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Associations of muscle mass, strength, and quality with all-cause mortality in China: a population-based cohort study

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Abstract

Background It remains unclear about the association of muscle mass, strength, and quality with death in the general Chinese population of diverse economical and geographical backgrounds. The present study aimed to comprehensively examine such associations across different regions in China.

Methods Based on the China Kadoorie Biobank study, the present study included 23,290 participants who were aged 38 to 88 years and had no prevalent cardiovascular diseases or cancer. Muscle mass and grip strength were measured using calibrated instruments. Arm muscle quality was defined as the ratio of grip strength to arm muscle mass. Low muscle mass, grip strength, and arm muscle quality were defined as the sex-specific lowest quintiles of muscle mass index, grip strength, and arm muscle quality, respectively. Cox proportional hazards models yielded hazard ratios (HRs) and 95% confidence intervals (CIs) for risks of all-cause mortality in relation to muscle mass, strength, and quality.

Results During a median follow-up of 3.98 years, 739 participants died. The HR (95% CI) of all-cause mortality risk was 1.28 (1.08–1.51) for low appendicular muscle mass index, 1.38 (1.16–1.62) for low total muscle mass index, 1.68 (1.41–2.00) for low grip strength, and 1.41 (1.20–1.66) for low arm muscle quality in models adjusted for sociodemographic characteristics, lifestyle factors, and medical histories.

Conclusion Low muscle mass, grip strength, and arm muscle quality are all associated with short-term increased risks of mortality, indicating the importance of maintaining normal muscle mass, strength, and quality for general Chinese adults.

Keywords: Muscle; All-cause mortality; Chinese; Prospective; Muscle mass; Muscle strength; Muscle quality

Introduction

The prevalence of sarcopenia in Chinese adults aged ≥65 years was 15.0% between 2007 and 2010[1] and continues to increase due to population ageing. As important indicators of sarcopenia, low muscle mass and low muscle strength may have adverse health effects such as increasing the risk of mortality.

Many cohort studies have been conducted to explore the risk of all-cause mortality in relation to muscle mass-related measures, muscle strength, and muscle quality. Muscle mass-related measures include lean mass (including muscle mass, bone mass, vital organs, extra-cellular fluid, and lipid in cellular membranes),[2] fat-free mass (lean mass devoid of lipid in cellular membranes),[2] muscle mass, and their adjustments (these measures divided by height squared, weight, or body mass index

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[BMI]). Cohorts from Western or Asian countries have reported inconsistent findings on the association of muscle mass-related measures with all-cause mortality.[3-12] Indicators of muscle strength such as grip strength and muscle quality (the ratio of muscle strength to muscle mass) may better predict mortality than muscle mass.[9] A meta-analysis of 28 cohorts (for Asian cohorts: seven from Japan, one from China,[13] and one cohort with a Chinese sub-cohort[14]) reported an inverse association of grip strength with all-cause mortality,[15] while only one cohort has assessed all-cause mortality in relation to muscle quality.[9]

Most previous studies were conducted in Western populations, while evidence from Asian populations, the Chinese population in particular, is very limited.[12,13] Body composition and muscle strength of Chinese adults are different from those of Western populations. Chinese adults have lower lean mass index, smaller decrease in 50th percentiles of lean mass index (lean mass divided by height squared) in older adults, lower total fat mass, greater central obesity, and lower grip strength.[16,17] Two small cohorts conducted in Taiwan of China reported a higher risk of mortality related to low muscle mass index (muscle mass divided by height squared) and low grip strength in older adults.[12,13] However, it remains unknown what the association is between muscle mass, strength, quality, and the risk of death in the general Chinese population of diverse economical and geographical backgrounds. In addition, assessing multiple muscle metrics in the same cohort is needed, since such analyses can help to identify metrics that are more of clinical and public health relevance.

The present study aimed to comprehensively examine the association of muscle mass, grip strength, and muscle quality with all-cause mortality based on the China Kadoorie Biobank study (CKB), which enrolled adults from 10 economically and geographically different regions across China.

Methods

Ethics approval

The CKB study was approved by the ethics committees of the China National Center for Disease Control and Prevention (Approval No. 005/2004) and the Oxford University (Approval No. 025-04). All participants provided their written informed consent.

Study population

The CKB study enrolled over half a million adults aged 30 to 79 years at baseline between 2004 and 2008 from 10 regions (five rural areas and five urban areas) in China. Thereafter, two resurveys were conducted among surviving participants, out of whom 5% were randomly selected. The present analysis was based on the second resurvey, at which data on muscle mass and strength were available. The second resurvey was conducted among 25,069 adults aged 38 to 88 years between 2013 and 2014.

We excluded participants with a previous diagnosis of cardiovascular diseases ($n = 1063$) or cancer ($n = 293$), or with missing data on muscle mass ($n = 355$), muscle strength ($n = 218$), or dietary frequency ($n = 28$). A total of 23,290 participants were included in the primary analysis.

Exposure assessment

Participants were measured for fat mass and fat-free mass in light clothes and with bare feet by Tanita BC418MA (Tanita Inc, Tokyo, Janpan), using the method of bioelectrical impedance analysis (BIA). And then muscle mass was predicted. The accuracy of BIA has been validated.[18-20] Muscle mass (kg) was divided by the square of height (m^2) to account for body size, and thus various muscle mass indices were derived, namely appendicular muscle mass index, total muscle mass index, arm muscle mass index, leg muscle mass index, and trunk muscle mass index [Supplementary Table 1, http://links.lww.com/CM9/B77]. A hydraulic hand dynamometer Jamar J00105 (Sammons Preston, Bolingbrook, IL, USA) was used to measure grip strength of both hands, the mean value of which was used in the present analysis. Arm muscle quality [Supplementary Table 1, http://links.lww.com/CM9/B77] was calculated as the ratio of grip strength (kg) to arm muscle mass (kg).

