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Association between muscle strength and cardiometabolic multimorbidity risk among middle-aged and older Chinese adults: a nationwide longitudinal cohort study

Jingxian Wang¹, Yi Yang¹, Qing Su¹, Juejin Wang¹, Hao Zeng¹, Yaqing Chen¹, Junxi Zhou¹ and Yi Wang^{1,2*}

Abstract

Background Cardiometabolic multimorbidity (CM) is emerging as a global health challenge. This study investigated the potential impact of muscle strength on the risk of CM in middle-aged and older Chinese adults.

Methods In total, 7610 participants were identified from the China Health and Retirement Longitudinal Study (CHARLS). Muscle strength was measured by absolute, relative grip strength (normalized for body mass index) and chair-rising time which were classified into three categories according to tertiles stratified by gender. Cox proportional hazards models were adopted to evaluate the effect of muscle strength on CM.

Results During follow-up, 235 (3.76%) participants from none cardiometabolic diseases (CMD), 140 (19.23%) from diabetes, 119 (21.17%) from heart disease, and 22 (30.56%) from stroke progressed to CM. In participants who had low relative grip strength, CM was more likely to occur in individuals with heart disease at baseline (HR: 1.89, 95%CI: 1.10 to 3.23). Those with high chair-rising time had a higher risk of CM than those with low chair-rising time in the individuals with diabetes (HR: 1.85, 95%CI: 1.20 to 2.86) and with heart disease (HR: 1.67, 95%CI: 1.04 to 2.70). However, we did not observe an association between muscle strength and CM in participants without CMD or with stroke at baseline.

Conclusions In Chinese middle-aged and older adults, low relative grip strength was associated with a higher risk of CM in individuals with heart disease, while high chair-rising time was associated with a higher risk of CM in individuals with diabetes or heart disease.

Keywords Muscle strength, Cardiometabolic multimorbidity, Handgrip strength, Chair rising, Cohort

Background

Cardiometabolic multimorbidity (CM), referring to the co-occurrence of at least two cardiometabolic diseases (CMD), including diabetes, heart disease and stroke [1, 2], is turning into a global challenge as the most common and severe multimorbidity [3, 4]. Multiple CMDs are associated with a substantially increased risk of death and significant life expectancy reduction compared to single CMD. The prevalence of CM has increased worldwide, with an estimated 10 million adults suffering from this disease in the United States

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and the European Union [5] and 6% of the population aged 30–80 years in China [4]. Middle-aged and older adults are at a high risk of CM development, and exploring the risk factors for CM needs to be taken urgently.

Studies reported that muscle strength decline in aging is associated with adverse health outcomes, such as frailty, functional decline, various cancers, and higher all-cause mortality rates [6–8]. Grip strength test and five-times chair stand test are simple, low-cost, and effective methods for assessing upper and lower body muscle strength in practice and routine procedures [9]. Many studies have investigated the impact of muscle strength on the incidence of a single type of CMD. A cross-sectional study conducted on Chinese, Malay, and Indian midlife women ($n=1201$; aged 45–69 years) found that lower absolute grip strength and prolonged chair rising time were associated with the incidence of diabetes [10]. Based on a longitudinal cohort ($n=2623$; aged over 45 years), Shan et al. also reported that lower relative grip strength and longer chair-rising time were independently associated with the incidence of diabetes [11]. Evidence from the UK Biobank has demonstrated a significant association between low absolute grip strength and increased risk of cardiovascular disease (CVD) [12, 13]. A cohort study of 2529 Norwegian women aged 65–88 elucidated that absolute handgrip strength and chair-rising time can predict CVD mortality [14]. A study of 8871 middle-aged and older people in China reported that absolute grip strength can serve as an independent predictor of stroke [15]. In contrast, limited studies examined the importance of muscle strength on CM combined with grip strength and chair-rising time measures. To our knowledge, only one cohort study based on the UK Biobank data investigated the role of absolute grip strength in the progression of CM in the general population aged 37–73 [16]. The results of this study indicated that absolute grip strength is associated with the progression from non-CMD or first cardiometabolic diseases (FCMD) to new-onset CM. However, this study only explored the relationship between absolute grip strength and CM. Moreover, whether these relationships still exist in individuals with different environments or genetic backgrounds is a question.

