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Association between Hand Grip Strength and Mortality: The North West, South Africa Prospective Urban Rural Epidemiology (PURE) Study

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SUMMARY

Hand Grip Strength (HGS) is employed in epidemiological contexts to measure muscle strength because it is inexpensive, easy to perform and interpret. Population-based investigations use protocols that incorporate HGS measurements in health-status evaluations. Our aim was to investigate the association of HGS with all-cause mortality in a South African population. Methods This study was based on the South African leg of the Prospective Urban and Rural Epidemiology (PURE) study, a community-based, prospective cohort study. This work was based on baseline HGS collected in 2005. Deterministic linkage to the mortality was performed using death status in 2018. The Cox regression was applied to investigate all-cause mortality risk in relation to HGS tertiles. A non-linear dose response analysis has been applied to investigate the shape of the relation between HGS and all-cause mortality risk. All the results were validated by numerous sensitivity analyses. Results Our work included 1 251 participants with a median age of 47 years (5th95th quantile range 36, 67) and 59.6% (n 746) of participants were women. During a median follow-up of 13.2 years, 374 deaths from all causes occurred. We observed a hazard ratio of 0.80 (95% CI = 0.61, 1.05) and 0.61(95% CI = 0.44, 0.85) decreased risk of all-cause mortality for the 2nd and 3rd tertiles of dominant hand grip strength compared to the 1st. A similar risk reduction was observed for the non-dominant hand. A linear monotone decreasing relation between HGS and all-cause mortality risk was reported. Conclusions HGS is inversely associated with mortality risk and can be used to predict mortality risk in the South African population.

Keywords: Hand grip; Mortality; Sub Saharan Africa; PURE study.

INTRODUCTION

Hand grip strength (HGS) is the force that the host of muscles in the hand and forearm can produce [1]. Although hand grip strength indicates muscular strength in the hand and forearm, it is a proxy of upper body muscle strength [2]. Measures of HGS are employed in clinical and epidemiological contexts to measure

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muscle strength because the test is inexpensive, easy to perform and easy to interpret [3,4]. Population-based investigations, such as the UK Biobank study, use protocols that incorporate HGS measurements [5].

Data from HGS assessments has been used to assess health-related issues [5–11]. Additionally, HGS gives an overall indication of muscle health and possible susceptibility to muscular disorders [12,13]. Muscle strength and endurance decrease due to aging and development of chronic diseases, resulting in a loss of functional performance [14]. Similarly, sickness and lifestyle factors affect muscular strength because muscle atrophy and lack of optimal nutrition contribute to the deterioration of muscle mass and muscle activation [13,15]. The lack of muscle mass and concomitant decrease in functional ability and performance, connects HGS to many other health-related factors, such as bone mineral density, nutritional status, and sleep related conditions [2]. Thus HGS is related to overall health in individuals and is influenced by lifestyle and daily living activities [4,16–18].

There is abundant information on the association between HGS and mortality on populations in high income countries (HIC). However, such information is scarce in low- and middle-income countries (LMIC). The aim of this study was to investigate the association of HGS with all-cause mortality in a South African population. We first investigated the association between dominant and non-dominant HGS with all-cause mortality at 13 years' follow-up. Afterwards, we investigated the shape of the association between HGS and all-cause mortality risk using a non-linear dose-response analysis. Numerous sensitivity analyses and adjusted models were adopted to exclude potential biases and reversal causation. Finally, we used an internally cross-validated analysis to investigate if HGS from dominant hand is a better all-cause mortality predictor than HGS from non-dominant hand.

METHODS

Study design

This research study is part of The Prospective Urban and Rural Epidemiology (PURE) study which is a community-based multi-country longitudinal prospective cohort research study conducted to investigate the association between risk factors and various health outcomes [3]. Overall, 27 countries are involved in the PURE study. This study is based on data collected on a random stratified sample of 6,000 randomly selected households in the North West Province in South Africa. The urban stratum was defined by established townships near a large city, and the rural stratum was defined by tribally governed communities [19]. Baseline data were collected in 2005, the present study is based on full covariate information about 1,251 participants; 622 rural and 629 urban participants.

