength and mortality in the oldest old population.

**Methods:** We included 555 participants (65% women) from the Leiden 85-plus study, a prospective population-based study of all 85-year-old inhabitants of Leiden, Netherlands. We measured the handgrip strength of participants at baseline and again at age 89 years. We collected baseline data on comorbidities, functional status, levels of physical activity, and adjusted for potential confounders. During the follow-up period, we collected data on mortality.

**Results:** During a follow-up period of 9.5 years (range 8.5–10.5 years), 444 (80%) participants died. Risk for all-cause mortality was elevated among participants in the lowest tertile of handgrip strength at age 85 years (hazard ratio [HR] 1.35, 95% confidence interval [CI] 1.00–1.82,  $p = 0.047$ ) and the lowest two tertiles of handgrip strength at age 89 years (HR 2.04, CI 1.24–3.35,  $p = 0.005$  and HR 1.73, CI 1.11–2.70,  $p = 0.016$ ). We also observed significantly increased mortality among participants in the tertile with the highest relative loss of handgrip strength over four years (HR 1.72, CI 1.07–2.77,  $p = 0.026$ ).

**Interpretation:** Handgrip strength, a surrogate measurement of overall muscular strength, is a predictor of all-cause mortality in the oldest old population and may serve as a convenient tool for prognostication of mortality risk among elderly people.

Inactivity is a major problem in this age group, owing to an increased prevalence of medical comorbidities and physical disability with age. Age-related stereotypes and misconceptions (e.g., that older people are invariably unhealthy), coupled with a perceived lack of benefits provided by physical activity, can also represent obstacles to exercise among the oldest old population.

The predisposing influence of a sedentary lifestyle on age-related cardiometabolic diseases (i.e., obesity, type 2 diabetes mellitus, hypertension and coronary artery disease) is well established. Evidence of the protective effects of physical activity against certain cancers, falls and mental health problems is accumulating.<sup>3,4</sup> Lack of exercise is also a significant risk factor for sarcopenia,<sup>5,6</sup> a progressive loss of skeletal muscle mass and strength with aging.<sup>7</sup> Sarcopenia is highly prevalent among those aged 80 years and older, with reported rates exceeding 50%.<sup>8</sup> Reduced muscular strength is associated in turn with outcomes such as physical disability,<sup>9,10</sup> cognitive decline<sup>11</sup> and mortality.<sup>12,13</sup>

Handgrip strength, a simple bedside tool, has been shown to be a valid surrogate measurement of overall muscular strength.<sup>14,15</sup> A recent systematic review has shown that low handgrip strength is associated consistently with premature mortality, disability and other health-related complications among various samples of middle-aged and older people.<sup>16</sup> Despite its prognostic value, handgrip dynamometry is rarely used in routine geriatric assessment. Epidemiologic studies evaluating the relation in the population of the oldest old are also lacking. We tested the association between handgrip strength and mortality in a prospective population-based study of the oldest old age group. We obtained approval for our study from the Medical Ethical Committee of the Leiden University Medical Center, and informed consent from all participants.

From the Department of Gerontology and Geriatrics (Ling, Taekema, de Craen, Westendorp, Maier); the Department of Public Health and Primary Care (Gussekloo); the Netherlands Consortium for Healthy Aging (de Craen, Westendorp, Maier), Leiden University Medical Center, Leiden, Netherlands; and the Department of Geriatric Medicine (Taekema), Alysus Zorggroep Rijnstate Hospital, Arnhem, Netherlands

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The fastest growing segment of the elderly population is the group older than 85 years, which is classified as the oldest old age group.<sup>1,2</sup> The average rate of growth of this group is reported to be 3.8% annually at a global level. By 2050, the oldest old age group will account for one-fifth of all older persons.<sup>2</sup>

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## Methods

### Participants

We obtained data from the prospective population-based Leiden 85-plus study, which involved all 85-year-old inhabitants of Leiden, The Netherlands. A total of 599 participants had been enrolled in the study (with a response rate of 87%) between September 1997 and September 1999. No selection criteria had been imposed for health status or demographic characteristics. Participants had been visited annually at their homes, where face-to-face interviews, blood samples and various functional tests were performed. Further information on the design of the Leiden 85-plus study and characteristics of its cohort is published elsewhere.<sup>17</sup>

In our analysis, we included 555 participants from whom we obtained reliable handgrip strength measurement at baseline (i.e., age 85 years). We performed a repeat measurement of handgrip strength in a total of 304 participants (55%) at 89 years of age.

### Study design

#### Strength assessment

We measured grip strength to the nearest kilogram of each participant's dominant hand using a Jamar hand dynamometer (Sammons Preston Inc., Bolingbrook, IL). We performed the measurement with the participant in an upright position and with the arm of the measured hand unsupported and parallel to the body. The width of the dynamometer's handle was adjusted to each participant's hand size so that the middle phalanges rested on the inner handle. We instructed participants to exert maximal force. For each participant, we allowed one test trial, then took three test measurements. We used the highest of the three recorded measurements in our analysis. We used the same protocol for each participant's follow-up visit at age 89 years.

To calculate the relative change in handgrip strength over four years, we divided the difference between the handgrip strength measurements taken at ages 85 and 89 years by the baseline value and multiplied the result by 100. We stratified the measurements of handgrip strength at ages 85 and 89 years and relative change in handgrip strength over four years into tertiles for men and women separately. We then created sex-specific tertiles by combining categories of tertiles for men and for women.

#### Potential confounders

We considered sex, anthropometric data, comorbidities, total number of prescription medications and smoking status to be potential confounders of an association between handgrip strength and mortality, and included these data in our analysis. Our measurement of body surface area was based on the Mosteller formula.<sup>20</sup> We recorded data on seven medical comorbidities, which were cardiovascular disease (comprising ischemic heart disease, cerebrovascular disease and peripheral vascular disease), hypertension, diabetes mellitus, chronic obstructive pulmonary disease, neoplasm, Parkinson disease, and arthritis (comprising osteoarthritis, rheumatoid arthritis and polymyalgia rheumatica).

We also considered scores on the Mini-Mental State Examination, Geriatric Depression Scale, Activities of Daily Living disability scale, Instrumental Activities of Daily Living disability scale and level of physical activity to represent potential confounders. We measured scores on the Activities of Daily Living and Instrumental Activities of Daily Living disability scales using the Groningen Activity Restriction Scale, where a score of 18 indicates not disabled and a score of 72 indicates severely disabled.<sup>18</sup>

To measure levels of physical exercise beyond routine, daily physical activity, we used four items from the Time-Spending Patterns questionnaire<sup>19</sup> related to walking for fun, cycling for fun, exercising (either alone or in groups) or other physical activity, and working in the garden. We scored each item from 0 (no activity) to 4 (daily participation in the activity), then added these values together to reach a sum score of physical activity level for each participant.

We also collected data on the living arrangements of participants (i.e., independent or in residential care). We did not include these data in the final model because living arrangement is determined primarily by factors already included in the multivariate model (i.e., functional abilities, cognition, comorbidities).

#### Follow-up

We collected data on mortality among participants until February 2008. The range of the follow-up period was 8.5–10.5 years. Information on follow-up for mortality was available for the whole study population. We obtained dates of deaths from the Dutch civic registry and specific data on causes of death from Statistics Netherlands, which assigns codes for all national death certificates according to the International Classification of Diseases and Related Disorders, 10th revision (ICD-10). Causes of death were divided into cardiovascular causes (ICD-10 codes I00-I99) and non-cardiovascular causes (all other ICD-10 codes). Cardiovascular causes were further classified into coronary artery disease, stroke and others. The non-cardiovascular causes were classified into infection with or without sepsis, pneumonia, neoplasm and others. Pneumonia was included because it is one of the major causes of death among elderly people.

#### Statistical analysis

Continuous variables with Gaussian distribution are presented as mean (standard deviation [SD]) and those with non-Gaussian distribution as median (interquartile range [IQR]). We used a paired *t* test to compare two groups of paired data that were of Gaussian distribution. To adjust for difference in physical capacity between men and women, we created sex-specific tertiles of handgrip strength, which were combined categories of tertiles for men and for women. We used a  $\chi^2$  test to compare categorical variables and a Kruskal-Wallis test to compare non-normally distributed variables between the tertiles of handgrip strength.

We applied Kaplan-Meier curves to display survival according to tertiles of handgrip strength for participants at age 85 years and for those at age 89 years, and for the relative change in handgrip strength over four years. We assessed the analysis of survival using Cox regression analyses. We

adjusted the hazard ratios (HR) of mortality for potential confounders using baseline data reflecting presence of comorbidities, total number of prescription medications and smoking status, and data collected at baseline or age 89 years for body surface area, for scores on the Mini-Mental State Examination, the Geriatric Depression Scale, the Activities of Daily Living disability scale and the Instrumental Activities of Daily Living disability scale, and for level of physical activity.

