

Physical Activity, Muscle Phenotypes, and Functional Health Outcomes Among Middle-Aged and Older Chinese Adults: A Multi-wave Cohort Study Using CHARLS

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Abstract

Background

Physical activity and muscle health are important public health targets for preventing functional decline in ageing populations. Evidence integrating physical activity, subsequent muscle abnormalities, and later functional outcomes within the same cohort remains limited.

Methods

This study used China Health and Retirement Longitudinal Study (CHARLS) 2011, 2015 and 2018 data. The baseline analytic cohort included 4,323 adults aged 50 years or older with assessable muscle phenotype and physical activity information. Primary physical activity exposures were participation (> 0 vs 0 min/week) in vigorous, moderate-intensity and walking activities. Four-category muscle phenotypes were analyzed using multinomial logistic regression, and binary muscle outcomes and functional outcomes were analyzed using modified Poisson regression with community-clustered robust standard errors.

Results

At baseline, 2,595 participants (60.0%) had normal muscle phenotype, 961 (22.2%) had isolated low muscle mass, 420 (9.7%) had isolated low grip strength and 347 (8.0%) had the sarcopenia phenotype. In cross-sectional analyses, moderate-intensity activity and walking were inversely associated with low-grip-strength phenotypes, whereas vigorous activity was positively associated with isolated low muscle mass. During 2011–2015 follow-up, 172 sarcopenia-phenotype events, 401 low-grip-strength events and 175 equation-estimated low-muscle-mass events were observed, and baseline physical activity was not consistently associated with these newly observed muscle abnormalities. In 2015–2018 analyses, isolated low grip strength was associated with incident instrumental activities of daily living (IADL) limitation (RR = 1.550, 95% CI 1.209–1.989) and self-rated health deterioration (RR = 1.115, 95% CI 1.010–1.231). The sarcopenia phenotype was also associated with self-rated health deterioration (RR = 1.186, 95% CI 1.053–1.336), while isolated low muscle mass showed weaker associations.

Conclusions

Physical activity was more consistently associated with concurrent muscle strength than with later newly observed muscle abnormalities. Low-grip-strength phenotypes in 2015 showed clearer prospective associations with later functional and self-rated health outcomes than equation-estimated low muscle mass.

1 Introduction

Population ageing is making muscle health an important public health issue among middle-aged and older adults in China. According to the National Bureau of Statistics of China, by the end of 2025 the population aged 60 years or older had reached 323 million, accounting for 23.0% of the total population, while the population aged 65 years or older was approximately 224 million, accounting for 15.9% [1]. Alongside this demographic shift, the burden of sarcopenia and muscle-function decline remains substantial. A study based on nationally representative CHARLS data reported that the weighted prevalence of sarcopenia among middle-aged and older Chinese adults remained high from 2011 to 2015, and that both possible sarcopenia and sarcopenia were associated with increased long-term mortality risk [2]. Another national cohort study also found that possible sarcopenia was associated with higher all-cause mortality and poorer functional independence [3].

Physical activity is an important and modifiable health behaviour in midlife and later life. A CHARLS 2020 study showed marked differences in physical activity levels among middle-aged and older adults, with the proportion meeting recommended activity levels decreasing with age [4]. Physical activity also changes over time; in CHARLS 2011–2015 data, remaining active or shifting from inactivity to activity was associated with lower risks of sarcopenia and low muscle strength [5]. These findings suggest that assessing overall physical activity at a single time point may not fully capture long-term exposure, and that different muscle-health indicators may respond differently to changes in physical activity.

The public health importance of impaired muscle health is also reflected in its close association with subsequent functional impairment, falls and fractures. Previous CHARLS studies have shown that possible sarcopenia and sarcopenia are associated with increased risks of incident IADL disability, hip fracture, falls and disability [6–9]. These findings further suggest that muscle mass, muscle strength and physical function may represent different dimensions of muscle health and may not have identical long-term health implications.