Data collection

Trained field workers used a standardized questionnaire to interview at least one household member for personal details and additional characteristics regarding the household [19]. Self-reported demographics, cardiovascular risk factors, comorbidity disorders, education levels, work position, physical activity levels, and dietary habits were collected through questionnaire-based interviews. A customized questionnaire was used to obtain data on prescribed medicines, alcohol, and tobacco use.

The Baecke physical activity questionnaire [20] is a short questionnaire for the measurement of habitual physical activity in epidemiological surveys. The questionnaire includes a total of 16 questions classified into three domains: work, sports, and non-sports leisure activity. Each domain has several questions scored on a five-point Likert scale, ranging from never to always or very often [20] . It defines three levels of occupational physical activity, namely low level (clerical work, driving, shop keeping, teaching, studying, housework, medical practice and most other occupations with a university education), middle level (factory work, plumbing, carpentry, farming) and high level (dock work, construction work, sport). Similarly, sports are categorized into three levels: low level (billiards, sailing, golf), middle level (badminton, cycling, dancing, tennis) and high level (boxing, rugby, football, rowing). A sport participation score is calculated from the intensity factor, the number of times per week participating in that type of sport and the proportion of the year in which the sport is played. Indices of physical activity for three dimensions, namely occupational physical activity, sport during leisure-time and physical activity during leisure time, excluding sport, can be established using the Baecke questionnaire (BQ). Test-retest reliability of the work index, sport index and leisure-time index varies between 0.74 and 0.88. The questionnaire can be used for the various socio-economic classes in the general population. The questionnaire has been used in the assessment of physical activity of study participants between the ages of 20 and 70 years and significant correlation coefficients ranging from 0.76 to 0.93 were found in reliability testing [20].

The Omron HEM-757 equipment (Omron Healthcare, Kyoto, Japan) was used to measure blood pressure with subjects in the supine position for at least five minutes. Hypertension is a systolic or diastolic blood pressure equal to or greater than 140mmHg systolic or 90mmHg diastolic blood pressure, as per the 2018 ESC/ESH guidelines [21]. Height was measured with a stadiometer and weight with a digital scale and used to calculate body mass index (BMI) in kg/m^2. HGS was measured by trained exercise professionals with a Jamar dynamometer, using a standardized protocol [3]. Three measurements to the nearest kilogram were recorded from the participant's dominant and non-dominant hand, the highest value was considered for the analysis.

Mortality data, as recorded on the participants' death certificates provided by Statistics South Africa dated 2018, was the outcome considered. The study adhered to the revised Helsinki Declaration and was approved by the North-West University Health Research Ethics Committee for Humans with ethics number 04M10 and NWU-00016-10-A1. All involved participants signed informed consent forms for data processing and handling. Participants were free to withdraw from the study at any time.

Statistical methods

Data description was performed by median and 5th to 95th percentile range for continuous variables, counts and percentages were used for categories. The Cox proportional hazards model was used to estimate the hazards of all-cause mortality by tertiles of dominant and non-dominant HGS and by one standard deviation increase. To this aim, the Cox proportional hazard model had sex, 10-years age categories and locality (rural or urban) as strata factors. The hazard ratios (HRs) for one standard deviation increase were performed after transforming the HGS variable with Blom's transformation, resulting in a normal standardized variable [22]. Moreover, all analyses were adjusted for medication use, socio-economic status (cross categories of employment and education above grade 8th), hypertension or use of anti-hypertensive medication, former or current tobacco use, former or current alcohol use, diabetes, any prevalent diseases such as HIV or TB, cardiovascular or respiratory diseases or cancer, physical activity index according to the Baecke questionnaire, and BMI. Supplementary analyses were performed excluding participants with positive baseline HIV or tuberculosis, cardiovascular diseases, and cancer. Sensitivity analyses were conducted excluding participants who experienced death in the first year of observation. A non-linear dose response analysis was performed to investigate the shape of the relation between HGS and mortality risk. To this aim, we used a restricted cubic spline with four knots placed at the 5th, 35th, 65th and 95th percentiles.