Based on the above, we speculate that muscle strength decline may be an independent predictor for the incidence of new-onset CM cases. Investigating the association between muscle strength decline and CM in middle-aged and older populations may contribute to advancing preventive strategies against CM. Therefore, this study aims to explore the association between muscle strength and the risk of CM in middle-aged and older Chinese adults based on a nationwide prospective cohort study, which comprehensively assesses grip strength and chair-rising time.

Methods

Study population

This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), a prospective cohort of Chinese community residents over 45. All participants were Chinese residents and underwent face-to-face interviews with structured questionnaires and physical measurements including muscle strength. The CHARLS was established in 2011 and followed at 2-year or occasionally 3-year intervals. Details about the study design of the CHARLS had been previously reported [17]. We applied CHARLS 2011, 2013, 2015, and 2018 data, available online at <http://charls.pku.edu.cn>. In this study, we set the CHARLS 2011 as the baseline, and the occurrence of CM during follow-up was considered as the outcome. The CHARLS cohort was conformed to the Declaration of Helsinki and approved by the Peking University Biomedical Ethics Committee, with all participants signing informed consent.

Of the 16,931 participants aged over 45 years who were recruited in the baseline (CHARLS 2011), individuals were excluded if they met the following criteria: (i) missing data of muscle strength at baseline; (ii) no CM data during the follow-up period; (iii) lack of values in main variables; (iv) suffering from CM in 2011; (v) loss follow-up to observe the CM event. The flowchart of the selection process of subjects is shown in Fig. 1.

Assessment of muscle strength

Muscle strength in this study was measured at baseline by well-trained assessors following standardized instructions and expressed as grip strength and chair-rising time [11]. Grip strength (kg) was measured by squeezing a standardized handgrip dynamometer [Yuejian™ WL-1000 dynamometer (Nantong Yuejian Physical Measurement Instrument Co., LTD., Nantong, China)] in kilograms [17]. Each dynamometer requires computerized testing and calibration before leaving the factory and periodic recalibration at the factory every two years. Furthermore, CHARLS ensures that dynamometers are returned to the factory for calibration before each wave of the survey. Participants were instructed to grasp the dynamometer with one hand, maintaining a 90° elbow flexion angle in a standing position. Then, they were required to firmly grasp the handle and exert maximum force until the pointer reached its peak. Each hand was measured twice, with an unnecessary recovery interval between each alternate measurement for the left and right hands, and a 30-s recovery interval between each continuous measurement with the same hand. The maximum value of four measurements was selected as the absolute grip strength for subsequent analyses [18]. In consideration of the substantial covariance between grip strength and body mass

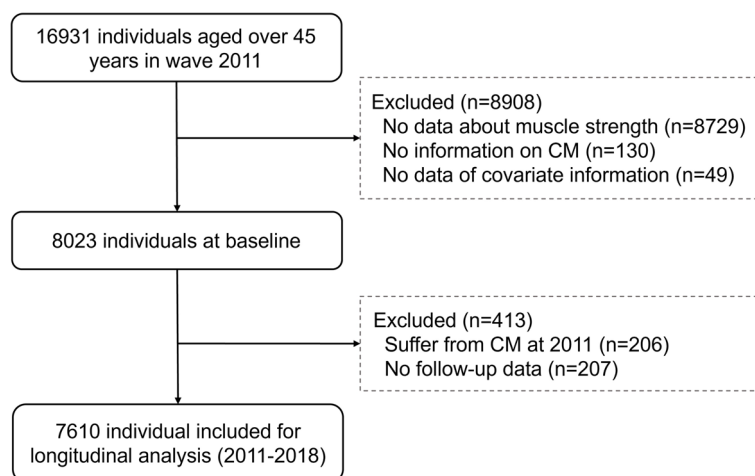


Fig. 1 Flowchart of the participants selection process. Abbreviations: CM, cardiometabolic multimorbidity

index (BMI), maximum grip strength was also converted into relative grip strength adjusted by BMI [grip strength (kg)/BMI (kg/m²)] [19, 20].