We corrected the HRs for relative change in handgrip strength using data on comorbidities, total number of prescription medications and smoking status at baseline, on body surface area at age 89 years, and on absolute change in scores on the Mini-Mental State Examination, Geriatric Depression Scale, Activities of Daily Living disability scale, Instrumental Activities of Daily Living disability scale, and in level of physical activity over four years. In addition, we

analyzed handgrip strength as a continuous variable in the multivariable model with adjustment for the above variables. For all fully adjusted models, we calculated the coefficient of determination (i.e.,  $R^2$ ) using the method of Nagelkerke.<sup>21</sup> We considered a two-tailed  $p$ -value of less than 0.05 to be significant.

## Results

The baseline clinical characteristics of the 555 participants in the study according to tertile of handgrip strength are presented in Table 1. Cardiovascular disease was the most prevalent comorbidity. At baseline, the median Mini-Mental State Examination score was 26, with evidence of severe cognitive impairment (i.e., score < 19) in 13% of participants. At age 89 years, impairment was evident in 25%. The median score on

**Table 1:** Clinical characteristics at baseline (age 85 years) of the study population by sex-specific tertile of handgrip strength

Variable	Total population <i>n</i> = 555	Sex-specific tertile of handgrip strength*			<i>p</i> value
		Low <i>n</i> = 184	Middle <i>n</i> = 177	High <i>n</i> = 194	
Sex, female, %	65.0	64.7	64.4	66.0	0.94
Living arrangement, %					< 0.001
Independent living	85.9	73.9	88.7	94.8	
Residential care	14.1	26.1	11.3	5.2	
Smoking status (%)					0.53
Nonsmoker	50.4	55.2	46.3	49.5	
Previous smoker	34.1	30.1	36.7	35.6	
Current smoker	15.5	14.8	16.9	14.9	
Comorbidity, %					
Cardiovascular disease	62.5	66.8	66.1	55.2	0.031
Hypertension	38.7	33.2	41.8	41.2	0.16
Diabetes mellitus	15.3	18.5	15.8	11.9	0.20
Chronic obstructive pulmonary disease	11.7	13.0	10.7	11.3	0.78
History of neoplasm	17.9	18.8	14.1	20.6	0.94
Parkinson disease	2.0	2.2	1.7	2.1	0.25
Arthritis	32.7	30.4	35.8	32.1	0.54
Total no. of prescription medications [ <i>n</i> = 526], median (IQR)	2 (1–4)	2 (1–4)	2 (1–4)	2 (1–4)	0.07
Mental status, median (IQR)					
MMSE score	26 (23–28)	24 (18–27)	27 (24–28)	27 (25–29)	< 0.001
GDS-15 score [ <i>n</i> = 484]	2 (1–3)	2 (1–4)	2 (1–3)	1 (0–2)	< 0.001
Functional status, median (IQR)					
ADL disability score [ <i>n</i> = 553]	10 (9–13)	11 (9–17)	10 (9–12)	9 (9–10)	< 0.001
IADL disability score [ <i>n</i> = 553]	17 (12–25)	24 (16–32)	17 (13–22)	14 (10–19)	< 0.001
GARS score [ <i>n</i> = 553]	27 (21–37)	36 (25–48)	27 (22–34)	24 (20–30)	< 0.001
PAS, median (IQR) [ <i>n</i> = 538]	7 (5–8)	6 (4–8)	7 (4–8)	7 (6–9)	< 0.001

Note: ADL = Activities of Daily Living (score range 9–36), GARS = Groningen Activity Restriction Scale (score range 18–72), GDS-15 = Geriatric Depression Scale-15 (score range 0–15), IADL = Instrumental Activities of Daily Living (score range 9–36), IQR = interquartile range, MMSE = Mini-Mental State Examination (score range 0–30), PAS = Physical Activity Score (sum score of four physically active items on the Time Spending Pattern questionnaire; score range 0–16).

\*Reference range for sex-specific handgrip strength tertiles: low (women: 1–16 kg; men: 10–27 kg), middle (women: 17–20 kg; men: 28–33 kg), high (women: 21–31 kg; men: 34–54 kg).

the Geriatric Depression Scale at baseline was 2 (IQR 1–3), with evidence of depression (i.e., score  $\geq 4$ ) in 113 participants, who represented 23.4% of those without severe cognitive impairment at baseline compared with 27.7% at age 89 years. At baseline, the median score on the Activities of Daily Living disability scale was 10 (IQR 9–13); on the Instrumental Activities of Daily Living disability scale it was 17 (IQR 12–25); and on the Groningen Activity Restriction Scale it was 27 (IQR 21–37). The median sum scores for level of physical activity at baseline was 7 (IQR 5–8).

Lower handgrip strength was significantly related to higher rates of cardiovascular disease ( $p = 0.031$ ) but not to other comorbidities. Lower handgrip strength was also significantly associated ( $p < 0.001$ ) with lower scores on the Mini-Mental State Examination and with higher scores on the Geriatric Depression Scale, the Activities of Daily Living disability scale and the Instrumental Activities of Daily Living disability scale, and, finally, with a lower score for level of physical activity. We also observed a significant difference in living arrangement among participants in different tertiles of handgrip strength, with a greater proportion of participants with lower handgrip strength living in residential care.

Anthropometric data and measurements of handgrip strength collected at ages 85 and 89 years and stratified by sex are presented in Table 2. Of the 555 participants, 357 (64.3%) lived to age 89 years. Measurements of handgrip strength were not available for 53 participants at age 89 years, most of whom withdrew from the study. Participants who were lost to follow-up measurement of handgrip strength did not differ significantly ( $p \geq 0.083$ ) from the group as a whole in comorbidities, cognitive status and functional status at baseline.

Handgrip strength among men was consistently higher than among women, both at baseline (30.6 kg [SD 8.2] v. 18.7 kg [SD 5.5],  $p < 0.001$ ) and at age 89 years (25.6 kg [SD 7.8] v. 16.4 kg [SD 5.0],  $p < 0.001$ ). Among both women and

men, handgrip strength declined significantly from age 85 to 89 years, with an average loss of strength of 1.53 kg per year among men and 0.85 kg per year among women. However, no significant difference was evident between men and women in relative loss of handgrip strength over four years ( $-19.2\%$  [SD 16.7] v.  $-15.9\%$  [SD 22.4],  $p = 0.156$ ).

During a follow-up period of 9.5 years (range 8.5–10.5 years), 444 deaths (80%) occurred, with a greater proportion of deaths among men, at 88.1%, compared with women, at 75.6% ( $p < 0.001$ ). Mean lifespan was 89.7 years (SD 3.0) among men and 91.0 years (SD 3.0) among women. Of the deaths, 36.7% had cardiovascular causes (coronary artery disease 30.1%, stroke 26.4%, unspecified 43.5%). Of the deaths that were attributed to noncardiovascular causes, 28.8% were caused by neoplasm, 10.0% were caused by infection (of which 85.7% were related to pneumonia) and 61.2% were unspecified.

Kaplan–Meier cumulative survival curves for all-cause mortality are presented in Figure 1. The curves are stratified by sex-specific tertile of handgrip strength at baseline, of handgrip strength at 89 years of age, and of relative change in handgrip strength over four years. The unadjusted and adjusted HRs for all-cause mortality are shown in Table 3. The HRs are stratified by tertile of handgrip strength at age 85 years, handgrip strength at age 89 years and relative change in handgrip strength from age 85 to 89 years.

After adjusting for possible confounders, we found a significant elevation in risk for all-cause mortality among participants in the lowest tertile of handgrip strength at age 85 years (HR 1.35, 95% CI 1.00–1.82,  $p = 0.047$ ) and the lowest two tertiles of handgrip strength at age 89 years (HR 2.04, 95% CI 1.24–3.35,  $p = 0.005$  and HR 1.73, CI 1.11–2.70,  $p = 0.016$ ), with greater HRs in the latter age group. We also observed a significantly increased mortality among participants in the tertile with the highest relative loss of handgrip strength over four years (HR 1.72, CI 1.07–2.77,  $p = 0.026$ ). The coeffi-

**Table 2:** Handgrip strength and anthropometrical measurements at baseline (age 85 years) and at age 89 years, by sex

Variable	Measurements for women, mean (SD)			Measurements for men, mean (SD)		
	Baseline ( <i>n</i> = 361)	Age 89 ( <i>n</i> = 255)	<i>p</i> value	Baseline ( <i>n</i> = 194)	Age 89 ( <i>n</i> = 102)	<i>p</i> value
Handgrip strength, kg	18.7 (5.5)	16.4 (5.0)*	< 0.001	30.6 (8.2)	25.6 (7.8)†	< 0.001
Absolute loss in handgrip strength, kg		–3.4 (4.2)			–6.1 (5.2)	
Relative loss in handgrip strength, %		–15.9 (22.4)			–19.2 (16.7)	
Weight, kg	67.7 (12.7)‡	65.5 (12.6)§	< 0.001	74.1 (11.9)**	71.1 (11.9)††	< 0.001
Height, m	1.56 (0.06)‡	1.55 (0.06)§	< 0.001	1.68 (0.06)**	1.67 (0.06) ††	< 0.001
BSA, m <sup>2</sup>	1.71 (0.18)‡	1.68 (0.18)§	< 0.001	1.86 (0.17)**	1.81 (0.17) ††	< 0.001
BMI, kg/m <sup>2</sup>	27.7 (4.8)‡	27.4 (4.7)§	0.049	26.1 (3.7)**	25.5 (3.8) ††	< 0.001

Note: BMI = body mass index, BSA = body surface area, SD = standard deviation.