Finally, we used a Least Absolute Shrinkage and Selection Operator (LASSO) analysis to determine which of the dominant or non-dominant hand was the best predictor of all-cause mortality. Briefly, we divided our data frame into two equal subsets, a training and a test data frame. A first model was performed on the training data frame, afterwards the model was validated by a LASSO approach on the test data frame. Variable selection was performed by means of the optimal Lambda parameter of the LASSO model [23–25]. The Cox proportional hazard assumption of the risk proportionality was assessed by a model having a multiplicative interaction term between HGS and the log-transformed time [26]. All statistical tests were two-tailed with a type-I error rate of 5% (α = 0.05). The HRs were estimated using the PHREG procedure of the SAS software vers 9.4. The non-linear dose-response analysis was performed using the mkspline function of the STATA software vers. 14. The LASSO analysis was performed by a customized approach based on the glmnet package of the R software.

RESULTS

This study included 1,251 participants with a median age of 47 years (5th to 95th range = 36; 67), 59.6% (n = 746) of participants were women and 50.3% (n = 629) were from the urban area. During a median follow-up of 13.2 years, 374 deaths from all causes occurred. Regarding behavioural risk factors, 59.6% of the participants were tobacco users, 48.2% were alcohol consumers and the median Baecke physical activity index was 7.5 (5th to 95th range = 4.6; 10.2). Regarding the metabolic risk factors, 47.5% had hypertension, 6.2% had type two diabetes, the median BMI was 22.3kg/m^2 (5th to 95th range = 16.2; 38.5), and the prevalence of obesity (BMI > 30 kg/m^2) was 21.1%. When looking at baseline prevalent diseases, 4.5% of participants had infectious diseases (HIV and TB), 6.2% participants had cardiovascular diseases (CVD) and respiratory infections (RI), 0.3% had cancer, and 13.3% were using medication. Among all participants, 69.2% were educated above grade 8 and employed. For HGS, the median measurement for the dominant hand was 32.0 N (5th to 95th range = 20.0; 52.0) and 30.0 N (5th to 95th range = 18,0; 50.0) for the non-dominant hand. There were 374 deaths at the end of the follow up. The median age at baseline of those that died was 51.0 (5th to 95th range = 36.0; 72.0). Of the deceased participants, 46.5% were women and 59.9% were from urban areas. The behavioural risk factors for the deceased were: 69.8% were tobacco users and 62% of them were alcohol consumers. Regarding the physical activity index, the median was 6.6 (5th to 95th range = 4.3; 9.8). Regarding the metabolic risk factors, 56.7% of the participants were hypertensive and 7.2% had type 2 diabetes. The median BMI for those that died was 20.7 kg/m^2 (5th to 95th range = 15.6; 36.8). The prevalent diseases for the deceased were 8% for infectious diseases (HIV and TB), 6.2% for CVD and RI, and 0.3% for cancer. In addition, the cause of death was undetermined for about 70% of the cases. Results indicate 14.7% of the deceased were using some type of medication. Among the deceased participants, the majority had a job and education above grade 8 (78.1%). The baseline characteristics of all participants in the study sample are reported in Table 1.

We observed hazard ratio (HR) of 0.80 (95% CI = 0.61; 1.05) and 0.61, (95% CI = 0.44; 0.85) for risk of all-cause mortality for the 2nd and 3rd tertiles of dominant hand grip strength compared to the 1st tertile. Similarly, there was a HR of 0.65

