MEASURING SENESCENCE THROUGH HANDGRIP STRENGTH

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J. J. E. Koopman, D. van Bodegom, D. van Heemst, R. G. J. Westendorp.
Handgrip strength, ageing and mortality in rural Africa.
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Background • Muscle strength measured as handgrip strength declines with increasing age and predicts mortality. While handgrip strength is determined by lifestyle through nutrition and physical activity, it has almost exclusively been studied in western populations with a sedentary lifestyle. This study aims to investigate the age pattern of handgrip strength and its relation with mortality in a population characterised by a predominance of malnutrition and manual labour.

Methods • From a traditional African rural population in Ghana, 923 community-dwelling individuals aged 50 years and older were included. Demographic characteristics were registered. At baseline, height, body mass index (BMI), and handgrip strength were measured and compared with those in a western reference population. Survival of the participants was documented during a period of up to two years.

Results • Handgrip strength was dependent on age, sex, height, and BMI. Compared with the western reference population, handgrip strength was lower due to a lower height and BMI, but declined with age similarly. Risk of mortality was lower in participants having higher handgrip strength, with a hazard ratio of 0.94 per kg increase (p = 0.002). After adjustment for age, sex, tribe, socioeconomic status, drinking water source, height, and BMI, only handgrip strength remained predictive of mortality.

Conclusion • In a traditional rural African population characterised by malnutrition and manual labour, handgrip strength declines with age and independently predicts mortality similarly to western populations. Handgrip strength can be used as a universal marker of biological age.

Muscle strength measured as handgrip strength is widely used as a simple and robust marker of biological age. Handgrip strength declines with increasing age in different ethnicities, especially after the age of 50 years.[1-7] At both middle and high ages, low handgrip strength is associated with increased risks of future disability;[8-14] of age-related diseases such as the metabolic syndrome,[15] cardiovascular disease,[16,17] diabetes mellitus,[18] and cognitive impairment,[12,19] of hospitalisation,[13,20] and of treatment-related complications.[13] Moreover, low handgrip strength predicts all-cause mortality[13-15,21-23] as well as mortality due to cardiovascular disease[6,24] and cancer.[15,23,24] Consequently, low handgrip strength is considered as an accurate indicator of frailty.[25]

Apart from age, sex, and ethnicity, handgrip strength is dependent on height, body mass index (BMI), nutritional status, and physical exercise.[11,26-29] While these determinants are closely related to lifestyle, research on handgrip strength has almost exclusively been conducted in western societies where an affluent and sedentary lifestyle is omnipresent.[3,30,31] In societies characterised by a predominance of malnutrition and manual labour, handgrip strength may be a reflection of dietary composition and muscle training rather than senescence. In addition, the association between age, handgrip strength, and mortality may be mediated by age-related diseases and be attenuated when these are uncommon.[27,32]

This study investigates the age pattern of handgrip strength and its relation with mortality in a traditional rural African population where a sedentary lifestyle is absent and age-related diseases are uncommon.[32-34] We show the age pattern of handgrip strength and it with that in a western reference population, we assess the individual characteristics that determine handgrip strength, and we assess whether handgrip strength predicts mortality in this population.

Methods

Research area and participants

This study was conducted in the Garu-Tempane District in the Upper East Region in Ghana. The area is rural, remote, and one of the least developed in the country. The vast majority of the inhabitants are involved in non-commercial agriculture performed by manual labour without proper means of transportation or mechanised farming. Hospital care is absent. Infectious diseases are highly endemic and constitute the main causes of death, although the prevalence of human immunodeficiency virus (HIV) is low (< 4%) compared with other African regions.[35]

Since 2002, we have kept a demographic registry of the population within a research area of 375 km^2 comprising 32 villages. During yearly visits, we registered the name, age, sex, tribe, and location of living of each inhabitant. In 2007, we determined the property value of each household. From this value, an index of the socioeconomic status with a standard normal distribution was calculated according to the Demographic and Health Survey method.[36] In addition, we registered the main drinking water source of each household. Water from boreholes was classified as safe and water from open wells and rivers as unsafe, based on their pathogen contents.[37] Annual migration relative to the study population's size was 2% into and 1% out of the research area. An elaborate description of this study population has been given elsewhere.[32,34,36,37]

Ethical approval was given by the Ethical Review Committee of Ghana Health Services, the Committee Medical Ethics of Leiden University Medical Center, and the local chiefs and elders. Because of illiteracy, informed consent was obtained orally from the participants after explanation of the purpose and conduction of this research project. Participation was only proceeded after verbal consent in the participant's own language.