Muscle mass indices, grip strength, and arm muscle quality were grouped into sex-specific quintiles. Low appendicular muscle mass index was defined as the lowest quintile of appendicular muscle mass index (<7.26 kg/m^2 for men and <6.23 kg/m^2 for women), according to the Asian Working Group for Sarcopenia (AWGS),[21] and the rest of the participants were defined as having "normal" appendicular muscle mass index. Similarly, low total muscle mass index (<16.79 kg/m^2 for men and <14.70 kg/m^2 for women), low muscle mass indices by body parts, low grip strength (<25.5 kg for men and <15.5 kg for women), and low arm muscle quality (10.23 kg/kg for men and <8.78 kg/kg for women) were defined as the lowest quintiles of the corresponding variables.

Assessment of covariates

Questionnaire information on covariates collected at the second resurvey included age, sex, marital status, occupation, household income, smoking status, alcohol intake, type and duration of physical activities, consumption frequency and amount of 20 food items, and self-reported diagnosis of diabetes, chronic bronchitis, and pulmonary emphysema. Additionally, trained health workers measured participants' body fat percentage, body weight, standing height, waist circumference, blood pressure, blood glucose, and lung function using standard instruments. Factor analysis derived two dietary patterns in the CKB population, namely the balanced dietary pattern, and the rice and meat dietary pattern.[22] Prevalent hypertension was defined as systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg, or taking anti-hypertensive medications. Prevalent diabetes was defined as a self-reported diagnosis of diabetes, a random glucose level $\geq$11.1 mmol/L, or a fasting glucose level ≥7.0 mmol/L. Prevalent chronic obstructive pulmonary disease (COPD) was defined as a self-reported diagnosis of chronic bronchitis or pulmonary emphysema, or the ratio of forced expiratory volume in 1 s over forced vital capacity <0.7.

Outcome assessment

Information on death was mostly obtained from Disease Surveillance Points in China, with supplementary information from the health insurance system, and active follow-up.

Statistical analysis

Participants with low or normal total muscle mass index, grip strength, and arm muscle quality were compared for characteristics at the second resurvey via linear (continuous variables) or logistic regressions (categorical variables) adjusted for age, sex, and study site, when appropriate.

The follow-up duration was calculated from the date of second resurvey to the date of death, loss to follow-up, or December 31, 2017, whichever came first. Cox proportional hazards models yielded hazard ratios (HRs) and 95% confidence intervals (CIs) for relative risks of all-cause mortality related to low muscle mass indices, grip strength, and arm muscle quality. We also calculated relative risks of all-cause mortality by quintiles of muscle mass indices, grip strength, and arm muscle quality.

Age was the time scale of Cox models, and models were stratified by age at study date (in a five-year interval: 38 to 42 years, 43 to 47 years, 48 to 52 years, 53 to 57 years, 58 to 62 years, 63 to 67 years, 68 to 72 years, 73 to 77 years, 78 to 82 years, and 83 to 88 years) and region. Covariates included sex, educational attainment, marital status, occupation, household income, smoking status, alcohol consumption, total levels of physical activities, scores of dietary patterns, prevalent hypertension, prevalent diabetes, and prevalent COPD (model 3). We adjusted for age, sex, socioeconomic status, lifestyle factors (including diet), and chronic diseases since they may affect muscle mass, strength, and quality.[23-26]

To explore the potential non-linear muscle–mortality relationship, Cox models based on model 3 were fitted by coding muscle mass indices, grip strength, or arm muscle quality as restricted cubic spine functions, with four knots set at the 5th, 35th, 65th, and 95th percentages of corresponding variables. Likelihood ratio tests comparing models with restricted cubic splines and models with only linear terms were used to test for non-linearity.

We conducted several sensitivity analyses based on model 3 separately by additionally including participants with a self-reported diagnosis of cardiovascular diseases or cancer in the analysis, by excluding participants who died within the first year of follow-up to minimize reverse causation, by excluding participants whose body weight changed >2.5 kg during the past 1 year, or by excluding participants who ever smoked.

Sub-group analyses were done according to participants' characteristics such as levels of physical activities at the second resurvey and residential areas. To test for potential multiplicative interactions, we performed likelihood ratio tests by comparing models with and without the interaction term between each of the exposures and each of the sub-grouping factors.

Statistical analyses were conducted via STATA 15.0 (StataCorp, College Station, TX, USA). All P values were two-sided, and $P < 0.007$ (0.05/7, Bonferroni correction for multiple exposures) was regarded as providing evidence of an association. We interpreted $P < 0.0009$ (Bonferroni correction) as providing some evidence of multiplicative interaction.

Results

Among the 23,290 participants included in the present study, the mean age was 59.1 years, 8803 (37.8%) were men, and 9852 (42.3%) were urban residents. Compared with adults with normal total muscle mass index, those with low total muscle mass index were older, had a lower level of household income, were more likely to smoke, to have lower BMI, body fat percentage, and scores of rice and meat dietary pattern, and to have prevalent COPD, and were less likely to have prevalent hypertension and prevalent diabetes [Table 1]. Compared with adults with normal grip strength or arm muscle quality, those with low grip strength or arm muscle quality were older, had lower educational attainment, lower household income, lower physical activities, and lower scores of the balanced dietary pattern, and were more likely to be unemployed [Table 1].

As of December 31, 2017, the median follow-up duration was 3.98 years, and 739 participants died during the follow-up.