Table 1. Baseline characteristics of the study sample

	All Participants n = 1,251	**Survivors n = 877**	**Deceased n = 374**
Age(years)	47.0 (36.0; 67.0)	46.0 (36.0; 65.0)	51.0 (36.0; 72.0)
Women	746 (59.6)	572 (65.2)	174 (46.5)
Urban	629 (50.3)	405 (46.2)	224 (59.9)
Educated and employed	866 (69.2)	574 (65.5)	292 (78.1)
Educated and unemployed	53 (4.2)	51 (5.8)	2 (0.5)
Uneducated and employed	238 (19.0)	185 (21.1)	53 (14.2)
Uneducated and unemployed	94 (7.5)	67 (7.6)	27 (7.2)
Smokers	746 (59.6)	485 (55.3)	261 (69.8)
Alcohol use	603 (48.2)	368 (42.0)	235 (62.8)
Hypertension	594 (47.5)	382 (43.6)	212 (56.7)
Type 2 Diabetes	78 (6.2)	51 (5.8)	27 (7.2)
Infectious diseases	56 (4.5)	26 (3.0)	30 (8.0)
CVD and RI	78 (6.2)	55 (6.3)	23 (6.2)
Cancer	4 (0.3)	3 (0.3)	1 (0.3)
Use of medication	166 (13.3)	111 (12.7)	55 (14.7)
Body mass index (kg/m^2)	22.3 (16.2; 38.5)	23.5 (16.8; 39.0)	20.7 (15.6; 36.8)
Physical Activity Index	7.5 (4.6; 10.2)	7.7 (4.7; 10.3)	6.6 (4.3; 9.8)
DHG (N)	32.0 (20.0; 52.0)	32.0 (20.0; 52.0)	32.0 (18.0; 50.0)
NHG (N)	30.0 (18.0; 50.0)	30.0 (20.0; 50.0)	30.0 (18.0; 50.0)

Notes. *Grade 8th was the threshold chosen for education, Infectious diseases: HIV and Tuberculosis (TB), CVD and RI: Cardiovascular Diseases and Respiratory Infections, DHG: Dominant hand grip, NHG: Non-dominant hand grip, N: Newtons (unit of measure)*

(95% CI = 0.49; 0.86) and 0.64, (95% CI = 0.46; 0.89) for all-cause mortality risk for the same analysis applied for the non-dominant hand. Moreover, we observed a HR of 0.75 (95% CI = 0.66; 0.86) for the dominant hand and 0.76 (0.66; 0.87) for the non-dominant hand for one standard deviation increase of HGS. After the exclusion of participants who died within the first year of the study, a HR of 0.82, (95% CI = 0.62; 1.09) and 0.66, (95% CI = 0.47; 0.93) for all-cause mortality risk was observed for the 2nd and 3rd tertile respectively compared to the 1st tertile for the dominant hand grip strength and HR of 0.70, (95% CI = 0.52; 0.94) and HR of 0.69, (95% CI = 0.49; 0.98) all-cause mortality risk for the 2nd and 3rd tertile compared to the 1st tertile, for the non-dominant hand. Additionally, we observed an all-cause mortality risk of 0.81 (95% CI = 0.69; 0.94) for the dominant hand and 0.83 (95% CI = 0.69; 0.98) for the non-dominant hand for one standard deviation increase for HGS.

The above results were confirmed by the sensitivity analysis performed regarding the exclusion of participants with infectious diseases, cardiovascular disease and/or respiratory infections, cancer, and those who were using any medication. When excluding the participants with any baseline infectious diseases, we observed a decreased all-cause mortality risk for the 2nd and 3rd tertile of dominant hand, likewise for the non-dominant hand grip strength, compared to the 1st tertile. Additionally, a HR of 0.75 (0.65; 0.86) for the dominant hand and 0.76 (0.66; 0.87) for the non-dominant hand for one standard deviation increase in HGS was observed after excluding participants with baseline infectious diseases. A decreased risk was also observed for the 2nd and 3rd tertile respectively compared to the 1st tertile for the dominant hand, similarly for the non-dominant hand, after the exclusion of participants with CVD and RI. Furthermore, we observed a HR of 0.74 (95% CI = 0.65; 0.84) for the dominant hand and 0.75 (95% CI = 0.65; 0.86) for the non-dominant hand for one standard deviation increase in HGS after exclusion of participants with baseline CVD or RI. After exclusion of participants with cancer, we observed an all- cause mortality risk reduction for the 2nd and 3rd tertile of dominant hand, correspondingly for the non-dominant hand grip strength with respect to the 1st tertile. In addition, when considering one standard deviation increase in HGS for the exclusion of participants with cancer, we observed a hazard ratio of 0.75 (95% CI = 0.66; 0.86) for the dominant hand and 0.76 (95% CI = 0.67; 0.87) for the non-dominant hand. Furthermore,

we observed an all-cause mortality risk decrease for the 2nd and 3rd tertile respectively compared to the 1st after the exclusion of participants using any medication for the dominant hand as well as the non-dominant hand. Moreover, we observed a hazard ratio of 0.73 (95% CI = 0.63; 0.84) for the dominant hand and 0.75 (95% CI = 0.64; 0.86) for the non-dominant hand after the exclusion of participants using any medication for one standard deviation increase in HGS.