Measurements

In 2009 and 2010, we measured handgrip strength among 923 inhabitants aged 50 and older, who were recruited in villages visited consecutively. To ensure maximal participation, we set up a mobile field work station in the villages and, if necessary, brought less mobile participants by car. Reasons of exclusion included death of the individual since the last registration (n = 48), refusal of participation (n = 35), absence from the research area during our visits because of migration or travelling (n = 30), and other reasons (n = 46).

Handgrip strength in kilograms was measured using a calibrated Jamar hand dynamometer (Sammons Preston, Bolingbrook, IL, USA), while the participant was standing in an upright position with the arms unsupported parallel to the body. The width of the dynamometer's handle was adjusted to each participant's hand size. Participants were instructed to exert maximal force with each hand once. The handgrip strength of the hand with the highest measurement was registered. Body height and weight were measured with a calibrated length scale and weighing scale. BMI was calculated as body weight in kilograms divided by squared body height in metres.

After the measurements in 2009 and 2010, follow-up data on 915 individuals (99.1%) were available in our demographic registry. Follow-up lasted until death, migration out of the research area, loss to follow-up or our last visit to the research area in 2011.

Reference population

To compare the Ghanaian study population with a western population, we retrieved data from the Leiden Longevity Study. This study included offspring of long-lived native Dutch siblings and the partners of the offspring without selection criteria on health or demographic characteristics. The design of the study has been previously described in more detail.[38] We used data on age, sex, height, BMI and handgrip strength measured in 316 offspring and 311 partners aged 50 to 80 years. Handgrip strength did not differ between offspring and partners. The measurements were performed with the same hand dynamometer and in the same position as described for the Ghanaian study population.[39]

Analyses

Differences between both populations in mean values of height, BMI, and handgrip strength and in the decline in handgrip strength per year of age were determined by linear regression with age as an independent variable and were restricted to participants aged 50 to 80 years. Determinants of handgrip strength in the Ghanaian study population were assessed by linear regression including all participants aged 50 to 97 years. Handgrip strength in the Ghanaian study population was standardised according to the age-group- and sex-specific mean height and BMI in the Dutch reference population, using the regression coefficients obtained for these determinants in the Ghanaian study population. To investigate whether handgrip strength predicted mortality, we constructed Kaplan-Meier survival curves with left truncation to account for different ages at baseline. Survival curves were separated between individuals classified as having low or high handgrip strength according to the age-group- and sex-specific medians. Hazard ratios were determined by Cox regression with follow-up starting at the time of the measurements of handgrip strength.

Results

Table 8.1 shows the characteristics of the Ghanaian study population at the moment of handgrip strength measurement in 2009 or 2010. For comparison, we used data from a Dutch reference population including 316 men and 311 women aged 50 to 80 years. As described previously for this population,[39] mean height (with standard deviation) was 177.9 (7.7) cm in men and 165.7 (5.9) cm in women; mean BMI was 27.1 (4.1) kg/m^2 in men and 26.4 (4.6) kg/m^2 in women and mean handgrip strength was 46.9 (8.1) kg in men and 29.3 (5.5) kg in women. These values of height and BMI were higher than those in the Ghanaian study population adjusted for age (both $p < 0.001$).

Figure 8.1A shows that mean handgrip strength was lower in the Ghanaian study population compared with the Dutch reference population. Overall, the difference (with 95% confidence interval) was 14.7 (13.6 to 15.8) kg in men and 5.7 (4.9 to 6.4) kg in women (both $p < 0.001$). In the Ghanaian study population, handgrip strength declined with 0.4 (0.3 to 0.5) kg per year of age in men and with 0.3 (0.2 to 0.4) kg per year of age in women (both $p < 0.001$). For comparison, handgrip strength in the Dutch reference population declined with a slightly higher rate of 0.6 (0.5 to 0.7) kg per year of age in men up to the age of 80 years ($p = 0.046$), with a similar rate in men up to the age of 75 years ($p = 0.384$) and with a similar rate in women ($p = 0.687$).