Although epidemiological evidence on sarcopenia among middle-aged and older Chinese adults continues to accumulate, existing studies have mostly used overall sarcopenia or possible sarcopenia as the exposure or outcome and have examined individual health outcomes separately [2, 3, 6–9]. Relatively little evidence is available from integrative longitudinal studies that distinguish muscle mass, muscle strength and their combined phenotypes within the same nationally representative cohort and examine their relations with physical activity and later functional outcomes across sequential follow-up windows. An integrated analysis separating muscle mass and grip strength across sequential follow-up windows may help clarify these associations.

Therefore, using multiple waves of CHARLS data from 2011, 2015 and 2018, this study first examined the cross-sectional association between physical activity and concurrent muscle phenotypes in 2011; then evaluated the longitudinal associations of 2011 physical activity with newly observed low grip strength, equation-estimated low muscle mass and the sarcopenia phenotype in 2015; and further investigated the associations of 2015 muscle phenotypes with functional health outcomes in 2018.

2 Methods

2.1 Study Population and Design

Data were obtained from the China Health and Retirement Longitudinal Study (CHARLS). CHARLS is a nationally representative longitudinal survey of Chinese adults aged 45 years or older, using a multistage, stratified, probability-proportional-to-size sampling design that covers 28 provinces, 150 counties or districts and 450 villages or communities in China. The national baseline survey was conducted in 2011, with follow-up surveys in 2013, 2015 and 2018 [10].

This study used data from the 2011, 2015 and 2018 waves and included three analytic stages: (1) a cross-sectional analysis of physical activity and concurrent muscle phenotypes in 2011; (2) analyses of 2011 physical activity and newly observed muscle abnormalities in 2015 among participants free of the corresponding abnormality at baseline; and (3) analyses of 2015 muscle phenotypes as exposures in relation to functional health outcomes in 2018.

Participants aged 50 years or older were eligible for inclusion. The main exclusion criteria were: (1) missing age information or age younger than 50 years; (2) missing grip-strength or muscle-mass-related information; and (3) missing physical activity participation information. Stage-specific analytic samples were further constructed according to the completeness of the relevant exposures, outcomes and covariates.

2.2 Physical Activity Classification

Based on the CHARLS physical activity questionnaire, physical activity was classified as vigorous physical activity, moderate-intensity physical activity and walking. The primary exposure was participation in each activity type (> 0 vs 0 min/week). Weekly frequency, duration per session and estimated weekly activity time were used for supplementary descriptive or sensitivity analyses.

In the 2015–2018 analyses, prior physical activity participation breadth was additionally calculated according to participation in the three activity types in 2011. Participation in 0–1 activity type was defined as limited participation, and participation in 2–3 activity types was defined as broader participation. This measure was an exploratory composite indicator used to evaluate the potential influence of prior physical activity participation on the association between muscle phenotypes and later health outcomes.

2.3 Muscle Phenotypes

Muscle strength was assessed using grip strength. In CHARLS, trained interviewers measured grip strength twice for each hand using a dynamometer. In this study, the maximum value among all valid grip-strength measurements was used for analysis. According to the age- and sex-specific cut-points recommended by the Asian Working Group for Sarcopenia 2025 (AWGS 2025), low grip strength was

defined as grip strength < 34 kg in men aged 50–64 years, < 20 kg in women aged 50–64 years, < 28 kg in men aged 65 years or older and < 18 kg in women aged 65 years or older [11].