\**n* = 215

†*n* = 89

‡*n* = 347

§*n* = 217

\*\**n* = 183

††*n* = 92

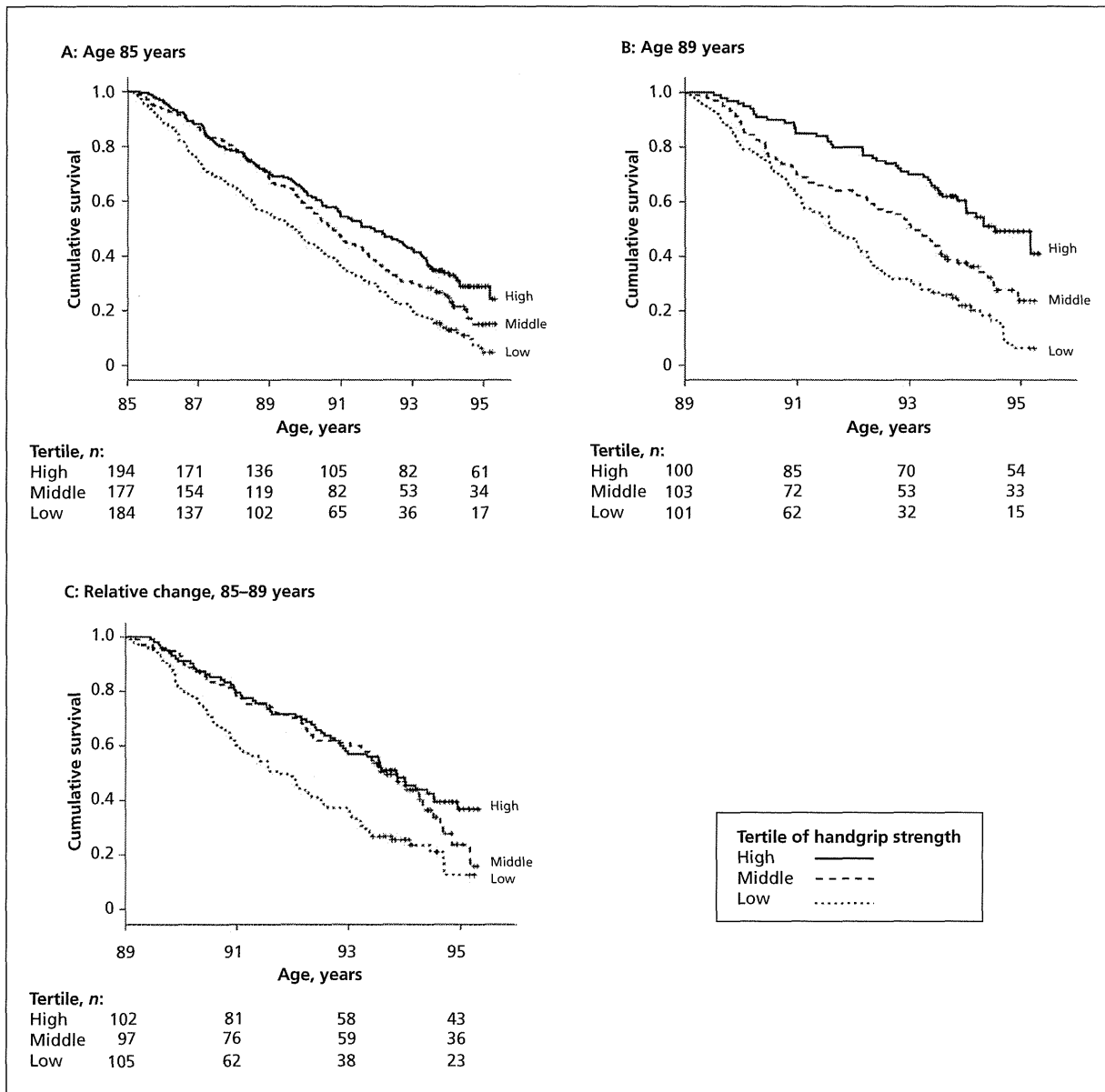
cients of determination were 0.18 for handgrip strength at baseline, 0.27 for handgrip strength at age 89 years and 0.23 for relative loss of handgrip strength. Baseline handgrip strength, handgrip strength at age 89 years and relative loss of handgrip strength were not associated with increased risk for mortality from specific causes.

When we analyzed handgrip strength as a continuous variable in our multivariable analysis, we found that, for each 5-kg reduction in handgrip strength, an increase in risk for all-cause mortality occurred at age 85 years (HR 1.11, CI

1.01–1.23,  $p = 0.040$ ) and at age 89 years (HR 1.24, CI 1.04–1.48,  $p = 0.019$ ). Similarly, we observed an increase in risk for all-cause mortality for every additional 5% loss of relative handgrip strength (HR 1.06, CI 1.01–1.12,  $p = 0.033$ ).

### Interpretation

Our results show that low handgrip strength at ages 85 and 89 years, and a greater decline in strength over time, are associated with increased all-cause mortality. Our findings also sug-



**Figure 1:** Kaplan–Meier cumulative survival curves for all-cause mortality based on sex-specific tertile of handgrip strength (A) at age 85 years, (B) at age 89 years and (C) by relative change in handgrip strength over four years. The highest tertile of relative change in handgrip strength refers to the tertile with the lowest loss of handgrip strength over four years.



**Table 3:** Mortality stratified by sex-specific tertiles of handgrip strength at baseline (age 85 years), handgrip strength at age 89 years, and relative change in handgrip strength over four years

Tertile (range, women/men)	Unadjusted		Adjusted*	
	n	HR (95% CI)	n	HR (95% CI)
<b>Age 85 years, kg</b>				
Low (1–16)/(10–27)	184	1.87 (1.48–2.34)	115	1.35 (1.00–1.82)
Middle (17–20)/(28–33)	177	1.30 (1.03–1.65)	153	1.24 (0.95–1.62)
High (21–31)/(34–54)	194	1.00 (ref)	170	1.00 (ref)
<b>Age 89 years, kg</b>				
Low (2–14)/6–21)	101	3.10 (2.16–4.44)	55	2.04 (1.24–3.35)
Middle (15–18)/(22–28)	103	1.90 (1.31–2.75)	80	1.73 (1.11–2.70)
High (19–31)/(29–48)	100	1.00 (ref)	90	1.00 (ref)
<b>Relative change in handgrip strength over time, %†</b>				
Low (–87.5 to –25.0)/(–76.9 to –26.3)	105	2.07 (1.47–2.90)	58	1.72 (1.07–2.77)
Middle (–23.8 to –6.7)/(–25.6 to –13.8)	97	1.18 (0.82–1.68)	82	1.29 (0.81–2.04)
High (–6.25 to 90.0)/(–13.6 to 20.0)	102	1.00 (ref)	84	1.00 (ref)

Note: CI = confidence interval, HR = hazard ratio, ref = reference group.

\*Hazard ratios for handgrip strength at ages 85 and 89 years were corrected for baseline data for comorbidities, total number of prescription medications and smoking status, and data at baseline or age 89 years for body surface area, for scores on the Mini-Mental State Examination, the Geriatric Depression Scale, the Activities of Daily Living disability scale and the Instrumental Activities of Daily Living disability scale, and for level of physical activity. Hazard ratios for relative change in handgrip strength were corrected for comorbidities, total number of prescription medications and smoking status at baseline, body surface area at age 89 years, and absolute change in scores on the Mini-Mental State Examination, Geriatric Depression Scale, Activities of Daily Living disability scale, Instrumental Activities of Daily Living disability scale, and level of physical activity over four years.

†The highest tertile (i.e., reference tertile) refers to that showing the least loss of handgrip strength over four years.

gest a greater association between handgrip strength and mortality with increasing age.

The mechanisms underlying the association between muscle strength and mortality are not well understood. We were unable to ascertain whether the relation between muscle strength and mortality is direct or whether muscular strength is a surrogate marker of other factors underlying mortality. Future studies of interventions like resistance training, which has been shown to be efficacious in preserving muscular strength,<sup>23</sup> could show whether maintenance of muscular strength translates into a reduction in mortality among weak elderly people. Our finding of increased risk for mortality among weak elderly people suggests that family physicians need to pay special attention to general prevention-related measures in these patients.

### Limitations

Our study had limitations. Our assessment of comorbidities was limited to common chronic diseases. We did not address severity of disease, which could affect probability of survival. Lower handgrip strength can be an indicator of subclinical diseases that affect mortality. In addition, we were unable to adjust for the interim development or progression of comorbidities.

We did not observe an association between handgrip strength and cause-specific mortality, although several previous studies have linked poorer grip strength to mortality resulting from cardiovascular diseases,<sup>24,25</sup> respiratory diseases<sup>25</sup> and cancer.<sup>24</sup> This finding may be explained by the relatively small

number of deaths from each specific cause in our study. The values for handgrip strength in our study population were comparable to other population-based studies involving older adults of similar ages.<sup>26</sup> However, handgrip strength has been shown to be associated with ethnicity, and is weaker among Asian populations compared with Western.<sup>27</sup> Given that our study was based on a homogenous Dutch population, the cutoff threshold for handgrip strength, below which is an increased risk for mortality, may not be generalizable to all elderly populations.