Determinants of handgrip strength in the Ghanaian study population are described in Table 8.2. In a multivariate analysis of

Table 8.1 • General characteristics of the Ghanaian study population

	Men	Women
Number of individuals	480	443
Age, median (iqr) years	67 (58–76)	61 (56–70)
Tribe, %		
Bimoba	69.5	68.6
Kusasi	22.5	25.5
other	8.1	5.9
Household property value, median (iqr) US$	1008 (500–1700)	1196 (583–2108)
Access to safe drinking water, %	86.7	88.5
Weight, kg	50.6 (7.9)	45.5 (7.6)
Height, cm	167.5 (6.8)	157.9 (6.8)
BMI, kg/m^2	18.0 (2.3)	18.2 (2.6)
Handgrip strength, kg	31.3 (8.7)	23.6 (5.9)

Data are presented as means with standard deviations unless specified otherwise. Iqr: interquartile range. BMI: body mass index.

demographic and anthropometric characteristics, handgrip strength in both sexes was higher in individuals with a higher age, with a higher height and with a higher BMI. When this analysis was not stratified by sex, handgrip strength was 6.0 (5.0 to 7.0) kg higher in men ($p < 0.001$).

Figure 8.1B shows that the differences in handgrip strength between the Ghanaian study population and the Dutch reference population were attenuated when handgrip strength in the Ghanaian study population was standardised according to the age-group- and sex-specific mean height and BMI of the Dutch reference population. Hereby accounting for the differences in height and BMI between both populations, handgrip strength was similar in men ($p = 0.350$) and 1.7 (0.9 to 2.4) kg higher in Ghanaian women ($p < 0.001$). Standardised handgrip strength declined with age with similar rates in men ($p = 0.067$) and women ($p = 0.233$) in both populations.

Figure 8.2 shows how mortality is predicted by handgrip strength in the Ghanaian study population. Data on follow-up were available for 476 men and 439 women. From the baseline measurements in 2009 and 2010 through the end of follow-up in 2011, we recorded 1492 person-years and 46 deaths. Mean individual follow-up was 20 (6) months. Individuals were classified as having low or high handgrip strength according to the age-group- and sex-specific medians. Risk of mortality was lower in individuals with high handgrip strength, with a hazard ratio of 0.45 adjusted for age and sex ($p = 0.010$).

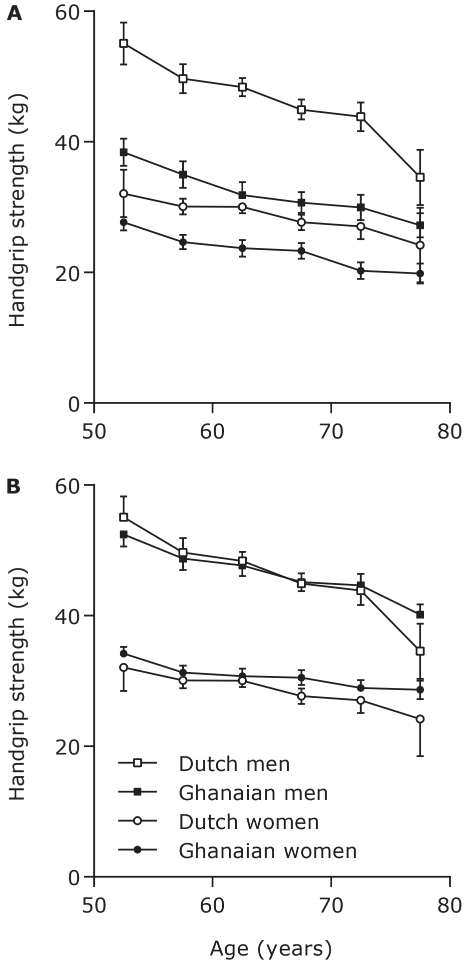

Figure 8.1 • Handgrip strength per sex and per age group in the Ghanaian study population compared with the Dutch reference population. A comparison of mean handgrip strength with 95% confidence intervals per 5-year age category and per sex as observed in the Ghanaian study population and the Dutch reference population (A).[39] Idem after standardisation of the individual handgrip strength measurements in the Ghanaian study population according to the age-group- and sex-specific height and BMI of the Dutch reference population (B).[39]