Chair-rising time was assessed through the five-times chair stand test and recorded with a stopwatch. During the five-times chair stand test, participants were instructed to perform five repetitions of standing up straight from a chair and sitting down at their fastest speed. Throughout this process, participants were required to keep their arms folded in front of their chest without pausing between each repetition or assistance from arm movements [11]. Considering the differences in muscle strength between the genders, muscle strength was categorized into tertiles within gender-specific stratification (Supplementary Table S1 – S3) [21].

Assessment of CM events

The outcome of this study was CM events, which were identified during the follow-up period. Consistent with previous studies, the incidence of CMD was identified in two ways. The first one is based on information from CHARLS's questionnaire, including the following: "Have you been told by a doctor that you have been diagnosed with diabetes?" "Have you been told by a doctor that you have been diagnosed with a heart attack, Angina, coronary heart disease, heart failure, or other heart problems?" or "Have you been told by a doctor that you have been diagnosed with a stroke?" [22]. Another one, according to the American Diabetes Association criteria, participants were considered diabetes if their blood test results from CHARLS met any of the following criteria: (i) fasting plasma glucose ≥ 7.0 mmol/L; (ii) random plasma glucose ≥ 11.1 mmol/L; (iii) HbA1c $\geq 6.5\%$ [23]. The date of CM onset was identified as the time of

diagnosis of the second CMD, at which time the individuals had two types of CMD. If the exact onset time of CMD was unavailable, the time to event was calculated as (the time of specific wave with CMD information - the time of interval wave)/2 + (the time of interval wave - the time of baseline investigation) [24].

Potential covariates

Information on covariates was acquired through the questionnaire by trained interviewers at baseline. Demographic covariates included age and gender ("men" and "women"). Socioeconomic factors included living residence ("rural" and "urban"), educational level ("primary school or below" and "middle school or above") and marital status ("married or partnered" and "single"). Health-related factors included BMI, smoking status ("yes" and "no"), alcohol drinking ("yes" and "no") and self-reported physician-diagnosed hypertension ("yes" and "no") (17). BMI was calculated as weight in kilograms divided by height in meters squared and then classified into four groups: underweight (BMI < 18.5 kg/m²), normal weight (BMI = 18.5–23.9 kg/m²), overweight (BMI = 24–27.9 kg/m²) and obesity (BMI ≥ 28 kg/m²) [25].

Statistical analysis

Continuous variables are presented as means \pm standard deviation (SD) if they are normal distribution or median and interquartile range if not, and categorical variables as numbers and percentages. The differences between continuous variables were assessed by the analysis of variance or the Kruskal–Wallis test, while the differences between categorical variables were evaluated through the Pearson Chi-square test. In the longitudinal analysis, we computed the follow-up time from baseline to the time

of the CM events, death, loss to follow-up, or the end of follow-up, whichever came first. Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs) between muscle strength in tertiles and incidence of CM. Before running the Cox regression model, the assumption of proportional hazard was checked using the Schoenfeld residual test with P -value > 0.05 , which considered to fulfill the assumption. Three models were fitted: Model 1 was not adjusted with covariates; Model 2 was performed by adjusting age and gender; Model 3, as a fully adjusted model, was controlled for age, gender, residence, educational level, marital status, BMI, smoking status, drinking status and hypertension.

Subgroup analyses were conducted in subjects stratified by age (≥ 60 years vs. < 60 years) and gender (men vs. women) for longitudinal analyses. All statistical analyses were performed by R software (Version 4.2.2) and the statistical significance was defined as $P < 0.05$ with two-sided.