### Conclusion

Our findings have substantial implications for care of a growing elderly population. Application of handgrip dynamometry as a screening tool in a multidimensional geriatric assessment may help identify older people at risk for disability and holds potential for use in prognostication of survival among elderly people. Further studies exploring factors that contribute to loss of muscular strength could provide valuable information toward the development of strategies for preserving muscular strength with advancing age.

This article has been peer reviewed.

**Competing interest:** None declared.

**Contributors:** Anton de Craen, Jacobijn Gussekloo and Rudi Westendorp were involved in the conceptual design of the study. Carolina Ling, Diana Taekema and Andrea Maier were involved in the analysis and interpretation of the data. Carolina Ling drafted the manuscript and wrote the final version. All of the authors critically reviewed the manuscript for important intellectual content and approved the final version submitted for publication.

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**Correspondence to:** Carolina Ling, Leiden University Medical Center, Department of Gerontology and Geriatrics, Albinusdreef 2, 2333 ZA Leiden, Netherlands; [c.h.y.ling@lumc.nl](mailto:c.h.y.ling@lumc.nl)

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概要 (800字まで)	<p>本研究は、オランダのLeiden 85-plus Studyに参加した男女555名を対象に、平均9.5年間の追跡調査を行い、握力と総死亡の関連について検討したものである。利き腕の握力を3回測定し、最大値を記録した。85歳をベースラインとし、89歳時に同様の測定をした。それぞれの測定値を低い準に3群に分類し、また4年間の変化率を低い準に3群に分類した。85歳時で握力の一番高いグループと比較すると、低いグループで総死亡のリスクが1.35(95%信頼区間:1.00-1.82)と有意に上昇した。89歳時で握力の一番高いグループと比較すると、低いグループで2.04(1.24-3.35)、中のグループで1.73(1.11-2.70)と総死亡のリスクが有意に上昇した。また、4年間の握力減少率が一番少なかったグループと比較すると、一番多かったグループでは1.72(1.07-2.77)と有意なリスク上昇がみられた。5kgの握力減少は、85歳時および89歳時で有意なリスク上昇が明らかとなり、また、相対的に5%の握力減少も有意なリスク上昇を示した。</p>																																																																											
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エキスパートによるコメント (200字まで)	<p>身体活動基準の策定に用いられた研究の1つである。握力と総死亡との関係については、これまでいくつかの報告がなされていたが、85歳という高齢においても検討がなされたという点で非常に意義深い。握力は全身の筋量や筋力の指標となり、85歳以上の高齢者でもそれを高く保つことの重要性が示唆された。</p>																																																																											

担当者:久保絵里子・村上晴香・宮地元彦

## Physical activity compensates for increased mortality risk among older people with poor muscle strength

E. Portegijs<sup>1,2</sup>, T. Rantanen<sup>1,2</sup>, S. Sipilä<sup>1,2</sup>, P. Laukkanen<sup>3</sup>, E. Heikkinen<sup>2</sup>

<sup>1</sup>Department of Health Sciences, Finnish Center for Interdisciplinary Gerontology, University of Jyväskylä, Jyväskylä, Finland,

<sup>2</sup>Finnish Center for Interdisciplinary Gerontology, University of Jyväskylä, Jyväskylä, Finland, <sup>3</sup>Health Center of the City of Jyväskylä, Jyväskylä, Finland

Corresponding author: Erja Portegijs, Department of Health Sciences, Finnish Center for Interdisciplinary Gerontology, University of Jyväskylä, PO Box 35 (viv), FI-40014 Jyväskylä, Finland. Tel: +358 14 260 2175, Fax: +358 14 260 4600, E-mail: erja.portegijs@sport.jyu.fi

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The aim of the study was to determine whether habitual physical activity can compensate for the increased mortality risk among older people with poor muscle strength. Mortality was followed up for 10 years after laboratory examination in 558 community dwelling 75- and 80-year-old men and women. Maximal isometric strength of five muscle groups was measured and tertile cut-off points were used to categorize participants. Participants, who reported moderate physical activity for at least 4 h a week, were categor-

ized as physically active and the others as sedentary. High muscle strength and physical activity both protected from mortality, but their effect was not additive. Within each muscle strength tertile, physically active people had a lower mortality risk than sedentary people, the effect being most pronounced among those with lower strength in all muscle groups. A high level of physical activity may thus compensate for the increased mortality associated with low muscle strength.

With increasing age, physical function declines and a sedentary lifestyle becomes more prevalent (DiPietro, 2001). Physical activity may help to counteract the age-related decline in or improve muscle, cardiovascular, respiratory and metabolic function. Additionally, physical activity may inhibit the onset of certain diseases as well as improve health and function among people with diseases, disabilities or depressive symptoms (e.g. reviewed by the American College of Sports Medicine Position Stand, 1998; Bean et al., 2004; Taylor et al., 2004). Consequently, longitudinal studies have demonstrated that high physical activity is protective for all-cause mortality (e.g. reviewed by Lee & Skerrett, 2001) and mortality from major chronic diseases such as cardiovascular disease (Kaplan et al., 1996; Kushi et al., 1997; Bijnen et al., 1998; Gregg et al., 2003), respiratory disease (Kushi et al., 1997) and cancer (Gregg et al., 2003).

Although sedentary lifestyle and poor muscle strength often coexist, they do not correlate fully (Rantanen et al., 1997). Some people with good muscle strength may be quite sedentary, while some people with low strength are physically quite active. Multiple factors underlying the individual differences in strength, including genetic factors (Tiainen et al., 2004), are a potential explanation for this. Previous longitudinal analyses have shown that the associa-

tion of strength and all-cause mortality persisted even after adjustment for multiple factors potentially explaining the association, such as age, presence of chronic conditions, inflammation, nutritional status and depressive symptoms (e.g. Rantanen et al., 2003). Therefore, it is possible that strength may be a constitutional marker of vulnerability to adverse health events, such as disease, disability, falls and injury or poor recovery from these conditions, thus also increasing mortality risk.

The aim of the study is to examine the combined effects of physical activity and muscle strength on all-cause mortality. The analyses were carried out to better understand whether physical activity may modify the risk of mortality among people with different levels of strength.

### Methods

#### Participants

This study is part of the Evergreen project, a longitudinal study on health and functional capacity among older residents in the city of Jyväskylä, Finland. A detailed description of the study design has been reported elsewhere (Heikkinen, 1997). Briefly, all community dwelling people of the city aged 75 and 80 years were invited to participate in the study and 663 people were found to be eligible. In the autumn of 1989 and the winter of 1990, 93% ( $n = 617$ ) of the eligible population agreed to

participate and were interviewed at home. Ninety percent of the participants responded to the question about physical activity (men: 109 aged 75 years and 67 aged 80 years; and women: 204 aged 75 years and 178 aged 80 years) and 81% ( $n = 500$ ) of them visited the laboratory for examination. Participation in the muscle strength measurements was contraindicated for six women and nine men due to cardiovascular diseases, musculoskeletal problems or poor cooperation (Rantanen et al., 1994, Rantanen & Heikkinen, 1998). Handgrip strength was the muscle strength test most commonly taken and was measured in 101 men aged 75 years and 55 aged 80 years, and in 186 women aged 75 years and 136 aged 80 years. In total, 478 people participated in at least one strength test, while 444 participated in the tests of all five muscle groups (Appendix A). All participants signed an informed consent before the examinations.

#### Clinical assessment

The presence of chronic medical conditions, with a minimum duration of 3 months, was ascertained by a physician in a clinical examination. Sixty-two percent of the participants had cardiovascular diseases, such as ischemic heart disease and hypertension. Additionally, musculoskeletal diseases (e.g. osteoarthritis) were present in 39% of the participants, and neurological (e.g. cerebrovascular ischemia) and sensory (e.g. glaucoma and cataract) diseases in 26% of the participants. Less prevalent disease categories were metabolic diseases (15%; e.g. diabetes), respiratory diseases (12%), diseases of the digestive system (10%), mental diseases (4%), cancer (9%) and other non-classified diseases (17%). Additionally, the physician assessed contraindications to the muscle strength tests.

#### Physical activity

A modified version of the multiple-choice question developed and validated by Grimby (1986) and Mattiasson-Nilo et al. (1990) was used to assess the level of physical activity related to leisure-time, work and carrying out daily activities. The participants were asked to choose the description that best pictured their level of physical activity over the last year: (1) hardly any activity, mostly sitting; (2) light physical activity, such as light household tasks; (3) moderate physical activity about 3 h a week; walking longer distances, cycling and domestic work; (4) moderate physical activity at least 4 h a week or heavier physical activity 1–2 h a week; (5) heavier physical activity or moderate exercise for at least 3 h a week; and (6) competitive sports. This scale is feasible in older independent populations as it is easy and quick to use and it also rates domestic activities. To avoid small group sizes in the analyses, the scale was dichotomized. Participants were considered physically active if they reported moderate physical activity for at least 4 h a week. The test–retest Pearson correlation coefficients were  $r = 0.634$  for men and  $r = 0.655$  for women (Sihvonen et al., 1998).