Muscle mass and all-cause mortality

The relative risk of all-cause mortality was 1.28 (95% CI: 1.08–1.51) for low appendicular muscle mass index compared with normal appendicular muscle mass index ($Z = 2.88$, $P = 0.004$) and 1.38 (95% CI: 1.16–1.62) for low total muscle mass index in comparison with normal total muscle mass index ($Z = 3.75$, $P < 0.001$) in models adjusted for sociodemographic characteristics, lifestyle factors, and medical histories (model 3, Table 2). Appendicular muscle mass index and total muscle mass index were further grouped into quintiles [Table 2]. Adults in the lowest quintile of appendicular muscle mass index (HR: 1.30, 95% CI: 1.03–1.64) or total muscle mass index (HR: 1.38, 95% CI: 1.11–1.73) were at a higher risk of all-cause mortality compared to those in the third quintile in model 3.

The present study also assessed risks of all-cause mortality in relation to low muscle mass indices by body parts [Table 3]. The HR (95% CI) was 1.54 (1.30–1.82) for low *vs*. normal arm muscle mass index ($Z = 5.05$, $P < 0.001$) and 1.57 (1.31–1.88) for low *vs*. normal trunk muscle mass index ($Z = 4.93$, $P < 0.001$) in model 3. No

Table 1: Characteristics of participants by total muscle mass index, grip strength, and arm muscle quality.

Characteristics	Total muscle mass index				Grip strength				Arm muscle quality			
	Normal*	Low*	Statistic†	*P* value	Normal*	Low*	Statistic†	*P* value	Normal*	Low*	Statistic†	*P* value
N of participants	18,621	4669			18,680	4610			18,639	4651		
Age (years)	58.2	62.5	695.36	<0.001	57.0	67.4	4731.44	<0.001	57.6	65.1	2257.30	<0.001
Male (%)	37.8	37.7	0.13	0.894	37.8	37.8	−0.01	0.990	37.8	37.8	−0.03	0.977
Rural areas (%)	59.1	52.2	8.49	<0.001	57.7	57.9	−0.28	0.777	57.6	58.3	−0.82	0.410
Married (%)	87.8	86.6	−2.35	0.019	87.9	86.6	−2.54	0.011	87.7	86.9	−1.71	0.087
Middle school or above (%)	47.4	48.3	1.30	0.195	48.5	42.9	−7.30	<0.001	48.3	44.3	−5.40	<0.001
Household income <20,000 Chinese yuan/year (%)	20.6	22.6	3.26	0.001	20.0	24.2	6.40	<0.001	20.5	22.5	3.24	0.001
Unemployed (%)	28.6	29.7	1.67	0.095	27.4	34.2	9.37	<0.001	27.9	32.8	7.07	<0.001
Current daily smoking (%)	22.4	26.5	7.50	<0.001	23.5	22.2	−2.12	0.034	23.6	21.9	−2.96	0.003
Current daily alcohol intake (%)	8.5	9.0	1.04	0.297	8.9	7.6	−2.67	0.008	8.8	7.7	−2.54	0.011
Physical activities (MET-h/day)	18.8	17.6	31.67	<0.001	18.8	17.6	255.96	<0.001	18.7	17.9	13.22	<0.001
BMI (kg/m^2)	25.1	20.4	9533.92	<0.001	24.3	23.6	99.74	<0.001	23.8	25.5	792.11	<0.001
Body fat percentage (%)	27.3	22.9	1930.58	<0.001	26.5	25.8	1034.98	<0.001	26.1	27.6	198.56	<0.001
Highest quintile of balanced dietary pattern (%)	20.2	19.2	−1.51	0.130	20.8	16.2	−6.63	<0.001	20.3	18.5	−2.93	0.003
Highest quintile of rice and meat dietary pattern (%)	23.7	19.7	−6.42	<0.001	23.3	20.4	−3.77	<0.001	22.9	22.4	−0.65	0.518
Prevalent hypertension (%)	52.2	37.0	−19.32	<0.001	49.2	48.6	−0.68	0.496	47.8	54.7	8.31	<0.001
Prevalent diabetes (%)	10.2	6.0	−8.77	<0.001	8.7	11.1	4.64	<0.001	8.2	13.1	9.90	<0.001
Prevalent COPD (%)	25.6	31.2	7.93	<0.001	26.2	28.7	3.29	0.001	26.5	27.6	1.44	0.150

All values were adjusted for age at baseline, sex, and study region, when appropriate. * According to the AWGS, low total muscle mass index, low grip strength, and low arm muscle quality were defined as the lowest sex-specific quintiles of total muscle mass index, grip strength, and arm muscle quality, respectively. Normal groups were defined as Q2–Q5 of total muscle mass index, grip strength, and arm muscle quality, respectively. † F statistics for continuous variables and Z statistics for categorical variables. AWGS: Asian Working Group for Sarcopenia; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease: MET: Metabolic equivalent.

Table 2: Associations of muscle mass indices with all-cause mortality.