Results

Baseline characteristics

Finally, 7610 individuals were included in this study. Comparisons between excluded ($n = 9231$) and included ($n = 7610$) individuals for this study were depicted in Supplementary Table S4. During a median follow-up of seven years, 516 (6.78%) incident CM cases were identified. The baseline characteristics of the participants grouped by CMD and muscle strength status were depicted in Table 1 and Supplementary Table S5-S7. There were significant differences in age, gender, residential area, BMI, smoking, alcohol consumption, hypertension and muscle strength among people with different health status. Individuals without CMD were more likely to be younger (57.99 ± 8.94 years), had more normal weight (BMI: 23.08 ± 3.52), and had lower prevalence of hypertension (19.37%). In individuals with FCMD, the stroke group was older (62.69 ± 9.16 years), more men (59.72%), weightless (BMI: 23.48 ± 3.45) and had more hypertension (56.94%) than the other two groups. Moreover, participants without CMD had the highest relative grip strength (1.46 ± 0.45 kg), highest absolute grip strength (33.29 ± 9.88 kg) and lowest chair-rising time (9.69 (7.89, 12.00) second). In individuals with FCMD, participants with heart disease showed the lowest relative grip strength (1.31 ± 0.45 kg) and absolute grip strength (31.03 ± 9.80 kg). However, regarding the five-times chair stand test, participants with a stroke spent the most time (12.43 (9.62, 15.56) second). Regarding muscle strength, participants in the low relative grip, absolute grip, and high chair duration groups were all older and had lower education level, higher single rate, and less drinking rate.

Associations of grip strength with risk of CM

Among participants without CMD, 235 (3.76%) individuals progressed to CM and 140 (19.23%) from diabetes, 119 (21.17%) from heart disease, 22 (30.56%) from stroke developed CM. In participants with heart disease, the risk of CM was increased with the declining tertiles of relative grip strength in all three Cox regression models. After fully adjusting, we observed that low relative grip strength was strongly associated with the risk of CM only in individuals with heart disease at baseline (HR: 1.89, 95% CIs: 1.10 to 3.23) but not those without CMD and those with diabetes or stroke (Table 2).

The results of the association between absolute grip strength with CM are shown in Table 3. We found no significant relationship between absolute grip strength and CM in all groups after controlling for covariates.

Associations of chair-rising time with risk of CM

In the longitudinal analysis of the association between chair-rising time and the incidence of CM, compared with low chair-rising time, high chair-rising time increased the risk of CM among those with diabetes (HR: 1.85, 95% CIs: 1.20 to 2.86) and those with heart disease (HR: 1.67, 95% CIs: 1.04 to 2.70) at baseline after fully adjusted covariates (Table 4). However, high chair-rising time was not related to an increased odds of CM in subjects without CMD or subjects suffering from a stroke at the time of inclusion.

Stratified subgroup analyses of the effect of muscle strength on the risk of CM

Subgroup analyses stratified by age and gender were presented in Supplementary Figure S1-S2. With adjustment of covariates, the association of relative grip strength with CM among individuals with heart disease at baseline was comparable in age and gender. Meanwhile, the association between chair-rising time and CM among individuals with diabetes or heart disease at baseline was also comparable in age and gender. Subgroup analyses for stroke were not carried out cause the small sample size.

Discussion

In this study, we investigated the association between muscle strength and CM risk in Chinese middle-aged and older population. We found that low relative grip strength positively correlated with CM risk in participants with heart disease, and high chair-rising time was associated with odds of CM risk in people with diabetes or heart disease. Previous studies suggested that low muscle strength was associated with CMD development. Bellettiere et al. demonstrated that patients with poor lower-extremity physical function were more likely to

Table 1 Baseline characteristics of participants in this study (n = 7610)