Table 8.2 • Determinants of handgrip strength in the Ghanaian study population

	Men	Women
	Difference in handgrip strength (95% CI), kg	**Difference in handgrip strength (95% CI), kg**
Age, per year	-0.3 (-0.3 to -0.2) **	-0.2 (-0.2 to -0.1) **
Tribe, Bimoba vs other	+1.3 (-0.1 to +2.6)	+0.1 (-0.9 to +1.1)
Socioeconomic status, per SD	+0.1 (-0.4 to +0.6)	-0.1 (-0.4 to +0.3)
Safe drinking water, vs unsafe	+1.1 (-0.8 to +2.9)	+1.1 (-0.3 to +2.5)
Height, per cm	+0.3 (+0.2 to +0.4) **	+0.3 (+0.2 to +0.3) **
BMI, per kg/m^2	+1.3 (+1.0 to +1.6) **	+0.6 (+0.4 to +0.8) **

Data are presented as kilograms difference in handgrip strength per unit increase for continuous variables or between categories for categorical variables. Differences are shown with 95% confidence intervals (95%CI) and are adjusted for all other variables. SD: standard deviation. ** $p < 0.001$.

Determinants of mortality in the Ghanaian study population are described in Table 8.3. While handgrip strength, age, and BMI determined mortality in the univariate analysis, only handgrip strength determined mortality in the multivariate analysis with a hazard ratio of 0.94 per kg increase (p = 0.016). The association between handgrip strength and mortality in the univariate analysis remained unchanged after the adjustments in the multivariate analysis. In the multivariate analysis, the association of handgrip strength with mortality was not different between

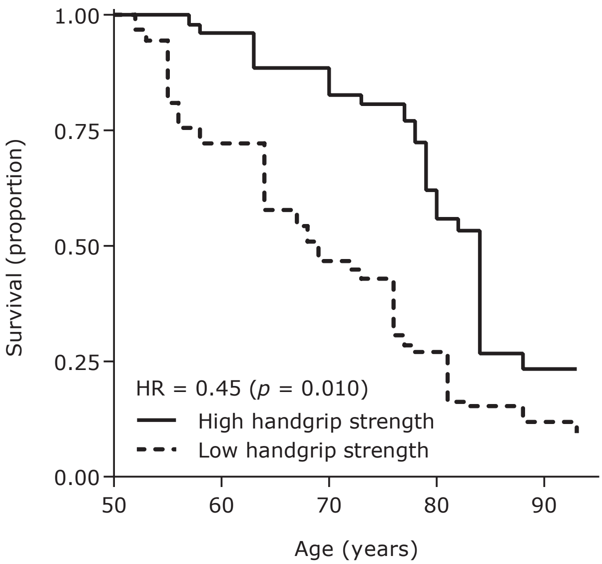

Figure 8.2 • Handgrip strength as a predictor of mortality in the Ghanaian study population. Age-specific survival is dependent on handgrip strength in the Ghanaian study population. Handgrip strength is classified as low or high according to the age-group- and sex-specific medians. The hazard ratio (HR) is given for individuals with high handgrip strength relative to those with low handgrip strength, adjusted for age and sex.

Table 8.3 • Determinants of mortality in the Ghanaian study population

	Univariate	Multivariate
	Difference in handgrip strength (95%CI), kg	**Difference in handgrip strength (95%CI), kg**
Handgrip strength, per kg	0.94 (0.90 to 0.98) *	0.94 (0.89 to 0.99) *
Age, per year	1.05 (1.02 to 1.08) *	1.02 (0.99 to 1.06)
Sex, men vs women	1.44 (0.79 to 2.62)	1.71 (0.76 to 3.84)
Tribe, Bimoba vs other	1.61 (0.80 to 3.25)	1.62 (0.79 to 3.31)
Socioeconomic status, per SD	0.81 (0.63 to 1.06)	0.88 (0.68 to 1.14)
Safe drinking water, vs unsafe	0.92 (0.39 to 2.18)	1.09 (0.46 to 2.57)
Height, per cm	0.99 (0.95 to 1.02)	1.00 (0.95 to 1.05)
BMI, per kg/m^2	0.81 (0.72 to 0.92) *	0.90 (0.79 to 1.03)