Muscle mass indices	Binary category		Quintiles				
	Normal*	Low*	Q1	Q2	Q3	Q4	Q5
Appendicular muscle mass index							
Median (kg)	7.3	6.1	6.1	6.5	6.8	7.2	8.0
Person-years	72,038	17,718	17,718	18,053	18,073	17,952	17,960
N of death	465	274	274	130	115	112	108
Crude mortality†	6.5	15.5	15.5	7.2	6.4	6.2	6.0
HR (Model 1)	1.00	1.24 (1.05–1.46)	1.28 (1.01–1.61)	0.95 (0.74–1.22)	1.00	1.09 (0.84–1.42)	1.14 (0.88–1.49)
HR (Model 2)	1.00	1.20 (1.02–1.42)	1.24 (0.99–1.57)	0.95 (0.74–1.22)	1.00	1.10 (0.85–1.43)	1.17 (0.89–1.52)
HR (Model 3)	1.00	1.28 (1.08–1.51)	1.30 (1.03–1.64)	0.96 (0.75–1.24)	1.00	1.07 (0.83–1.40)	1.09 (0.84–1.43)
Total muscle mass index							
Median (kg)	17.0	14.5	14.5	15.3	15.9	16.7	18.5
Person-years	71,975	17,781	17,781	18,021	17,944	18,047	17,963
N of death	480	259	259	134	123	114	109
Crude mortality†	6.7	14.6	14.6	7.4	6.9	6.3	6.1
HR (Model 1)	1.00	1.33 (1.13–1.57)	1.34 (1.07–1.67)	0.96 (0.75–1.23)	1.00	1.02 (0.79–1.32)	1.08 (0.83–1.41)
HR (Model 2)	1.00	1.29 (1.09–1.52)	1.30 (1.04–1.63)	0.96 (0.75–1.23)	1.00	1.04 (0.80–1.35)	1.12 (0.86–1.45)
HR (Model 3)	1.00	1.38 (1.16–1.62)	1.38 (1.11–1.73)	0.98 (0.76–1.26)	1.00	1.02 (0.79–1.32)	1.06 (0.81–1.38)

HRs were estimated using stepwise models and shown as point estimate value (95% confidence interval). Model 1 was stratified by age at baseline and study region, and was adjusted for sex. Model 2 was adjusted for educational attainment, marital status, occupation, household income, smoking status, alcohol consumption, levels of physical activities, scores of dietary patterns, and variables in model 1. Model 3 was adjusted for prevalent hypertension, prevalent diabetes, prevalent COPD, and variables in model 2. * Low muscle mass indices were defined as the lowest quintiles of sex-specific muscle mass indices. The normal groups were defined as Q2–Q5 of corresponding muscle mass indices. † Per 1000 person-years. COPD: Chronic obstructive pulmonary disease; HR: Hazard ratio.

Table 3: Associations of muscle mass indices with all-cause mortality by body parts.

Muscle mass indices	Binary category		Quintiles				
	Normal*	Low*	Q1	Q2	Q3	Q4	Q5
Arm muscle mass index							
Person-years	71,712	18,044	18,044	17,981	17,626	17,844	18,261
N of death	448	291	291	123	127	105	93
Crude mortality†	6.3	16.1	16.1	6.8	7.2	5.9	5.1
HR (Model 1)	1.00	1.47 (1.25–1.74)	1.30 (1.04–1.62)	0.80 (0.62–1.03)	1.00	0.93 (0.71–1.20)	0.83 (0.63–1.10)
HR (Model 2)	1.00	1.44 (1.22–1.69)	1.27 (1.02–1.58)	0.79 (0.61–1.01)	1.00	0.93 (0.72–1.21)	0.85 (0.64–1.11)
HR (Model 3)	1.00	1.54 (1.30–1.82)	1.33 (1.07–1.67)	0.79 (0.62–1.02)	1.00	0.91 (0.70–1.18)	0.77 (0.59–1.02)
Leg muscle mass index							
Person-years	71,821	17,934	17,934	17,613	17,999	18,409	17,800
N of death	475	264	264	132	111	110	122
Crude mortality†	6.6	14.7	14.7	7.5	6.2	6.0	6.9
HR (Model 1)	1.00	1.12 (0.94–1.32)	1.17 (0.92–1.47)	0.98 (0.76–1.27)	1.00	1.03 (0.79–1.34)	1.23 (0.95–1.60)
HR (Model 2)	1.00	1.09 (0.92–1.28)	1.13 (0.89–1.43)	0.98 (0.76–1.26)	1.00	1.02 (0.78–1.33)	1.24 (0.96–1.62)
HR (Model 3)	1.00	1.15 (0.97–1.36)	1.17 (0.93–1.48)	0.98 (0.76–1.27)	1.00	0.98 (0.75–1.28)	1.17 (0.90–1.53)
Trunk muscle mass index							
Person-years	71,971	17,784	17,784	18,035	18,114	17,941	17,882
N of death	493	246	246	106	135	129	123
Crude mortality†	6.9	13.8	13.8	5.9	7.5	7.2	6.9
HR (Model 1)	1.00	1.56 (1.31–1.86)	1.46 (1.16–1.83)	0.85 (0.65–1.10)	1.00	0.97 (0.76–1.23)	0.95 (0.74–1.22)
HR (Model 2)	1.00	1.49 (1.24–1.77)	1.40 (1.11–1.76)	0.85 (0.65–1.10)	1.00	0.97 (0.76–1.24)	0.99 (0.77–1.26)
HR (Model 3)	1.00	1.57 (1.31–1.88)	1.47 (1.16–1.85)	0.86 (0.66–1.11)	1.00	0.96 (0.75–1.22)	0.94 (0.73–1.21)

HRs were estimated using stepwise models and shown as point estimate value (95% confidence interval). Models 1 to 3 were adjusted for the same variables as corresponding models in Table 2. * Low muscle mass indices were defined as the lowest quintiles of sex-specific muscle mass indices. Normal groups were defined as Q2–Q5 of corresponding skeletal muscle mass indices. † Per 1000 person-years. HR: Hazard ratio.