Characteristics	Without any CMD (N = 6248)	With diabetes only (N = 728)	With heart disease only (N = 562)	With stroke only (N = 72)	P-value
Age(years)	57.99 ± 8.94	59.18 ± 8.77	61.24 ± 9.19	62.69 ± 9.16	< 0.001
Gender					< 0.001
Men	3075 (49.22)	358 (49.18)	230 (40.93)	43 (59.72)	
Women	3173 (50.78)	370 (50.82)	332 (59.07)	29 (40.28)	
Residential area					< 0.001
Rural	4165 (66.66)	436 (59.89)	312 (55.52)	52 (72.22)	
Urban	2083 (33.34)	292 (40.11)	250 (44.48)	20 (27.78)	
Education					0.171
Primary school or below	4281 (68.52)	492 (67.58)	364 (64.77)	54 (75.00)	
Middle school or above	1967 (31.48)	236 (32.42)	198 (35.23)	18 (25.00)	
Marital status					0.106
Married or partnered	1967 (31.48)	641 (88.05)	481 (85.59)	60 (83.33)	
Single	715 (11.44)	87 (11.95)	81 (14.41)	12 (16.67)	
BMI (kg/m ²)	23.08 ± 3.52	24.43 ± 3.69	24.18 ± 4.13	23.48 ± 3.45	< 0.001
BMI classification					< 0.001
Underweight	451 (7.22)	32 (4.40)	39 (6.94)	5 (6.94)	
Normal weight	3547 (56.77)	309 (42.45)	247 (43.95)	36 (50.00)	
Overweight	1683 (26.94)	268 (36.81)	187 (33.27)	22 (30.56)	
Obesity	567 (9.07)	119 (16.35)	89 (15.84)	9 (12.50)	
Smoking	2061 (32.99)	221 (30.36)	131 (23.31)	22 (30.56)	< 0.001
Drinking	2164 (34.64)	257 (35.30)	135 (24.02)	22 (30.56)	< 0.001
Hypertension	1210 (19.37)	250 (34.34)	257 (45.73)	41 (56.94)	< 0.001
Relative grip strength	1.46 ± 0.45	1.38 ± 0.45	1.31 ± 0.45	1.41 ± 0.47	< 0.001
Relative grip strength classification					1.000
High	2087 (33.40)	244 (33.52)	188 (33.45)	25 (34.72)	
Middle	2080 (33.29)	242 (33.24)	186 (33.10)	23 (31.94)	
Low	2081 (33.31)	242 (33.24)	188 (33.45)	24 (33.33)	
Absolute grip strength (kg)	33.29 ± 9.88	33.07 ± 10.48	31.03 ± 9.80	32.58 ± 10.65	< 0.001
Absolute grip strength classification					0.924
High	1988 (31.82)	220 (30.22)	182 (32.38)	24 (33.33)	
Middle	2161 (34.59)	256 (35.16)	190 (33.81)	21 (29.17)	
Low	2099 (33.59)	252 (34.62)	190 (33.81)	27 (37.50)	
Chair-rising time (second)	9.69 (7.89,12.00)	9.87 (8.10,12.00)	11.23 (8.97,13.96)	12.43 (9.62,15.56)	< 0.001
Chair-rising time classification					1.000
Low	2083 (33.34)	243 (33.38)	188 (33.45)	24 (33.33)	
Middle	2086 (33.39)	242 (33.24)	188 (33.45)	23 (31.94)	
High	2079 (33.27)	243 (33.38)	186 (33.10)	25 (34.72)	

Values were shown as mean ± standard deviation, median (interquartile range) or numbers (percentages)

Abbreviations: CMD cardiometabolic diseases, BMI body mass index

develop CVD [26]. Data from a European cohort revealed that those with high chair-rising time had a higher incidence rate of diabetes in the top quartile of chair-rising time in comparison with the bottom quartile and the HRs(95% CIs) were 1.32 (1.17–1.48) [27], and a study from Mexican American reported that those with low relative grip strength had a significantly increased risk of

diabetes [28]. Extending these studies, we observed that individuals with low muscle strength were more likely to develop one-set CM in participants with pre-existing diabetes or heart disease. This result suggests that individuals with diabetes or heart disease should be concerned about muscle strength, as low muscle strength is a risk factor for developing CM.