Complete HR values for the sensitivity analysis were given in Table 2. The graph of the non-linear dose-response relation between HGS and all-cause mortality risk appears as a monotone deceasing relation for both dominant and non-dominant hand. According to the Wald test of the spline terms, we observed a significant result for the linear terms while the quadratic and the cubic terms were not (Figure 1).

Table 2. Association between Hand grip strength and mortality for all causes

Total Sample				
Dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	135	4614.3	1 (Ref.)	0.75 (0.66; 0.86)
2nd tertile	118	4754.8	0.80 (0.61; 1.05)	
3rd tertile	121	4686.4	0.61 (0.44; 0.85)	
Non dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	142	4675.6	1 (Ref.)	0.76 (0.66; 0.87)
2nd tertile	98	4837.7	0.65 (0.49; 0.86)	
3rd tertile	134	4542.3	0.64 (0.46; 0.89)	
Exclusion of participants who died in the first year of observation				
Dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	124	3715.63	1 (Ref.)	0.81 (0.69; 0.96)
2nd tertile	109	4017.63	0.82 (0.62; 1.09)	
3rd tertile	116	3853.92	0.66 (0.47; 0.93)	
Non dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	129	3770.13	1 (Ref.)	0.83 (0.69; 0.98)
2nd tertile	93	4172.60	0.70 (0.52; 0.94)	
3rd tertile	127	3644.46	0.69 (0.49; 0.98)	
Exclusion of participants with infectious disease				
Dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	125	4472.3	1 (Ref.)	0.75 (0.65; 0.86)
2nd tertile	111	4569.1	0.81 (0.61; 1.07)	
3rd tertile	108	4510.7	0.58 (0.41; 0.82)	
Non dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	133	4510.8	1 (Ref.)	0.76 (0.66; 0.87)
2nd tertile	92	4721.2	0.65 (0.49; 0.87)	
3rd tertile	119	4320.1	0.62 (0.44; 0.88)	
Exclusion of participants with cardiovascular diseases and/or respiratory diseases				
Dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	126	4286.0	1 (Ref.)	0.74 (0.65; 0.84)
2nd tertile	112	4424.1	0.80 (0.60; 1.06)	
3rd tertile	113	4451.2	0.57 (0.41; 0.80)	
Non dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	134	4357.6	1 (Ref.)	0.75 (0.65; 0.86)
2nd tertile	89	4475.0	0.64 (0.48; 0.85)	
3rd tertile	128	4328.6	0.61 (0.44; 0.86)	

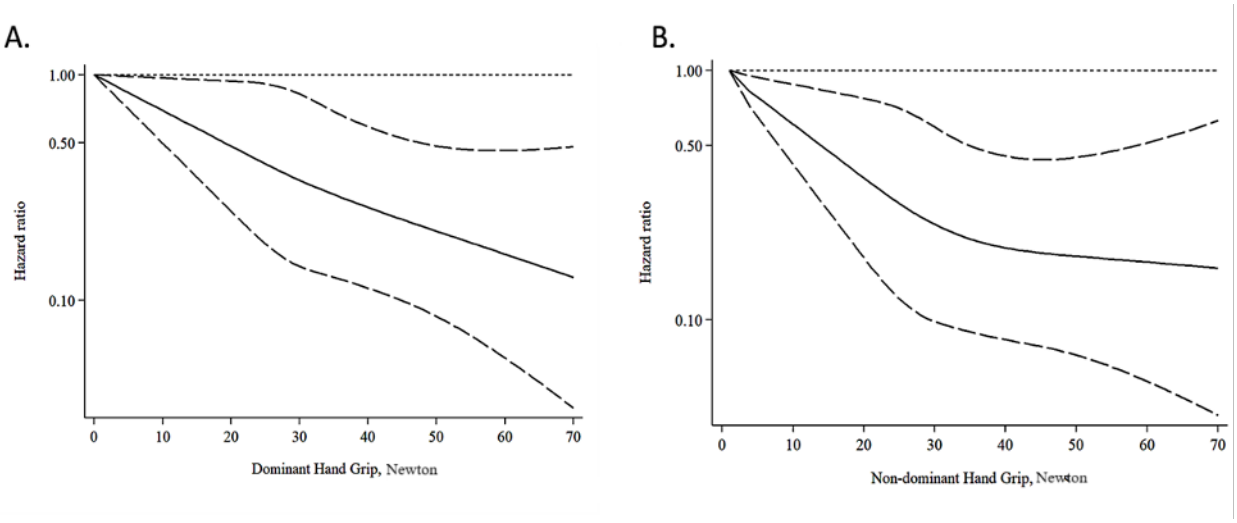
(*continued*)