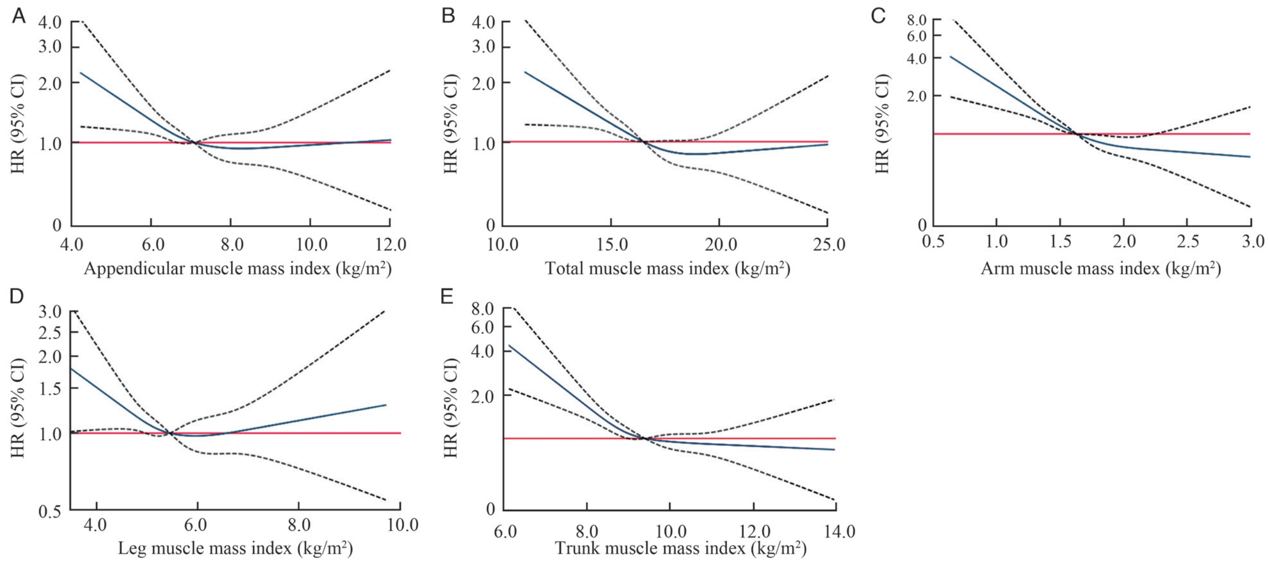

Figure 1: Restricted cubic splines for associations between muscle mass indices and all-cause mortality. The four knots for restricted cubic splines were set at the 5th, 35th, 65th, and 95th percentages of muscle mass indices, and the median values of muscle mass indices were the reference points. Solid lines represent HRs and dashed lines represent 95% CIs. Likelihood ratio tests were used to test for non-linearity (appendicular muscle mass index: $P = 0.103$; total muscle mass index: $P = 0.107$; arm muscle mass index: $P = 0.071$; leg muscle mass index: $P = 0.126$; trunk muscle mass index: $P = 0.009$). Models were adjusted for variables in model 3 of Table 2. CIs: Confidence intervals; HRs: Hazard ratios.

association between leg muscle mass index and all-cause mortality was observed ($Z = 1.59$, $P = 0.113$).

Cox models with restricted cubic splines indicated trends of non-linear associations of appendicular muscle mass index and total muscle mass index with all-cause mortality, but the non-linear trends were not statistically significant [Figure 1].

Muscle strength, muscle quality, and all-cause mortality

The relative risk of all-cause mortality was 1.68 (1.41–2.00) for low *vs*. normal grip strength ($Z = 5.88$, $P < 0.001$) and 1.41 (1.20–1.66) for low *vs*. normal arm muscle quality ($Z = 4.17$, $P < 0.001$) in model 3 [Table 4]. Grip strength and arm muscle quality were further grouped into quintiles. Adults in the lowest quintile of grip strength were 2.22 (95% CI: 1.54–3.21) times as likely to die as those in the highest quintile of grip strength, and the relative risk of all-cause mortality was 1.49 (95% CI: 1.18–1.87) for participants in the lowest quintile *vs*. in the third quintile of arm muscle quality.

The restricted cubic spline model showed a linear association of grip strength with all-cause mortality risk [Supplementary Figure 1, http://links.lww.com/CM9/B77], and each standard deviation (SD) decrease in grip strength was associated with a 69% (95% CI: 50–91%) increased risk of all-cause mortality.

Sensitivity analysis and sub-group analysis

For associations of muscle mass indices, grip strength, or arm muscle quality with all-cause mortality, changes in risk estimates were minor in sensitivity analyses [Supplementary Table 2, http://links.lww.com/CM9/B77].

Sub-group analyses indicated that increased risks of all-cause mortality for low appendicular muscle mass index, low leg muscle mass index, and low grip strength were limited to participants with lower levels of total physical activities. But no interactions between exposures and sub-grouping variables including total physical activities and residential areas (urban *vs*. rural) were observed after Bonferroni correction [Supplementary Tables 3–10, http://links.lww.com/CM9/B77].

Discussion

The present cohort study which involved 23,290 adults from 10 diverse regions in China observed that the short-term (median 3.98 years) increased risk of all-cause mortality was 28% for low appendicular muscle mass index, 38% for low total muscle mass index, 68% for low grip strength, and 41% for low arm muscle quality after adjusting for sociodemographic factors, lifestyle factors, and medical histories. Grip strength was linearly inversely associated with all-cause mortality, with per-SD decrease in grip strength associated with a 69% short-term increased risk of all-cause mortality.