Table 2 Cox proportional hazards regression of association between relative grip strength and CM

Variables	cases, No	Model1 ^a	HR (95%CI) Model2 ^b	Model3 ^c
Without CMD at baseline				
High	60	Reference	Reference	Reference
Middle	76	1.27(0.90,1.78)	1.19(0.85,1.67)	0.90(0.64,1.28)
Low	99	1.73(1.26,2.39) [§]	1.47(1.06,2.05) [*]	0.83(0.57,1.20)
<i>P</i> for trend		1.32(1.13,1.55) [§]	1.21(1.03,1.43) [*]	0.91(0.76,1.09)
With diabetes at baseline				
High	36	Reference	Reference	Reference
Middle	50	1.46(0.95,2.24)	1.39(0.90,2.14)	1.11(0.71,1.75)
Low	54	1.68(1.10,2.57) [*]	1.54(0.98,2.42)	1.04(0.63,1.71)
<i>P</i> for trend		1.29(1.05,1.58) [*]	1.23(0.99,1.54)	1.01(0.79,1.29)
With heart disease at baseline				
High	25	Reference	Reference	Reference
Middle	41	1.69(1.03,2.77) [*]	1.73(1.05,2.85) [*]	1.57(0.94,2.63)
Low	53	2.49(1.55,4.00) [§]	2.60(1.59,4.23) [§]	1.89(1.10,3.23) [*]
<i>P</i> for trend		1.56(1.24,1.97) [§]	1.60(1.26,2.02) [§]	1.36(1.04,1.76) [*]
With stroke at baseline				
High	8	Reference	Reference	Reference
Middle	7	1.11(0.40,3.06)	1.08(0.39,3.00)	1.14(0.38,3.38)
Low	7	1.12(0.41,3.10)	1.39(0.49,3.97)	1.53(0.43,5.47)
<i>P</i> for trend		1.06(0.64,1.76)	1.18(0.69,2.00)	1.23(0.65,2.31)

Abbreviation: HR hazard ratio, CIs confidence interval, CM cardiometabolic multimorbidity, CMD cardiometabolic diseases

^a Model 1 was unadjusted

^b Model 2 was adjusted for age, gender

^c Model 3 was adjusted for age, gender, residence, marital status, educational level, drinking status, smoking status, body mass index and hypertension

* $P < 0.05$

$P < 0.01$

§ $P < 0.001$

Different from the outcome of the UK biobank, we did not find an association between absolute grip strength and CM [16], which may result from population differences. Similar to previous studies, we found inconsistent associations between relative and absolute grip strength and consequence. In Korean adults, absolute and relative grip strength were found to be inversely associated with metabolic syndrome [21]. Gao et al. declared that grip strength/weight or grip strength/BMI, but not absolute grip strength, predicted cardiovascular disease risk factors in Chinese community residents [29]. The utilization of absolute grip strength may introduce a potential bias compared to relative grip strength, which accounts for confounding factors related to mass and evaluates concurrent health risks associated with increased body size and low muscle strength [30]. Therefore, in the Chinese middle age and older population, it is recommended that the CM risks be evaluated by considering grip strength in relation to BMI status, rather than assuming absolute grip strength. Moreover, we did not monitor a relationship between grip strength and CM

in participants with diabetes, which may be because of a mixture of factors at baseline. No association between muscle strength and CM in participants with stroke was detected, probably because the relatively small sample size or muscle strength was significantly affected by stroke events [31]. Notably, as far as our information, the association between muscle strength and progression from non-CMD to CM was not proven, possibly due to the relatively short follow-up time. A work from Kadoorie Biobank in China indicated that the age gap between participants with non-CMD and CM is beyond ten years [4]. Therefore, given the correlation between muscle strength and the progress of CMD, as well as the development of CM from FCMD, muscle strength may be a meaningful predictor of the development of CM in people without CMD.

The underlying mechanism of the association between low muscle strength and increased odds of CM has yet to be fully figured out, yet several explanations may exist. First, poor muscle strength is correlated with unfavorable cardiometabolic markers, such

Table 3 Cox proportional hazards regression of association between absolute grip strength and CM