Table 2. Association between Hand grip strength and mortality for all causes (continued)

Total Sample				
Exclusion of participants with cancer				
Dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	134	4596.4	1 (Ref.)	0.75 (0.66; 0.86)
2nd tertile	118	4728.2	0.80 (0.61; 1.05)	
3rd tertile	121	4686.4	0.61 (0.44; 0.85)	
Non dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	141	4657.6	1 (Ref.)	0.76 (0.67; 0.87)
2nd tertile	98	4811.2	0.66 (0.50; 0.87)	
3rd tertile	134	4542.3	0.64 (0.46; 0.89)	
Exclusion of participants using any medication				
Dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	115	4043.9	1 (Ref.)	0.73 (0.63; 0.84)
2nd tertile	102	4172.9	0.76 (0.56; 1.03)	
3rd tertile	102	4065.9	0.56 (0.39; 0.81)	
Non dominant hand	Cases	Persons-year	HR_1 (95% CI)	HR_2 (95% CI)
1st tertile	121	4119.1	1 (Ref.)	0.75 (0.64; 0.86)
2nd tertile	82	4186.4	0.65 (0.48; 0.89)	
3rd tertile	116	3977.3	0.64 (0.45; 0.92)	

HR_1 = Multivariate adjusted all-cause mortality risk by tertiles, HR_2 Multivariate adjusted for one standard deviation increase

Figure 1. The non-linear dose-response analysis of HGS and all-cause mortality risk. The analysis of dominant and non-dominant HGS are reported on panes A and B, respectively. Units were measured in Newtons (N)



Finally, the LASSO analysis confirmed that dominant hand should be considered as a better predictor of mortality than the non-dominant hand. This result was confirmed after the exclusion of participants died during the first year of observation and after excluding subjects with baseline conditions such as cardiovascular disease and respiratory infections, cancer or using any medication.

DISCUSSION

This is the first long follow-up investigation reporting HGS in relation to mortality in Black South Africans. Firstly, we showed that the relation between HGS and all-cause mortality is robust after adjusting for numerous factors. This demonstrates that HGS was independently associated with all-causes mortality

risk thus confirming its application as a valid proxy of health status in this South African population. Moreover, we showed that HGS serves as an indicator of health status in the general population excluding any reversal causation as our results were consistent after the exclusion of participants who died within the first year of observation.

The validity of our results in the general population were confirmed by numerous sensitivity analyses corroborating the association between HGS and all-cause mortality without the direct influence of other comorbidities. We observed a monotone decreasing risk of all-cause mortality with increasing hand grip strength, for both the dominant and non-dominant hand. Using a cross validated LASSO model, we confirmed that HGS of the dominant hand is a better mortality predictor than the HGS measured in the non-dominant hand.