#### Muscle strength

Maximal isometric strength of handgrip, elbow flexion and knee extension were measured on the dominant side in a sitting position using an adjustable dynamometer chair, and expressed in Newton (N) (Heikkinen et al., 1984). For the measurement of handgrip strength, a dynamometer was fixed to the arm of the chair. Elbow flexion strength was measured with a strain-gauge system at the wrist, the elbow supported at an angle of 90° and the hand in the neutral position (thumb

up). Knee extension strength was measured at a knee angle of 60° from the fully extended leg toward flexion. The ankle was attached to a strain-gauge system. Maximal isometric trunk flexion and trunk extension strength were measured in a standing position according to Viitasalo et al. (1977).

After two to three practice trials, each strength test was performed three times with an inter-trial rest period of 1 min. The best result was used as the measure of maximal strength in the analyses. The test–retest Pearson correlation coefficients were  $r = 0.97$  for handgrip, knee extension and trunk flexion strength, and  $r = 0.90$  for elbow flexion, and  $r = 0.92$  for trunk extension (Rantanen et al., 1997). As muscle strength is highly dependent on gender and age, tertile cut-off points were determined for 75- and 80-year-old men and women separately (Appendix A). In this way, an equal number of men and women were placed in each tertile.

#### Confounders

The number of chronic diseases, obtained from the clinical assessment, was used as an indicator of morbidity. Depressive symptoms, smoking and the level of education were assessed by means of a questionnaire. The self-rated Center for Epidemiologic Studies-Depression Scale (Radloff, 1977) was used to assess the presence of depressive symptoms (cut-off score 16). The respondents were asked to rate the frequency, ranging from 0 (rarely or none of the time) to 3 (most or all of the time), of 20 listed symptoms over the past week. Additionally, participants were classified as (1) non-smoker and (2) previous or current smoker, and the level of education was described as (1) less than primary school, (2) primary or junior high school, (3) senior high school or (4) technical school or university. Age and gender were registered and body height and weight were measured at the research laboratory.

#### Mortality

All-cause mortality was followed up at 10 years from baseline. Death dates were received from the Population Register. Survival time was calculated from baseline to the day the subject died. Subjects not known to have died or lost to the follow-up were given a survival time of 10 years.

#### Statistical methods

The gender-specific differences in the characteristics of the sedentary and physically active groups were determined by an independent *T*-test, or cross-tabulation with a chi-square test. Mortality rates relative to survival time were calculated and expressed as the number of deaths/100 person years.

Cox proportional hazard analyses were first executed separately for both age and gender groups to investigate the association of the level of physical activity and muscle strength, separately and combined, with all-cause mortality. Eventually, the data were combined in a single model, as the direction of the associations was similar and the group sizes were small for meaningful separate analysis. The results were adjusted for age, gender, body height and weight, number of chronic diseases, presence of depressive symptoms, smoking and level of education.

SPSS computer software was used for the analyses. Significance was set at  $P < 0.05$ .

Table 1. Means and standard deviations (SD) of the baseline characteristics of sedentary and physically active 75- and 80-year-old men and women with at least one muscle strength measure

	Men					Women				
	Sedentary*		Active†		<i>t</i> -test <i>P</i>	Sedentary		Active		<i>t</i> -test <i>P</i>
	<i>n</i>	Mean ± SD	<i>n</i>	Mean ± SD		<i>n</i>	Mean ± SD	<i>n</i>	Mean ± SD	
Body height (cm)	98	169.2 ± 6.6	59	169.4 ± 5.8	0.826	221	155.8 ± 5.6	101	155.4 ± 5.4	0.563
Body weight (kg)	98	75.0 ± 12.1	59	73.4 ± 9.7	0.387	221	67.5 ± 11.9	101	63.8 ± 8.8	0.007
Chronic diseases ( <i>n</i> )	98	2.6 ± 1.4	58	1.8 ± 1.3	0.002	222	2.7 ± 1.7	101	2.4 ± 1.6	0.109
Handgrip strength (N)	97	343.3 ± 83.4	59	396.0 ± 86.3	<0.001	221	208 ± 57.6	101	227.5 ± 63.4	0.007
Elbow flexion strength (N)	97	231.4 ± 56.8	59	271.3 ± 42.6	<0.001	222	148.2 ± 40.5	101	156.4 ± 43.2	0.100
Knee extension strength (N)	96	318.2 ± 104.1	59	378.7 ± 81.4	<0.001	220	218.1 ± 71.2	101	232.7 ± 80.9	0.104
Trunk extension strength (N)	87	478.5 ± 214.4	58	657.1 ± 176.9	<0.001	207	293.4 ± 133.8	97	326.1 ± 140.9	0.051
Trunk flexion strength (N)	88	459.4 ± 176.7	57	544.2 ± 133.0	0.002	204	270.2 ± 96.0	95	294.6 ± 112.6	0.053

\*Sedentary: about 3 h of moderate physical activity a week or less.

†Active: moderate physical activity at least 4 h a week.

## Results

In this study, 38% of the men and 31% of the women were considered to be physically active. These men and women reported to engage in moderate physical activity for at least 4 h a week (28% and 29%, respectively) or in heavier physical activity and moderate exercise for at least 3 h a week (10% and 3%, respectively). None of the participants took part in competitive sports. The sedentary men and women (in total 62% and 69%, respectively) reported hardly any activity (12% and 6%, respectively), light physical activity (19% and 21%, respectively) or moderate physical activity about 3 h a week (33% and 42%, respectively). The sedentary participants had lower strength in all the muscle groups (Table 1). However, among the women, some of the strength differences did not reach statistical significance. Depressive symptoms were more common among the sedentary men (37%) than active men (20%,  $P = 0.024$ ), whereas among both the sedentary and active women the corresponding prevalence was 40%. Twenty-nine percent of the men and 92% of the women had never smoked.

During the 10-year follow-up period, 56% of the participants included in the analyses died (men: 63 aged 75 years and 48 aged 80 years; and women: 89 aged 75 years and 111 aged 80 years). After checking that the association of physical activity with mortality was similar in both the gender and age groups, all participants were jointly included in subsequent analyses. In the sedentary participants, the relative risk (RR) for mortality was 1.7 times (95% confidence interval: 1.3–2.2) that of physically active participants and adjusting for confounders did not change the risk estimate (RR = 1.7, 95% confidence interval: 1.2–2.2). Table 2 presents the crude and adjusted mortality risks according to the level of

strength in each muscle group. Crude RR for death was approximately twofold among those in the lowest muscle strength tertile compared with the highest; adjusting for confounders did not materially change the estimates. Similar results were obtained for all muscle groups.

To study the combined effects of the muscle strength tertiles and physical activity categories, six groups were formed for each muscle group tested. For example, for grip strength, 78% of those in the lowest tertile were sedentary, while the corresponding figures in the middle and highest tertile were 65% and 58%, respectively. Figure 1 shows the mortality rates of sedentary and physically active men and women by the strength tertiles in each muscle group. A highly similar mortality rate pattern according to muscle strength and physical activity was observed for men and women even though the rates were generally lower in women. Within each strength tertile, the mortality rate was lower among the physically active than sedentary participants. This difference was particularly evident among those in the lowest strength tertile where the overall mortality rate was higher. Among those in the highest strength tertile with a lower overall mortality rate, physical activity was not equally systematically associated with a lower death rate. The crude and adjusted RRs of mortality according to the level of strength in the groups of sedentary and physically active are shown in Table 2. For each group of muscles tested, the crude risk for death was 2–3 times higher among sedentary participants in the lowest strength tertile than among physically active participants in the highest strength tertile. The results show that the elevated risk of death associated with lower strength was substantially lower among those who were physically active. However, among those with higher strength, the risks of death were generally lower and

Table 2. Relative risks (RR) for mortality and 95% confidence intervals (95%CI)\* according to muscle strength tertiles for each muscle group (all) and for groups based on physical activity and muscle strength