Appendicular skeletal muscle mass (ASM) was estimated using an anthropometric prediction equation validated in Chinese adults [12]: $ASM (kg) = 0.193 \times \text{weight (kg)} + 0.107 \times \text{height (cm)} - 4.157 \times \text{sex} - 0.037 \times \text{age (years)} - 2.631$, where men = 1 and women = 2. The appendicular skeletal muscle mass index (ASMI) was calculated as ASM divided by height squared. AWGS 2025 DXA reference cut-points were applied to equation-estimated ASMI to construct operational phenotype categories; therefore, this study uses the term equation-estimated low muscle mass rather than dual-energy X-ray absorptiometry (DXA)- or bioelectrical impedance analysis (BIA)-measured muscle mass[11, 12]. For participants aged 50–64 years, low ASMI was defined as < 7.2 kg/m² in men and < 5.5 kg/m² in women; for those aged ≥ 65 years, the corresponding thresholds were < 7.0 kg/m² and < 5.4 kg/m², respectively.

Participants were classified into four mutually exclusive muscle phenotypes according to the combined status of low grip strength and equation-estimated low muscle mass: normal muscle phenotype, isolated low muscle mass, isolated low grip strength and the sarcopenia phenotype. The normal muscle phenotype was used as the reference group in regression models.

2.4 Functional Health Outcomes in 2018

Two co-primary outcomes were defined in 2018: incident instrumental activities of daily living (IADL) limitation and self-rated health deterioration. Incident IADL limitation was assessed only among participants without IADL limitation in 2015 and was defined as new difficulty, need for help or inability to perform any standard IADL item in 2018. Self-rated health deterioration was dichotomized using the 2018 question on health status compared with the previous wave, with participants reporting worse health than in the previous wave coded as events.

Secondary outcomes included ADL limitation, depressive symptoms, self-rated health, falls, pain and social participation. ADL limitation was defined as difficulty, need for help or inability to perform any of six basic ADL items; IADL limitation was defined analogously using standard IADL items available in CHARLS. Depressive symptoms were defined as a CES-D10 score ≥ 10 using complete 10-item responses. Incident falls were based on reported falls during follow-up, pain was defined as moderate or severe body pain in 2018 among participants without body pain in 2015, and absence of social activity was defined from the CHARLS social participation items. Detailed variable construction rules are provided in the Supplementary Methods and Supplementary Table S6.

2.5 Covariates and Statistical Analysis

Covariates included sociodemographic factors, health behaviours and comorbidity burden. Sociodemographic factors included age, sex, residence, region, education, marital status and employment status; health behaviours included current smoking status, alcohol consumption and sleep duration; and comorbidity burden was represented by the number of chronic diseases, categorized as 0, 1 and ≥ 2. Obesity in 2015 was defined as BMI ≥ 28 kg/m² or central obesity, with central obesity defined

as waist circumference ≥ 90 cm in men or ≥ 85 cm in women [11]. Obesity status was included only in sensitivity analyses. Continuous variables were described using means and standard deviations or medians and interquartile ranges, and categorical variables were described using counts and percentages.

Four-category muscle phenotypes were analyzed using multinomial logistic regression with the normal muscle phenotype as the reference group, and relative risk ratios (RRRs) were reported. Supplementary cross-sectional analyses treating low grip strength and equation-estimated low muscle mass as separate binary outcomes used modified Poisson regression and reported prevalence ratios (PRs). Longitudinal binary outcomes were analyzed using modified Poisson regression to estimate risk ratios (RRs) and 95% confidence intervals, with community-clustered HC1 robust standard errors [13].

For analyses of 2011 physical activity with concurrent and 2015 muscle outcomes, sequential adjustment models were used: Model 1 was unadjusted; Model 2 adjusted for age and sex; Model 3 additionally adjusted for residence, region, education, marital status and employment status; Model 4 additionally adjusted for smoking, alcohol consumption and sleep duration; and Model 5 additionally adjusted for the number of chronic diseases. The 2011–2015 longitudinal analyses used risk sets free of the corresponding muscle abnormality at baseline. For these longitudinal analyses, Model 4 was considered the primary adjusted model because chronic disease burden may partly reflect health status on pathways linking physical activity with later muscle health; Model 5 provided additional adjustment for chronic disease burden. BH-FDR correction was applied across the 2011–2015 physical activity-muscle outcome comparison family [14]. The analyses focused on association estimation rather than population prevalence estimation and were therefore conducted without survey weights; clustering at the community level was accounted for using robust standard errors.