Previous cohort studies on the relationship between muscle mass-related measures and all-cause mortality reported inconsistent results, with some observing inverse associations[3-6,10,12] while others finding no clear association of muscle mass with all-cause mortality.[8,9,11] These studies were mostly conducted in Western populations and the inconsistent findings might be due to differences in sample sizes, muscle mass-related indicators, durations of follow-up, and covariates adjusted in models. To the best of our knowledge, only one cohort study on this issue has been conducted among Chinese adults. The study involved 1512 adults aged ≥65 years from Taiwan of China with a median follow-up of 7.9 years and found that low total

Table 4: Associations of grip strength and arm muscle quality with all-cause mortality.

Muscle mass indices	Binary category		Quintiles				
	Normal*	Low*	Q1	Q2	Q3	Q4	Q5
Grip strength							
Median (kg)	26.0	14.0	14.0	18.0	21.0	24.0	30.0
Person-years	72,263	17,492	17,492	17,181	17,537	17,956	19,590
N of death	351	388	388	160	85	62	44
Crude mortality†	4.9	22.2	22.2	9.3	4.9	3.5	2.3
HR (Model 1)	1.00	1.79 (1.51–2.12)	2.46 (1.71–3.55)	1.65 (1.14–2.39)	1.18 (0.80–1.73)	1.12 (0.75–1.67)	1.00
HR (Model 2)	1.00	1.72 (1.45–2.04)	2.29 (1.59–3.31)	1.58 (1.09–2.29)	1.13 (0.77–1.67)	1.09 (0.73–1.62)	1.00
HR (Model 3)	1.00	1.68 (1.41–2.00)	2.22 (1.54–3.21)	1.58 (1.09–2.29)	1.12 (0.76–1.65)	1.07 (0.72–1.59)	1.00
Arm muscle quality							
Median (kg/kg)	12.5	7.9	7.9	10.3	11.7	13.3	15.4
Person-years	71,995	17,761	17,761	17,842	17,709	18,323	18,120
N of death	424	315	315	164	108	77	75
Crude mortality†	5.9	17.7	17.7	9.2	6.1	4.2	4.1
HR (Model 1)	1.00	1.52 (1.30–1.79)	1.61 (1.28–2.02)	1.23 (0.96–1.57)	1.00	0.85 (0.63–1.14)	0.99 (0.73–1.34)
HR (Model 2)	1.00	1.49 (1.27–1.75)	1.56 (1.24–1.97)	1.20 (0.94–1.54)	1.00	0.84 (0.63–1.13)	1.01 (0.75–1.37)
HR (Model 3)	1.00	1.41 (1.20–1.66)	1.49 (1.18–1.87)	1.19 (0.93–1.52)	1.00	0.85 (0.63–1.14)	1.05 (0.78–1.42)

HRs were estimated using stepwise models and shown as point estimate value (95% confidence interval). * Low grip strength and low arm muscle quality were defined as the lowest quintiles of sex-specific grip strength and arm muscle quality, respectively. The normal groups were defined as Q2–Q5 of corresponding indices. † Per 1000 person-years. HR: Hazard ratio.

muscle mass index (the lowest sex-specific quartile) was associated with a 40% (95% CI: 13–74%) higher risk of all-cause mortality after adjustment for age, BMI, physical activities, and comorbidities.[12] The present study, which included Chinese adults of more diverse backgrounds and followed them for a shorter duration, also found that low total muscle mass index was associated with all-cause mortality. We observed potential non-linear associations of appendicular muscle mass index and total muscle mass index with short-term all-cause mortality, but the *P* values for tests of non-linearity were >0.007 (0.05/7), which may be due to the limitation of statistical power. Only one previous study has reported such a non-linear relationship.[27] The Health Professionals Follow-Up Study followed 38,006 US men for 21.4 years and reported that the risk of all-cause mortality declined with increased lean mass until 56 kg of lean mass, and increased with increased lean mass afterwards.[27] Therefore, extremely high muscle mass may not exert an excess protective effect on all-cause mortality. Larger cohort studies conducted in the Chinese population are needed to further explore such potential non-linear associations. Few studies have assessed associations between muscle mass indices in different body parts and all-cause mortality. The present study observed that low arm and trunk muscle mass indices but no low leg muscle mass index were associated with increased risks of all-cause mortality, indicating that among Chinese adults muscle mass in the arms or trunk may better predict mortality from all causes than muscle mass in legs.

The present study observed that grip strength was inversely associated with the risk of all-cause mortality, with per-SD (9.1 kg) decrease in grip strength associated with a 69% higher risk of short-term mortality. A meta-analysis integrating results from 28 cohort studies with follow-up duration ranging from 1 year to 40 years also observed the linear strength–mortality relation.[15] There seems to be a difference between short-term and long-term effects of grip strength. The meta-analysis found that each 5 kg decrease in grip strength was associated with a 28% increased risk of all-cause mortality within <10 years of follow-up, and the increased risk was 9% when the follow-up duration was ≥10 years.[15] Cohort studies included in this meta-analysis were mostly conducted in the Western population and only two studies[13,14] involved Chinese adults. The Prospective Urban Rural Epidemiology study enrolled 142,861 participants (including 46,036 Chinese) from 17 countries and reported that the relative risk of all-cause mortality was 1.16 (95% CI: 1.13–1.20) for per 5 kg reduction in grip strength during a median follow-up of 4.0 years.[14] A cohort study including 558 Chinese men aged ≥75 years in Taiwan of China reported that the relative risk of all-cause mortality was 2.00 (95% CI: 1.04–3.85) for the highest *vs*. the lowest quartile of grip strength after adjustment for age, lifestyle factors, BMI, and medical histories during a mean follow-up of 2.5 years.[13] Results from the present study were similar to findings from the study conducted in Taiwan of China.