Tertile	Crude						Adjusted <sup>†</sup>					
	All		Sedentary <sup>‡</sup>		Active <sup>§</sup>		All		Sedentary		Active	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Handgrip												
Lowest	1.8	1.3–2.5	2.2	1.5–3.4	1.2	0.7–2.2	1.7	1.2–2.5	2.0	1.2–3.3	1.2	0.6–2.4
Medium	1.3	0.9–1.7	1.7	1.1–2.6	0.9	0.5–1.6	1.4	1.0–2.0	1.8	1.1–2.9	1.0	0.5–1.8
Highest	1.0		1.1	0.7–1.8	1.0		1.0		1.2	0.7–2.0	1.0	
Elbow flexion												
Lowest	2.0	1.5–2.7	2.7	1.7–4.2	1.2	0.6–2.3	1.9	1.3–2.7	2.6	1.6–4.3	1.4	0.7–2.9
Medium	1.3	1.0–1.8	1.7	1.1–2.7	1.2	0.7–2.1	1.3	0.9–1.8	1.8	1.1–2.9	1.2	0.7–2.2
Highest	1.0		1.2	0.8–2.0	1.0		1.0		1.4	0.8–2.4	1.0	
Knee extension												
Lowest	2.2	1.6–3.0	3.3	2.0–5.3	1.9	1.1–3.6	2.0	1.4–2.9	3.0	1.8–5.1	2.1	1.1–4.2
Medium	1.8	1.3–2.5	2.6	1.6–4.2	1.9	1.0–3.3	1.7	1.2–2.5	2.6	1.5–4.4	1.9	1.0–3.6
Highest	1.0		1.5	0.9–2.6	1.0		1.0		1.7	1.0–3.0	1.0	
Trunk extension												
Lowest	2.3	1.6–3.2	2.9	1.8–4.6	2.2	1.2–4.1	1.9	1.3–2.8	2.3	1.4–3.9	1.8	0.9–3.8
Medium	1.5	1.0–2.1	2.1	1.3–3.3	1.3	0.7–2.3	1.4	1.0–2.1	2.1	1.2–3.5	1.1	0.6–2.0
Highest	1.0		1.4	0.8–2.4	1.0		1.0		1.3	0.7–2.3	1.0	
Trunk flexion												
Lowest	1.9	1.3–2.6	2.8	1.7–4.4	1.5	0.8–2.8	1.6	1.1–2.4	2.3	1.4–3.9	1.2	0.6–2.4
Medium	1.3	0.9–1.8	1.8	1.1–3.0	1.3	0.7–2.4	1.1	0.8–1.7	1.6	0.9–2.7	1.0	0.5–2.0
Highest	1.0		1.5	0.9–2.5	1.0		1.0		1.4		1.0	

\*Obtained from Cox proportional hazard analysis.

<sup>†</sup>Adjusted for age, gender, body height and weight, number of diseases, presence of depressive symptoms, smoking and education level.

<sup>‡</sup>About 3 h of moderate physical activity a week or less.

<sup>§</sup>Moderate physical activity at least 4 h a week.

physical activity did not show a noticeable association with reduced risk. Adjusting for the confounders did not materially change the results.

## Discussion

We found that a high level of physical activity may compensate for the increased mortality risk among older people with poorer muscle strength. To our knowledge, this was the first study to determine the combined effects of physical activity and muscle strength on all-cause mortality, an indicator of general health, in older people. However, many longitudinal studies, including this one, using a large variety of measures, have found that poor muscle strength (e.g. Metter et al., 2002; Rantanen et al., 2003) and low physical activity (e.g. Lee & Skerrett, 2001, for a review) are consistently associated with an increased risk for mortality.

Muscle strength is a potential marker for resiliency to poor health in old age. Our observation that mortality risk was lower among the physically active people with poorer strength than among the sedentary suggests that physical activity may partly compensate for less favorable expected health trajectory among those with poorer strength. The associations

remained after adjusting for morbidity, body height and weight, depressive symptoms, smoking history and educational background. Age did not affect the associations either, as the age range was relatively small. The severity of the diseases could not be taken into account and therefore, some residual confounding may have remained in the models. However, we do not believe that disease severity would fully explain the current findings. Taking into account the cause of death could have added information about the pathway leading to death. However, as the independent effects of muscle strength (Rantanen et al., 2003) and physical activity (Kaplan et al., 1996; Bijnen et al., 1998; Gregg et al., 2003) on all-cause and cause-specific mortality have been found to be similar, the results of this study would likely not have changed.

Participants were considered physically active if they reported moderate physical activity for at least 4 h a week, which is approximately the same amount of activity as currently recommended for maintaining a healthy life. Leisure walking is the most common activity among older people (DiPietro, 2001; Taylor et al., 2004); however, its intensity may not be high enough for it to be associated with higher muscle strength (American College of Sports Medicine Position Stand, 1998). The health benefits, including

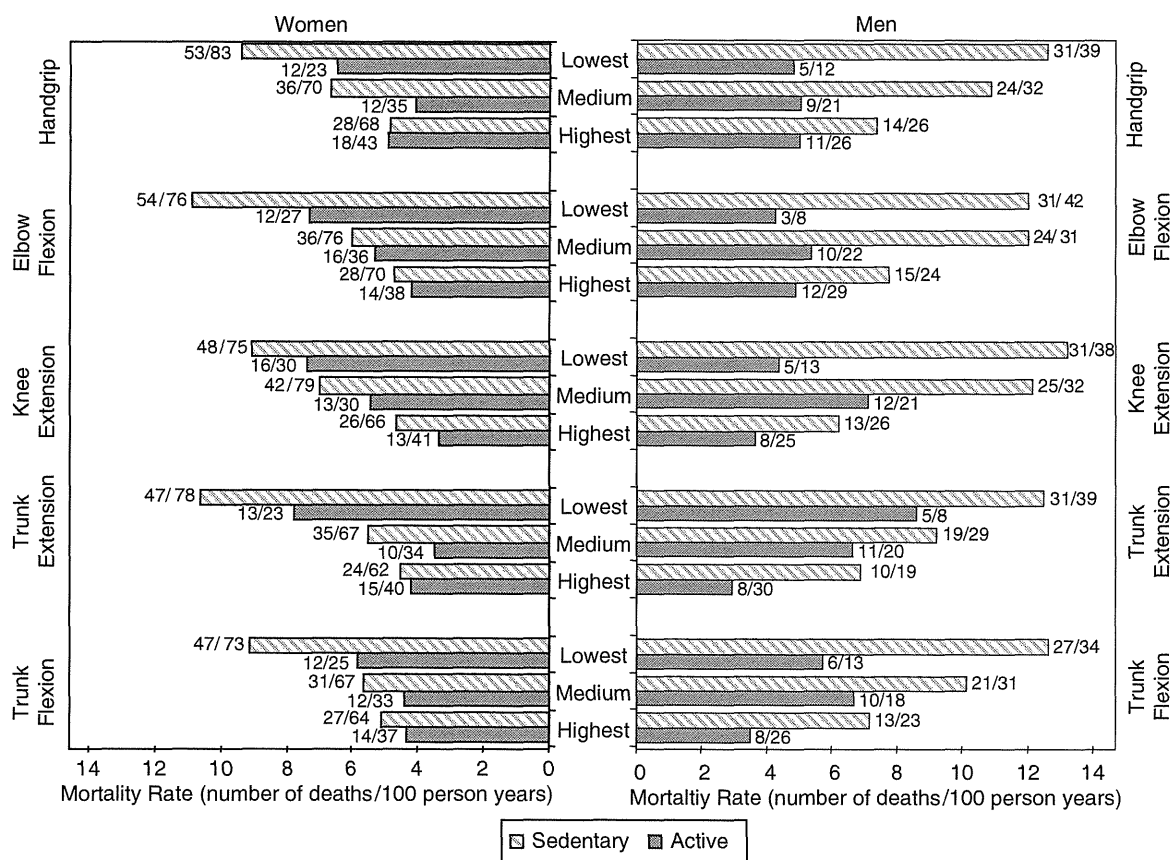


Fig. 1. Mortality rate (number of deaths/100 person years over follow-up) in sedentary and physically active (moderate physical activity for at least 4 h a week) men and women according to strength tertiles for each muscle group. The number of deaths relative to the group size is noted at the end of each bar.

reduced mortality, associated with physical activity were thus more likely to be induced by improvements in cardiovascular and respiratory function.

Having high muscle strength and being physically active did not seem to have an additional effect in reducing mortality in this study population. However, high levels of both muscle strength and physically activity may be important for other health outcomes or for disability.

The amount of physical activity needed to maintain good health in older age is still unclear, and currently there is no standardized method to assess physical activity in older people. In this study, physical activity was assessed by a short and easy self-report question, which was dichotomized for the analyses. Even this rough indicator of physical activity was predictive of mortality. Potentially larger effects of physical activity on mortality may be found when a more precise measure, differentiating people more adequately, is used. The association between isometric muscle strength and mortality was similar in the five muscle groups. Additionally, 83.1% of the participants were assigned to the same category for at least three muscle groups, while 8.3% had at least

one measure missing. These missing values altered the distribution of the data in the respective muscle groups. Handgrip strength may be preferred as an indicator of general muscle strength, considering its frequent use in previous studies (Philips, 1986; Fujita et al., 1995; Al Smih et al., 2002; Metter et al., 2002; Rantanen et al., 2003) and its high correlation with muscle strength in other muscle groups (Rantanen et al., 1997). Additionally, handgrip strength is easy and quick to assess.

The population used in this study was representative of the urban, community-dwelling population of this age in Central Finland. However, we believe that the range of muscle strength was truncated at the lower end, as those unable to attend the laboratory for the examinations and those with contraindications for the muscle strength assessments generally had poorer health status. Of those unable to participate in the muscle strength tests, 68% were 80 years old, and the mortality rate was 12.8 deaths/100 person years among the men and 8.3 deaths/100 person years among the women. In comparison, men with at least one muscle strength measurement had a mortality rate of 6.7 deaths/100 person years



and women a mortality rate of 5.2 deaths/100 person years, respectively. The mortality rate and risk estimates found in this study may therefore underestimate the effect of muscle strength.