The above results agree with multiple other studies [3,7,13,27–30]. However, the majority of those studies were conducted on Caucasian populations or having a small percentage of black participants. The originality of the results presented in this study lies in the investigation of a population with a high bone mineral density compared to a Caucasian population. This study further presents the non-linear dose-response analysis for the HGS in the dominant and non-dominant hand in relation to mortality. We confirmed that the HGS from the dominant hand is preferably used as a quantifiable measure of muscle strength in epidemiological studies [2,31,32]. As previously stated, HGS is used to evaluate muscle strength as it reflects the strength of the whole body [14,17,33] which is a proxy of the overall health status of individuals. Therefore, muscle strength, as assessed by HGS, is indicative of muscle health and even of possible changes in physiological functioning [6,8,34,35]. Several studies reported the prospective association between muscle strength and mortality [12,27,36]. On the one hand, low HGS and muscle weakness, which is linked with low physiological function, have been associated with an increased risk of all-cause mortality [8,14,17]. Conversely, higher muscle strength is associated with reduced mortality [37,38]. Higher levels of HGS were associated with reduced risk of all-cause mortality in a study involving approximately 2 million healthy men and women [12]. Moreover, our results also agree with a study based on numerous mortality predictors showing that muscle strength is a reliable predictor of long-term mortality in initially healthy individuals [39]. Our findings are supported by numerous possible biological mechanisms. Increased strength could be an indicator of better early life nutrition as this can influence and affect mid-life muscle strength [2]. Additionally, mid-life strength may be affected by earlier life-style characteristics, such as physical activity [17]. In support of this, previous studies have shown that muscle strength is associated with physical activity and low mortality risk [10,35,40]. Furthermore, poor muscle strength could be an indicator of undetected or undiagnosed diseases in healthy adults [41]. Poor muscle strength in people with chronic conditions and diseases affects muscle protein synthesis [2,42,43]. Further, our dose response analysis indicates that the risk of mortality decreases linearly with increased HGS. This is consistent with results reported in a previous study where it was found that higher HGS was linearly associated with lower risk of all-cause mortality in middle- aged people [38].

The above results confirm numerous studies conducted on caucasian populations. On the other hand, different results may be expected due to the Black population possessing a higher bone mineral content and protein composition [44,45]. As a result of the physiological differences, the Black population is expected to have a higher muscle composition than the Caucasian population and therefore a higher HGS. However, our mean value of HGS for the dominant hand was 32.0 which is quite similar to that of the total PURE study (30.6 N) [3]. Other studies confirmed our results showing that the association between HGS and mortality remains independent after adjusting for different factors [13,28].

Strengths and limitations

Our study is based on robust statistical methodology based on the use of a multivariate adjusted model, thus addressing potential confounders. Additionally, our results are robust because we confirmed our findings by means of numerous sensitivity analyses. Moreover, using a nonlinear dose response we showed the linearity of the relation between HGS and all-cause mortality risk. The mortality in our population was expectantly high, i.e. about 30% of the subjects died after a 13-year follow-up in a population with a mean age of 47 at entry. This adds interest for the specificities of the population. However, our study is not free of limitations. A possible weakness is that our analysis is limited to the investigation of all-cause mortality and over 70% of deaths were due to undetermined causes. However, this does not affect the value of our study because all-cause mortality is an important epidemiological proxy of health. Moreover, considering specific mortality would have reduced the statistical power of our models resulting in many false negative results. However, its application in a South African target population had not been confirmed prior to this study. The accumulation of numerous scientific evidence about HGS and health, the existence of possible underlying mechanisms that explain this relation and finally, but not least, the evident dose-response association observed corroborates our results.

CONCLUSION

The observation that HGS is inversely associated with mortality risk is applicable in a South African

population irrespectively of potential physiological differences with Caucasians. We showed that this association is not affected when considering either the dominant or non-dominant hand. We also showed that HGS, and dominant HGS in particular, is a reliable proxy of general health in a population.

AUTHOR CONTRIBUTIONS

KM performed the statistical analyses and draft the first version of the manuscript, SK HM and MP were responsible for data collection and study design, MCM DS and CL provided technical support to manuscript writing and epidemiological interpretation of the data, CR conceived the work and the statistical analysis and supervised KM for the drafting of the first version of the manuscript. All authors revised and approved the last version of the manuscript.

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COMPETING INTERESTS

Authors have no conflicts of interest to declare

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