Existing evidence on the association between muscle quality and mortality from all causes is scarce. The health, aging, and body composition study involving 2292 Americans aged 70 to 79 years reported that per SD reduction in arm muscle quality was associated with a 23% higher risk of all-cause mortality.[9] The present study also found that low arm muscle quality was associated with increased risk of death, adding prospective evidence on this issue from the Chinese population.

The associations of all-cause mortality with low grip strength, low arm muscle mass index, and low trunk muscle mass index were much stronger than its associations with low appendicular muscle mass index, low total muscle mass index, low leg muscle mass index, and low arm muscle quality [Tables 2–4]. This indicates that grip strength and muscle mass index in the arm and trunk are of more clinical and public health relevance and should be given priority when assessing population mortality risk using different muscle metrics.

Muscle mass and strength can be markers of nutritional status and physical functioning, while malnutrition and physical decline are associated with increased mortality risks.[28-30] In the present study, the association of muscle mass and muscle strength with all-cause mortality existed even after adjustment for dietary patterns and levels of physical activities. Many factors affect mass, strength, and quality of muscle and their associations with adverse health outcomes might be joint effects of these factors. More studies are warranted to explore mechanisms of the muscle–mortality association.

The present study has several strengths, including the general population from diverse regions in China, comprehensively assessing multiple muscle metrics including muscle mass, strength, and quality to explore the muscle–mortality association, and stringent quality control during data collection. Nevertheless, there are some limitations. First, AWGS recommended using muscle mass, muscle strength, and physical performance for the diagnosis of sarcopenia.[21] The present study did not measure participants' physical performance such as gait speed. More large-scale prospective studies are warranted to assess the mortality predicting effect of gait speed in the general Chinese population. Second, muscle mass was measured using the method of BIA, which is less accurate than the other commonly used method in epidemiological studies, the dual energy X-ray absorptiometry method. Nevertheless, BIA has the advantage of reasonable cost, fast processing, non-invasiveness, radiation-free functions, and convenience of use,[21] and is therefore more feasible in large-scale epidemiological studies. Third, for muscle strength, the present study did not measure knee extension muscle strength, but a previous study has shown that grip strength and knee extension muscle strength were highly correlated.[31] Fourth, due to the relatively shorter duration of follow-up, findings from the present study could only reflect the short-term predicting effects of muscle metrics on all-cause mortality.

Conclusions

The CKB study provides evidence for the general Chinese population that low muscle mass, low grip strength, and low arm muscle quality are risk factors for short-term all-cause mortality, indicating the importance of maintaining normal muscle mass, strength, and quality.

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Conflicts of interest

None.