The mortality rates were strikingly similar in the different muscle groups, and in men and women. However, considering the small group sizes, especially those of active men, further study is warranted. Larger studies are needed to allow for gender-specific analyses and more comprehensive analysis of confounding factors.

### Perspectives

Low level of physical activity (e.g. Lee & Skerrett, 2001, for review) and muscle strength (Philips, 1986; Fujita et al., 1995; Al Smih et al., 2002; Metter et al., 2002; Rantanen et al., 2003) are acknowledged risk factors for mortality. This study showed that physical activity may counteract the increased mortality risk associated with poor muscle strength. Physical activities, not specifically targeting at increasing muscle strength, such as leisure walking, are likely

to induce health benefits, reflected in reduced mortality, as the effects of high muscle strength and high physical activity were not additive. Especially, people with low muscle strength are likely to benefit from strategies promoting high levels of physical activity and should therefore be targeted for prevention and intervention. However, further study is needed to determine the mechanisms through which physical activity and muscle strength jointly affect mortality and health in older men and women.

**Key words:** physical exercise, sedentary, muscle force, survival, aged.

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**Appendix A**

Appendix A1. Age- and gender-specific cut-off points for strength, expressed in Newton, in each muscle group

Tertile	Men		Women	
	75-year-old	80-year-old	75-year-old	80-year-old
<b>Handgrip (n = 478)</b>				
Lowest	< 328.0	< 316.3	< 205.0	< 177.3
Medium	328.0–404.0	316.3–371.3	205.0–253.0	177.3–219.0
Highest	≥ 404.0	≥ 371.3	≥ 253.0	≥ 219.0
<b>Elbow flexion (n = 478)</b>				
Lowest	< 231.0	< 206.0	< 144.0	< 118.3
Medium	231.0–267.0	206.0–266.0	144.0–178.0	118.3–156.7
Highest	≥ 276.0	≥ 266.0	≥ 178.0	≥ 156.7
<b>Knee extension (n = 476)</b>				
Lowest	< 330.3	< 257.6	< 209.7	< 160.0
Medium	330.3–402.0	257.7–343.0	209.7–268.3	160.0–221.0
Highest	≥ 402.0	≥ 343.0	≥ 268.3	≥ 221.0
<b>Trunk extension (n = 449)</b>				
Lowest	< 504.0	< 375.0	< 285.0	< 183.3
Medium	504.0–681.0	375.0–559.0	285.0–409.7	183.3–278.3
Highest	≥ 681.0	≥ 559.0	≥ 409.7	≥ 278.3
<b>Trunk flexion (n = 444)</b>				
Lowest	< 455.0	< 423.0	< 265.3	< 200.0
Medium	455.0–590.0	423.0–536.0	265.3–339.7	200.0–278.0
Highest	≥ 590.0	≥ 536.0	≥ 339.7	≥ 278.0

論文名	Physical activity compensates for increased mortality risk among older people with poor muscle strength																																																																																																																																																																																																																																																																																																																			
著者	Portegijs E, Rantanen T, Sipilä S, Laukkanen P, Heikkinen E																																																																																																																																																																																																																																																																																																																			
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図表	<p>Table 2. Relative risks (RR) for mortality and 95% confidence intervals (95%CI)* according to muscle strength tertiles for each muscle group (all) and for groups based on physical activity and muscle strength</p> <table border="1"> <thead> <tr> <th rowspan="3">Tertile</th> <th colspan="6">Crude</th> <th colspan="6">Adjusted<sup>†</sup></th> </tr> <tr> <th colspan="2">All</th> <th colspan="2">Sedentary<sup>‡</sup></th> <th colspan="2">Active<sup>§</sup></th> <th colspan="2">All</th> <th colspan="2">Sedentary</th> <th colspan="2">Active</th> </tr> <tr> <th>RR</th> <th>95% CI</th> <th>RR</th> <th>95% CI</th> <th>RR</th> <th>95% CI</th> <th>RR</th> <th>95% CI</th> <th>RR</th> <th>95% CI</th> <th>RR</th> <th>95% CI</th> </tr> </thead> <tbody> <tr> <td>Handgrip</td> <td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td> <tr> <td>  Lowest</td> <td>1.8</td><td>1.3-2.5</td> <td>2.2</td><td>1.5-3.4</td> <td>1.2</td><td>0.7-2.2</td> <td>1.7</td><td>1.2-2.5</td> <td>2.0</td><td>1.2-3.3</td> <td>1.2</td><td>0.6-2.4</td> </tr> <tr> <td>  Medium</td> <td>1.3</td><td>0.9-1.7</td> <td>1.7</td><td>1.1-2.6</td> <td>0.9</td><td>0.5-1.6</td> <td>1.4</td><td>1.0-2.0</td> <td>1.8</td><td>1.1-2.9</td> <td>1.0</td><td>0.5-1.8</td> </tr> <tr> <td>  Highest</td> <td>1.0</td><td></td> <td>1.1</td><td>0.7-1.8</td> <td>1.0</td><td></td> <td>1.0</td><td></td> <td>1.2</td><td>0.7-2.0</td> <td>1.0</td><td></td> </tr> <tr> <td>Elbow flexion</td> <td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td> <tr> <td>  Lowest</td> <td>2.0</td><td>1.5-2.7</td> <td>2.7</td><td>1.7-4.2</td> <td>1.2</td><td>0.6-2.3</td> <td>1.9</td><td>1.3-2.7</td> <td>2.6</td><td>1.6-4.3</td> <td>1.4</td><td>0.7-2.9</td> </tr> <tr> <td>  Medium</td> <td>1.3</td><td>1.0-1.8</td> <td>1.7</td><td>1.1-2.7</td> <td>1.2</td><td>0.7-2.1</td> <td>1.3</td><td>0.9-1.8</td> <td>1.8</td><td>1.1-2.9</td> 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CI	Handgrip													Lowest	1.8	1.3-2.5	2.2	1.5-3.4	1.2	0.7-2.2	1.7	1.2-2.5	2.0	1.2-3.3	1.2	0.6-2.4	Medium	1.3	0.9-1.7	1.7	1.1-2.6	0.9	0.5-1.6	1.4	1.0-2.0	1.8	1.1-2.9	1.0	0.5-1.8	Highest	1.0		1.1	0.7-1.8	1.0		1.0		1.2	0.7-2.0	1.0		Elbow flexion													Lowest	2.0	1.5-2.7	2.7	1.7-4.2	1.2	0.6-2.3	1.9	1.3-2.7	2.6	1.6-4.3	1.4	0.7-2.9	Medium	1.3	1.0-1.8	1.7	1.1-2.7	1.2	0.7-2.1	1.3	0.9-1.8	1.8	1.1-2.9	1.2	0.7-2.2	Highest	1.0		1.2	0.8-2.0	1.0		1.0		1.4	0.8-2.4	1.0		Knee extension													Lowest	2.2	1.6-3.0	3.3	2.0-5.3	1.9	1.1-3.6	2.0	1.4-2.9	3.0	1.8-5.1	2.1	1.1-4.2	Medium	1.8	1.3-2.5	2.6	1.6-4.2	1.9	1.0-3.3	1.7	1.2-2.5	2.6	1.5-4.4	1.9	1.0-3.6	Highest	1.0		1.5	0.9-2.6	1.0		1.0		1.7	1.0-3.0	1.0		Trunk extension													Lowest	2.3	1.6-3.2	2.9	1.8-4.6	2.2	1.2-4.1	1.9	1.3-2.8	2.3	1.4-3.9	1.8	0.9-3.8	Medium	1.5	1.0-2.1	2.1	1.3-3.3	1.3	0.7-2.3	1.4	1.0-2.1	2.1	1.2-3.5	1.1	0.6-2.0	Highest	1.0		1.4	0.8-2.4	1.0		1.0		1.3	0.7-2.3	1.0		Trunk flexion													Lowest	1.9	1.3-2.6	2.8	1.7-4.4	1.5	0.8-2.8	1.6	1.1-2.4	2.3	1.4-3.9	1.2	0.6-2.4	Medium	1.3	0.9-1.8	1.8	1.1-3.0	1.3	0.7-2.4	1.1	0.8-1.7	1.6	0.9-2.7	1.0	0.5-2.0	Highest	1.0		1.5	0.9-2.5	1.0		1.0		1.4		1.0	
Tertile	Crude						Adjusted <sup>†</sup>																																																																																																																																																																																																																																																																																																													
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Medium	1.3	1.0-1.8	1.7	1.1-2.7	1.2	0.7-2.1	1.3	0.9-1.8	1.8	1.1-2.9	1.2	0.7-2.2																																																																																																																																																																																																																																																																																																								
Highest	1.0		1.2	0.8-2.0	1.0		1.0		1.4	0.8-2.4	1.0																																																																																																																																																																																																																																																																																																									
Knee extension													Lowest	2.2	1.6-3.0	3.3	2.0-5.3	1.9	1.1-3.6	2.0	1.4-2.9	3.0	1.8-5.1	2.1	1.1-4.2	Medium	1.8	1.3-2.5	2.6	1.6-4.2	1.9	1.0-3.3	1.7	1.2-2.5	2.6	1.5-4.4	1.9	1.0-3.6	Highest	1.0		1.5	0.9-2.6	1.0		1.0		1.7	1.0-3.0	1.0		Trunk extension													Lowest	2.3	1.6-3.2	2.9	1.8-4.6	2.2	1.2-4.1	1.9	1.3-2.8	2.3	1.4-3.9	1.8	0.9-3.8	Medium	1.5	1.0-2.1	2.1	1.3-3.3	1.3	0.7-2.3	1.4	1.0-2.1	2.1	1.2-3.5	1.1	0.6-2.0	Highest	1.0		1.4	0.8-2.4	1.0		1.0		1.3	0.7-2.3	1.0		Trunk flexion													Lowest	1.9	1.3-2.6	2.8	1.7-4.4	1.5	0.8-2.8	1.6	1.1-2.4	2.3	1.4-3.9	1.2	0.6-2.4	Medium	1.3	0.9-1.8	1.8	1.1-3.0	1.3	0.7-2.4	1.1	0.8-1.7	1.6	0.9-2.7	1.0	0.5-2.0	Highest	1.0		1.5	0.9-2.5	1.0		1.0		1.4		1.0																																																																																																																																																										
Lowest	2.2	1.6-3.0	3.3	2.0-5.3	1.9	1.1-3.6	2.0	1.4-2.9	3.0	1.8-5.1	2.1	1.1-4.2																																																																																																																																																																																																																																																																																																								
Medium	1.8	1.3-2.5	2.6	1.6-4.2	1.9	1.0-3.3	1.7	1.2-2.5	2.6	1.5-4.4	1.9	1.0-3.6																																																																																																																																																																																																																																																																																																								
Highest	1.0		1.5	0.9-2.6	1.0		1.0		1.7	1.0-3.0	1.0																																																																																																																																																																																																																																																																																																									
Trunk extension													Lowest	2.3	1.6-3.2	2.9	1.8-4.6	2.2	1.2-4.1	1.9	1.3-2.8	2.3	1.4-3.9	1.8	0.9-3.8	Medium	1.5	1.0-2.1	2.1	1.3-3.3	1.3	0.7-2.3	1.4	1.0-2.1	2.1	1.2-3.5	1.1	0.6-2.0	Highest	1.0		1.4	0.8-2.4	1.0		1.0		1.3	0.7-2.3	1.0		Trunk flexion													Lowest	1.9	1.3-2.6	2.8	1.7-4.4	1.5	0.8-2.8	1.6	1.1-2.4	2.3	1.4-3.9	1.2	0.6-2.4	Medium	1.3	0.9-1.8	1.8	1.1-3.0	1.3	0.7-2.4	1.1	0.8-1.7	1.6	0.9-2.7	1.0	0.5-2.0	Highest	1.0		1.5	0.9-2.5	1.0		1.0		1.4		1.0																																																																																																																																																																																																														
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概要 (800字まで)	<p>本研究は、フィンランドのThe Evergreen Projectに参加した高齢男女558名を対象に、10年間の追跡調査を行い、低筋力における身体活動量と全死因死亡リスクとの関連を検討したものである。質問紙により、過去1年間の身体活動実施状況を尋ね、週当たり4時間以上の中強度身体活動を実施している集団をActive、それ以下の集団をSedentaryとした。また、握力、肘屈曲、脚伸展、体幹伸展、体幹屈曲の測定を実施し、各項目とも年齢ごとに3群に分類した。全ての集団において、それぞれの筋力測定の最高分位と比較すると、握力は最も低い集団で全死因死亡リスクが1.7(95%信頼区間:1.2-2.5)に上昇し、肘屈曲では最も低い集団で1.9(1.3-2.7)に、脚伸展では第2分位の集団と最も低い集団でそれぞれ1.7(1.2-2.5)、2.0(1.4-2.9)に、体幹伸展では最も低い集団で1.9(1.3-2.8)に、体幹屈曲では最も低い集団で1.6(1.1-2.4)に上昇した。また、Sedentaryの集団においては、全ての筋力測定において第2分位以上で全死因死亡リスクが有意に上昇した。Activeの集団では、それらの有意なリスク上昇はみられな</p>																																																																																																																																																																																																																																																																																																																			
結論 (200字まで)	筋力の低い高齢集団においては、身体活動レベルを高めることで全死因死亡リスクを軽減させることが示唆された。																																																																																																																																																																																																																																																																																																																			
エキスパートによるコメント (200字まで)	身体活動基準の策定に使用された研究である。体力と身体活動の相互作用を検討した点に意義がある。サンプルサイズが小さい研究なので、今後より多くの参加者で同様の知見が得られるか否かを検討する必要がある。																																																																																																																																																																																																																																																																																																																			