For analyses of 2015 muscle phenotypes and 2018 functional health outcomes, Model A adjusted for age, sex, education, residence and marital status; Model B additionally adjusted for smoking, alcohol consumption, sleep duration and number of chronic diseases; and Model C additionally included prior physical activity participation breadth in 2011. The two co-primary outcomes were not FDR-corrected. Overall P values for muscle phenotype were obtained from global 3-df Wald tests for the muscle phenotype variable in Model C. Secondary 2015–2018 phenotype-outcome comparisons were corrected as a separate BH-FDR family.

Loss to follow-up was assessed using stabilized inverse probability of censoring weights (IPCW) in sensitivity analyses. For each longitudinal stage, stabilized IPCW models estimated the probability of outcome observation at the corresponding follow-up wave using covariates measured at the relevant baseline. For the 2011–2015 stage, weights estimated observation of 2015 muscle outcomes; for the 2015–2018 stage, weights estimated observation of 2018 functional health outcomes. P1/P99 truncation was used as a sensitivity procedure [15]. Obesity status was further adjusted for in sensitivity analyses, and an additional sensitivity analysis for self-rated health deterioration adjusted for baseline self-rated health in 2015. Joint exposure analyses combined 2015 muscle abnormality, defined as

isolated low muscle mass, isolated low grip strength or the sarcopenia phenotype, with 2011 prior physical activity participation breadth and evaluated interaction using multiplicative interaction terms, the relative excess risk due to interaction (RERI) and the attributable proportion (AP); additive interaction was interpreted according to epidemiological recommendations [16]. All statistical analyses were performed using R version 4.6.1. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

3 Results

3.1 Study Population

Baseline characteristics are shown in Table 1. In 2011, 4,323 participants with classifiable muscle phenotypes were included. The mean age was 62.17 ± 8.24 years, and 2,080 participants (48.1%) were men. According to muscle mass and grip-strength status, 2,595 participants (60.0%) were classified as having a normal muscle phenotype, 961 (22.2%) as isolated low muscle mass, 420 (9.7%) as isolated low grip strength and 347 (8.0%) as the sarcopenia phenotype. Overall, the sarcopenia phenotype group was the oldest and had the lowest BMI and estimated ASMI, as well as higher proportions of ADL and IADL limitations; the isolated low grip strength and sarcopenia phenotype groups had substantially lower maximum grip strength than the normal muscle phenotype group.

Table 1. Baseline characteristics by muscle phenotype in 2011

Variable	Total n=4323	Normal muscle phenotype n = 2595	Isolated low muscle mass n = 961	Isolated low grip strength n = 420	Sarcopenia phenotype n = 347
Age, years	62.17 ± 8.24	60.39 ± 7.24	64.45 ± 8.45	63.18 ± 8.33	67.91 ± 10.01
Sex, n/N (%)					
Male	2080(48.1%)	1222(47.1%)	413(43.0%)	253(60.2%)	192(55.3%)
Female	2243 (51.9%)	1373(52.9%)	548(57.0%)	167(39.8%)	155(44.7%)
BMI, kg/m ²	23.34 ± 3.90	25.03 ± 3.32	19.55 ± 1.66	24.92 ± 3.54	19.27 ± 1.86
Residence, n/N (%)					
Rural	2733 (63.2%)	1513(58.3%)	707(73.6%)	259(61.7%)	254(73.2%)
Urban	1590 (36.8%)	1082(41.7%)	254(26.4%)	161(38.3%)	93(26.8%)
Education, n/N (%)					
Primary school and below	3175(73.5%)	1763(63.9%)	783(81.5%)	234(77.2%)	306(88.2%)
Junior high school and above	1147(26.5%)	832(32.1%)	178(18.5%)	96(22.8%)	41(11.8%)
Currently employed, n/N (%)	2852(66.0%)	1737(67.0%)	687(71.6%)	233(55.6%)	195(56.2%)
Current smoking, n/N (%)	1726 (39.9%)	993(38.2%)	390(40.6%)	182(43.3%)	161(46.4%)
Alcohol consumption, n/N (%)	1385(32.0%)	846(32.6%)	298(31.0%)	127(30.2%)	114(32.9%)
Sleep duration, hours/night	6.32 ± 1.88	6.44 ± 1.75	6.16 ± 2.05	6.22 ± 1.96	5.99 ± 2.12
ADL limitation, n/N (%)	764(25.4%)	392(22.7%)	158(23.8%)	107(30.7%)	107(39.2%)
IADL limitation, n/N (%)	925(21.4%)	438(16.9%)	229(23.9%)	131(31.2%)	127(36.8%)