Variables	cases, No	HR (95% CIs)		
		Model1 ^a	Model2 ^b	Model3 ^c
Without CMD at baseline				
High	83	Reference	Reference	Reference
Middle	76	0.85(0.62,1.16)	0.72(0.52,0.98) *	0.79(0.58,1.09)
Low	76	0.92(0.67,1.26)	0.63(0.45,0.89) #	0.77(0.55,1.10)
<i>P</i> for trend		0.96(0.82,1.12)	0.79(0.67,0.94) #	0.88(0.74,1.05)
With diabetes at baseline				
High	42	Reference	Reference	Reference
Middle	56	1.16(0.78,1.73)	1.01(0.67,1.52)	1.21(0.79,1.84)
Low	42	0.93(0.60,1.42)	0.69(0.42,1.12)	0.86(0.52,1.42)
<i>P</i> for trend		0.96(0.78,1.18)	0.83(0.66,1.06)	0.94(0.73,1.19)
With heart disease at baseline				
High	37	Reference	Reference	Reference
Middle	41	1.17(0.75,1.83)	1.20(0.76,1.88)	1.20(0.76,1.90)
Low	41	1.31(0.84,2.04)	1.35(0.83,2.17)	1.44(0.90,2.32)
<i>P</i> for trend		1.14(0.92,1.43)	1.16(0.91,1.47)	1.20(0.95,1.52)
With stroke at baseline				
High	8	Reference	Reference	Reference
Middle	7	1.25(0.45,3.45)	1.37(0.49,3.81)	1.36(0.45,4.08)
Low	7	1.01(0.36,2.79)	1.37(0.47,3.95)	1.34(0.40,4.52)
<i>P</i> for trend		1.01(0.61,1.65)	1.17(0.70,1.97)	1.17(0.64,2.12)

Abbreviation: HR hazard ratio, CIs confidence interval, CM cardiometabolic multimorbidity, CMD cardiometabolic diseases

^a Model 1 was unadjusted

^b Model 2 was adjusted for age, gender

^c Model 3 was adjusted for age, gender, residence, marital status, educational level, drinking status, smoking status, body mass index, and hypertension

**P* < 0.05

P < 0.01

as glycosylated hemoglobin (HbA1c) [32] and uric acid (UA) [33]. In many fields, HbA1c plays a pivotal role in facilitating the identification of diabetes while also offering valuable insights into the pathogenesis of CVD [34]. Clinical research and experiments have reported that UA can induce insulin resistance by stimulating adenosine monophosphate dehydrogenase and inhibiting adenosine monophosphate kinase. It can also instigate oxidative stress-mediated vascular damage, ultimately culminating in CVD [35]. Second, lower muscle strength results in higher inflammation levels. For instance, C-reactive protein, a marker of both acute and chronic phase inflammation, is associated with a higher risk of the development of diabetes and CVD [11, 36]. Meanwhile, inflammatory conditions enhance muscle strength loss and fat accumulation in skeletal muscle in a vicious circle [37]. Third, during physical activity, skeletal muscle can produce various myokines that regulate energy expenditure, insulin sensitivity, lipid metabolism, and metabolism within the organism. For instance, insufficient IL-6 functionality may result

in impaired lipolysis, fat oxidation, and peripheral insulin-stimulated glucose uptake, leading to diabetes and CVD progression [38, 39]. Finally, low muscle strength may attenuate physical function and thus bring about less time for physical exercise or obesity, regarded as common causes of the development of diabetes, heart disease, and stroke [40, 41].

Our research has several strengths. First, our data were derived from a nationally longitudinal survey with a large sample size of middle-aged and older Chinese adults. Second, this is the first study to examine the longitudinal association between muscle strength and CM in Chinese population after adjustment for potential confounding. Despite the strength of this study, some limitations need to be taken into consideration. Firstly, although a series of confounding factors had been adjusted based on prior knowledge, residual confounding from physical activity and diet status still existed. Secondly, physician-diagnosed diabetes, heart disease, and stroke were obtained through self-report, which may lead to some degree of information bias. However, Xie et al. reported that 77.5%

Table 4 Cox proportional hazards regression of association between chair-rising time and CM