担当者:久保絵里子・村上晴香・宮地元彦

# Handgrip Strength and Cause-Specific and Total Mortality in Older Disabled Women: Exploring the Mechanism

Taina Rantanen, PhD,\*<sup>†</sup> Stefano Volpato, MD, MPH,\* Luigi Ferrucci MD, PhD,<sup>‡</sup> Eino Heikkinen MD, PhD,<sup>†</sup> Linda P. Fried, MD, MPH,<sup>§</sup> and Jack M. Guralnik, MD, PhD\*

**OBJECTIVES:** To examine the association between muscle strength and total and cause-specific mortality and the plausible contributing factors to this association, such as presence of diseases commonly underlying mortality, inflammation, nutritional deficiency, physical inactivity, smoking, and depression.

**DESIGN:** Prospective population-based cohort study with mortality surveillance over 5 years.

**SETTING:** Elderly women residing in the eastern half of Baltimore, Maryland, and part of Baltimore County.

**PARTICIPANTS:** Nine hundred nineteen moderately to severely disabled women aged 65 to 101 who participated in handgrip strength testing at baseline as part of the Women's Health and Aging Study.

**MEASUREMENTS:** Cardiovascular disease (CVD), cancer, respiratory disease, other measures (not CVD, respiratory, or cancer), total mortality, handgrip strength, and interleukin-6.

**RESULTS:** Over the 5-year follow-up, 336 deaths occurred: 149 due to CVD, 59 due to cancer, 38 due to respiratory disease, and 90 due to other diseases. The unadjusted relative risk (RR) of CVD mortality was 3.21 (95% confidence interval (CI) = 2.00–5.14) in the lowest and 1.88 (95% CI = 1.11–3.21) in the middle compared with the highest tertile of handgrip strength. The unadjusted RR of respiratory mortality was 2.38 (95% CI = 1.09–5.20) and other mortality 2.59 (95% CI = 1.59–4.20) in the lowest versus the highest grip-strength tertile. Cancer mortality was not associated with grip strength. After adjusting for age, race, body height, and weight, the RR of CVD mortality decreased to 2.17 (95% CI = 1.26–3.73) in the lowest and 1.56 (95% CI = 0.89–2.71) in the middle, with the highest grip-strength tertile as the reference.

From the \*Laboratory of Epidemiology, Demography and Biometry, National Institute on Aging, National Institutes of Health, Bethesda, Maryland; <sup>†</sup>Department of Health Sciences, University of Jyväskylä, Jyväskylä, Finland; <sup>‡</sup>Geriatric Department, I Fraticini, National Research Institute, Florence, Italy; and <sup>§</sup>Johns Hopkins Medical Institutions, Baltimore, Maryland.

Address correspondence to Taina Rantanen, PhD, Department of Health Sciences, PO Box 35, Fin-40014, University of Jyväskylä, Finland. E-mail: Taina@maila.jyu.fi

Further adjustments for multiple diseases, physical inactivity, smoking, interleukin-6, C-reactive protein, serum albumin, unintentional weight loss, and depressive symptoms did not materially change the risk estimates. Similar results were observed for all-cause mortality.

**CONCLUSION:** In older disabled women, handgrip strength was a powerful predictor of cause-specific and total mortality. Presence of chronic diseases commonly underlying death or the mechanisms behind decline in muscle strength in chronic disease, such as inflammation, poor nutritional status, disuse, and depression, all of which are independent predictors of mortality, did not explain the association. Handgrip strength, an indicator of overall muscle strength, may predict mortality through mechanisms other than those leading from disease to muscle impairment. Grip strength tests may help identify patients at increased risk of deterioration of health. *J Am Geriatr Soc* 51:636–641, 2003.

**Key words:** handgrip strength; muscle strength; predictor of mortality; older disabled women

Handgrip strength, an easy test that correlates with elbow flexion strength ( $r = 0.672$ ), knee extension strength ( $r = 0.514$ ), and trunk extension strength ( $r = 0.541$ ) and thus gives an approximation of total body muscle strength,<sup>1</sup> has been found to be a robust predictor of mortality and disability.<sup>2,3</sup> The association between grip strength and mortality has been observed in multiple populations ranging from hospitalized female geriatric patients to healthy middle-aged men followed for 30 years,<sup>3–6</sup> but neither the association between strength and cause-specific mortality nor the potential mechanisms explaining the association between muscle strength and mortality have been examined.

Chronic conditions, such as coronary heart disease, stroke, chronic obstructive pulmonary disease (COPD), and diabetes mellitus are common underlying causes of death in old age. The presence of these diseases is associated with decreased muscle strength.<sup>7</sup> The suggested pathways from disease to muscle impairment include