Data are presented as hazard ratio per unit increase for continuous variables or comparing categories for categorical variables. Differences are shown with 95% confidence intervals (95%CI) and are adjusted in the multivariate analysis for all other variables. SD: standard deviation. * $p < 0.05$.

individuals below or above the age of 65 (p = 0.920), between men and women (p = 0.380), between individuals with a low or high BMI (p = 0.188), or between individuals with a low or high socioeconomic status (p = 0.890).

Additional adjustment for family relations by clustering on the household level did not materially change the results.

Discussion

This study aims to study the age pattern of handgrip strength and its relation with mortality in a traditional rural African population with a non-western lifestyle. Handgrip strength was lower compared with a western reference population due to a lower height and BMI, but it declined with age with a similar rate. Lower levels of handgrip strength predicted mortality independent of its other determinants related to nutritional and socioeconomic status. Its predictive value was comparable with that known for western populations.[6,13,21,24]

The Ghanaian study population contrasts sharply with western populations, as a sedentary lifestyle is absent and age-related diseases are uncommon.[32-34] Because handgrip strength is dependent on nutritional status,[29] this contrast is most relevantly characterised by a low BMI and near absence of obesity (Chapter 9 of this thesis).[32] In line with this, handgrip strength was closely related to BMI and low compared with a Dutch reference population due to a lower BMI. Besides nutrition, handgrip strength is associated with physical activity and socioeconomic status.[26,27,40-42] Unlike western populations, almost all inhabitants in the research area engage in lifelong physical exercise. Manual labour in farming and housekeeping is necessary for subsistence up to the highest ages. Meanwhile, mechanical means of farming and transportation are lacking. Most inhabitants live in poverty[33] and common property is confined to cattle, fertiliser, and iron roofing.[36] Despite these differences, the variation in handgrip strength in the Ghanaian study population was similar to that in the Dutch reference population and as reported for other western populations.[2,43,44] Moreover, handgrip strength declined with age in these populations similarly.

Few other studies have described handgrip strength in traditional lean populations in Africa. Absolute levels of handgrip strength have been reported to be up to 4 kg lower in rural Kenya, rural Malawi, and among refugees from Rwanda compared with those found at similar ages in the Ghanaian study population.[31,45,46] Handgrip strength in these populations was also, though less, dependent on BMI. The decline in handgrip strength with age was similar to that in the Ghanaian study population. In a population-wide study in South Africa, handgrip strength did not differ between ethnicities or between rural and urban areas, but it was associated with age, anthropometry, and health.[30] None of these studies related handgrip strength with mortality.

As a western reference population, we used the Leiden Longevity Study.[39] Handgrip strength in this study is slightly higher compared with other western populations. This difference can be a result of international variations in the level of handgrip strength, while the declines with age are similar.[4] Alternatively, this difference can be a result of variations in body position during the measurements. Body position influences the estimation of handgrip strength, although it is not likely to influence its decline with age or its relation with mortality.[47-50] When using reference data from a meta-analysis of handgrip strength in twelve western study populations with a body position different from the Leiden Longevity Study, the decline in handgrip strength with age was similar to that in the Ghanaian study population.[7] Suitably, the body position during the measurements in the Ghanaian study population was identical to that in the Leiden Longevity Study.

This study has the following limitations. First, handgrip strength was measured only once, while it might have been valuable to relate individual age-related changes in handgrip strength with anthropometry and mortality. Second, nutritional status was documented by BMI, while it might have been valuable to relate dietary composition and physical activity with the level of handgrip strength as well as its predictive value of mortality, but these determinants were not formally documented. Lastly, because diseases were not registered, the possible effects of diseases on handgrip strength could not be studied and neither could handgrip strength be assessed as a predictor of morbidity.

In conclusion, this study shows that handgrip strength declines with age with a similar rate and functions equally well as an independent predictor of mortality in a traditional rural African population compared with western populations. Across divergent environments, in different populations, and despite variations in lifestyle, handgrip strength can be easily and universally used to identify frail people at increased risk of mortality.

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