References

1. Tyrovolas S, Koyanagi A, Olaya B, Ayuso-Mateos JL, Miret M, Chatterji S, *et al*. Factors associated with skeletal muscle mass, sarcopenia, and sarcopenic obesity in older adults: a multi-continent study. J Cachexia Sarcopenia Muscle 2016;7:312–321. doi: 10.1002/jcsm.12076.
2. Yu S, Visvanathan T, Field J, Ward LC, Chapman I, Adams R, *et al*. Lean body mass: the development and validation of prediction equations in healthy adults. BMC Pharmacol Toxicol 2013;14:53. doi: 10.1186/2050-6511-14-53.
3. Li R, Xia J, Zhang XI, Gathirua-Mwangi WG, Guo J, Li Y, *et al*. Associations of muscle mass and strength with all-cause mortality among US older adults. Med Sci Sports Exerc 2018;50:458–467. doi: 10.1249/mss.0000000000001448.
4. Pasco JA, Mohebbi M, Holloway KL, Brennan-Olsen SL, Hyde NK, Kotowicz MA. Musculoskeletal decline and mortality: prospective data from the Geelong Osteoporosis Study. J Cachexia Sarcopenia Muscle 2017;8:482–489. doi: 10.1002/jcsm.12177.
5. Batsis JA, Mackenzie TA, Emeny RT, Lopez-Jimenez F, Bartels SJ. Low lean mass with and without obesity, and mortality: results from the 1999–2004 national health and nutrition examination survey. J Gerontol A Biol Sci Med Sci 2017;72:1445–1451. doi: 10.1093/gerona/glx002.
6. Balogun S, Winzenberg T, Wills K, Scott D, Jones G, Aitken D, *et al*. Prospective associations of low muscle mass and function with 10-year falls risk, incident fracture and mortality in community-dwelling older adults. J Nutr Health Aging 2017;21:843–848. doi: 10.1007/s12603-016-0843-6.
7. Graf CE, Karsegard VL, Spoerri A, Makhlouf AM, Ho S, Herrmann FR, *et al*. Body composition and all-cause mortality in subjects older than 65 y. Am J Clin Nutr 2015;101:760–767. doi: 10.3945/ajcn.114.102566.
8. Wijnhoven HA, Snijder MB, van Bokhorst-de van der Schueren MA, Deeg DJ, Visser M. Region-specific fat mass and muscle mass and mortality in community-dwelling older men and women. Gerontology 2012;58:32–40. doi: 10.1159/000324027.
9. Newman AB, Kupelian V, Visser M, Simonsick EM, Goodpaster BH, Kritchevsky SB, *et al*. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. J Gerontol A Biol Sci Med Sci 2006;61:72–77. doi: 10.1093/gerona/61.1.72.
10. Han SS, Kim KW, Kim KI, Na KY, Chae DW, Kim S, *et al*. Lean mass index: a better predictor of mortality than body mass index in elderly Asians. J Am Geriatr Soc 2010;58:312–317. doi: 10.1111/j.1532-5415.2009.02672.x.
11. Otsuka R, Matsui Y, Tange C, Nishita Y, Tomida M, Ando F, *et al*. What is the best adjustment of appendicular lean mass for predicting mortality or disability among Japanese community dwellers? BMC Geriatr 2018;18:8. doi: 10.1186/s12877-017-0699-6.
12. Chuang SY, Chang HY, Lee MS, Chia-Yu Chen R, Pan WH. Skeletal muscle mass and risk of death in an elderly population. Nutr Metab Cardiovasc Dis 2014;24:784–791. doi: 10.1016/j.numecd.2013.11.010.
13. Chen PJ, Lin MH, Peng LN, Liu CL, Chang CW, Lin YT, *et al*. Predicting cause-specific mortality of older men living in the veterans home by handgrip strength and walking speed: a 3-year, prospective cohort study in Taiwan. J Am Med Dir Assoc 2012;13:517–521. doi: 10.1016/j.jamda.2012.02.002.
14. Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, *et al*. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. Lancet 2015;386:266–273. doi: 10.1016/s0140-6736(14)62000-6.
15. Wu Y, Wang W, Liu T, Zhang D. Association of grip strength with risk of all-cause mortality, cardiovascular diseases, and cancer in community-dwelling populations: a meta-analysis of prospective cohort studies. J Am Med Dir Assoc 2017;18:551.e517–551.e535. doi: 10.1016/j.jamda.2017.03.011.
16. Xiao Z, Guo B, Gong J, Tang Y, Shang J, Cheng Y, *et al*. Sex- and age-specific percentiles of body composition indices for Chinese adults using dual-energy X-ray absorptiometry. Eur J Nutr 2017;56:2393–2406. doi: 10.1007/s00394-016-1279-9.
17. Leong DP, Teo KK, Rangarajan S, Kutty VR, Lanas F, Hui C, *et al*. Reference ranges of handgrip strength from 125,462 healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study. J Cachexia Sarcopenia Muscle 2016;7:535–546. doi: 10.1002/jcsm.12112.
18. Chien MY, Huang TY, Wu YT. Prevalence of sarcopenia estimated using a bioelectrical impedance analysis prediction equation in community-dwelling elderly people in Taiwan. J Am Geriatr Soc 2008;56:1710–1715. doi: 10.1111/j.1532-5415.2008.01854.x.
19. Mijnarends DM, Meijers JM, Halfens RJ, ter Borg S, Luiking YC, Verlaan S, *et al*. Validity and reliability of tools to measure muscle mass, strength, and physical performance in community-dwelling older people: a systematic review. J Am Med Dir Assoc 2013;14:170–178. doi: 10.1016/j.jamda.2012.10.009.
20. Nigam P, Misra A, Colles SL. Comparison of DEXA-derived body fat measurement to two race-specific bioelectrical impedance equations in healthy Indians. Diabetes Metab Syndr 2013;7:72–77. doi: 10.1016/j.dsx.2013.02.031.
21. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, *et al*. Sarcopenia in Asia: consensus report of the Asian Working Group for sarcopenia. J Am Med Dir Assoc 2014;15:95–101. doi: 10.1016/j.jamda.2013.11.025.
22. Yu C, Shi Z, Lv J, Guo Y, Bian Z, Du H, *et al*. Dietary patterns and insomnia symptoms in Chinese adults: the China Kadoorie Biobank. Nutrients 2017;9:232. doi: 10.3390/nu9030232.
23. Liu Q, Wu M, Wen QR, Du HD, Lyu J, Guo Y, *et al*. The correlation of dietary patterns with low muscle mass, strength and quality in adults from 10 regions of China (in Chinese). Chin J Epidemiol 2021;42:780–786. doi: 10.3760/cma.j.cn112338-20200618-00855.
24. Wen QR, Wu M, Liu Q, Lyu J, Guo Y, Bian Z, *et al*. Correlation between chronic diseases and low muscle mass, strength and quality in adults in China (in Chinese). Chin J Epidemiol 2021;42:1948–1954. doi: 10.3760/cma.j.cn112338-20200910-01146.
25. McCormick R, Vasilaki A. Age-related changes in skeletal muscle: changes to life-style as a therapy. Biogerontology 2018;19:519–536. doi: 10.1007/s10522-018-9775-3.
26. Kalyani RR, Corriere M, Ferrucci L. Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other

diseases. Lancet Diabetes Endocrinol 2014;2:819–829. doi: 10.1016/s2213-8587(14)70034-8.
27. Lee DH, Keum N, Hu FB, Orav EJ, Rimm EB, Willett WC, *et al*. Predicted lean body mass, fat mass, and all cause and cause specific mortality in men: prospective US cohort study. BMJ 2018;362: k2575. doi: 10.1136/bmj.k2575.
28. Heymsfield SB, McManus C, Stevens V, Smith J. Muscle mass: reliable indicator of protein-energy malnutrition severity and outcome. Am J Clin Nutr 1982;35:1192–1199. doi: 10.1093/ajcn/35.5.1192.
29. Norman K, Stobaus N, Gonzalez MC, Schulzke JD, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. Clin Nutr 2011;30:135–142. doi: 10.1016/j.clnu.2010.09.010.
30. Schaap LA, Koster A, Visser M. Adiposity, muscle mass, and muscle strength in relation to functional decline in older persons. Epidemiol Rev 2013;35:51–65. doi: 10.1093/epirev/mxs006.
31. Bohannon RW, Magasi SR, Bubela DJ, Wang YC, Gershon RC. Grip and knee extension muscle strength reflect a common construct among adults. Muscle Nerve 2012;46:555–558. doi: 10.1002/mus.23350.

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