Variables	cases, No	Model1 ^a	HR (95%CIs) Model2 ^b	Model3 ^c
Without CMD at baseline				
Low	61	Reference	Reference	Reference
Middle	69	1.15(0.81,1.62)	1.07(0.76,1.52)	0.95(0.67,1.34)
High	105	1.81(1.32,2.48) [§]	1.57(1.13,2.17) [#]	1.37(0.99,1.90)
<i>P</i> for trend		1.36(1.16,1.60) [§]	1.27(1.08,1.50) [#]	1.19(1.01,1.41) [*]
With diabetes at baseline				
Low	35	Reference	Reference	Reference
Middle	44	1.32(0.85,2.06)	1.29(0.83,2.02)	1.24(0.79,1.94)
High	61	2.10(1.38,3.18) [§]	1.98(1.29,3.05) [#]	1.85(1.20,2.86) [#]
<i>P</i> for trend		1.46(1.19,1.80) [§]	1.42(1.14,1.76) [#]	1.37(1.10,1.71) [#]
With heart disease at baseline				
Low	29	Reference	Reference	Reference
Middle	45	1.60(1.00,2.56) [*]	1.62(1.01,2.59) [*]	1.42(0.88,2.29)
High	45	1.80(1.13,2.87) [*]	1.82(1.13,2.93) [*]	1.67(1.04,2.70) [*]
<i>P</i> for trend		1.32(1.06,1.65) [*]	1.33(1.06,1.67) [*]	1.28(1.02,1.62) [*]
With stroke at baseline				
Low	9	Reference	Reference	Reference
Middle	7	0.77(0.29,2.08)	0.69(0.26,1.87)	0.95(0.30,3.03)
High	6	0.69(0.24,1.93)	0.80(0.28,2.31)	0.92(0.26,3.26)
<i>P</i> for trend		0.82(0.49,1.39)	0.88(0.51,1.51)	0.96(0.51,1.80)

Abbreviation: HR hazard ratio, CIs confidence interval, CM cardiometabolic multimorbidity, CMD cardiometabolic diseases

^a Model 1 was unadjusted

^b Model 2 was adjusted for age, gender

^c Model 3 was adjusted for age, gender, residence, marital status, educational level, drinking status, smoking status, body mass index, and hypertension

**P* < 0.05

P < 0.01

§ *P* < 0.001

of self-reported coronary heart disease events were confirmed by medical records [42]. Thirdly, information on death for wave 3 and wave 4 has not yet been released, thereby, outcomes of participants were not fully available, which may underestimate the association between muscle strength and CM. Fourthly, our study exclusively recruited Chinese participants; therefore, further investigations would be required to generalize our findings to other ethnic populations. Fifthly, the selection bias might occur because the difference in baseline characteristics between the included and excluded populations. Finally, this longitudinal cohort study is an observational study, a further community intervention study was warranted to infer causality.

Conclusion

This study provided evidence that, among middle-aged and older Chinese adults, low relative grip strength was associated with a higher risk of incident CM in

individuals with heart disease, while high chair-rising time was associated with a higher risk of incident CM in individuals with diabetes or heart disease. Therefore, building up both upper and lower limb muscle strength may be a feasible measure to delay the development of CM in Chinese middle-aged and older populations with diabetes or heart disease.

Abbreviations

CM	Cardiometabolic multimorbidity
CMD	Cardiometabolic Diseases
CVD	Cardiovascular Disease
FCMD	First Cardiometabolic Diseases
CHARLS	China Health and Retirement Longitudinal Study
BMI	Body Mass Index
SD	Standard Deviation
HR	Hazard Ratios
CIs	Confidence Intervals
HbA1c	Glycosylated Hemoglobin
UA	Uric Acid

Supplementary Material 1.

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Authors' contributions

WJX contributed to conceptualization, data collection, data analysis, writing the original draft and editing of the paper. YY, SQ, and WJJ contributed to data analysis, review and editing of the paper. ZH, ZJX and CYQ contributed to data collection, data analysis and review of the paper. WY contributed to study conceptualization, methodology, supervision, review and editing of the paper. All authors have read and approved the manuscript.

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Availability of data and materials

Data supporting the findings are from the China Health and Retirement Longitudinal Study (CHARLS), which are available online at <http://charls.pku.edu.cn>.

Declarations

Ethics approval and consent to participate

This study was conformed to the Declaration of Helsinki and approved by the Peking University Biomedical Ethics Committee, with all participants signing informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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