Variable	Total n=4323	Normal muscle phenotype n = 2595	Isolated low muscle mass n = 961	Isolated low grip strength n = 420	Sarcopenia phenotype n = 347
Maximum grip strength, kg	31.61 ± 10.20	34.96 ± 9.35	31.00 ± 8.21	21.59 ± 7.49	20.44 ± 7.50
ASMI, kg/m ²	6.69 ± 1.15	7.05 ± 1.00	5.78 ± 0.96	7.20 ± 1.01	5.87 ± 1.00
Number of chronic diseases, n/N (%)					
0	1632(38.5%)	946(37.2%)	444(47.1%)	114(27.8%)	128(37.6%)
1	1419(33.5%)	847(33.3%)	311(33.0%)	132(32.2%)	129(37.9%)
≥2	1188(28.0%)	753(29.6%)	188(19.9%)	164(40.0%)	83(24.4%)
Vigorous PA participation, n/N (%)	1475(34.1%)	855(32.9%)	389(40.5%)	130(31.0%)	101(29.1%)
Moderate PA participation, n/N (%)	2441(56.5%)	1532(59.0%)	572(59.5%)	182(43.3%)	155(44.7%)
Walking participation, n/N (%)	3480(80.5%)	2123(81.8%)	785(81.7%)	319(76.0%)	253(72.9%)

Abbreviations: ADL, activities of daily living; ASMI, appendicular skeletal muscle mass index; IADL, instrumental activities of daily living; PA, physical activity.

3.2 Cross-sectional Associations Between Physical Activity and Muscle Phenotypes in 2011

Physical activity participation differed across muscle phenotype groups in 2011 (Table 1). After full covariate adjustment, with the normal muscle phenotype as the reference group, moderate-intensity physical activity was associated with lower relative risks of isolated low grip strength (RRR = 0.592, 95% CI 0.443–0.765) and the sarcopenia phenotype (RRR = 0.707, 95% CI 0.529–0.960). Walking was also inversely associated with isolated low grip strength (RRR = 0.633, 95% CI 0.457–0.869) and the sarcopenia phenotype (RRR = 0.636, 95% CI 0.468–0.878), but was not significantly associated with isolated low muscle mass (Table 2).

Vigorous activity was positively associated with isolated low muscle mass in the multinomial analysis (Model 5 RRR = 1.295, 95% CI 1.071–1.580), although this association was not consistently supported in the binary or FDR-adjusted analyses. When low grip strength and equation-estimated low muscle mass

were further analyzed as separate outcomes, moderate-intensity physical activity and walking remained more consistently associated with lower prevalence of low grip strength, whereas their associations with equation-estimated low muscle mass were more limited (Supplementary Table S1).

Table 2. Cross-sectional associations between physical activity participation and muscle phenotypes in 2011

Activity	Muscle phenotype	Model 5 RRR (95% CI)
Vigorous activity	Normal muscle phenotype	Reference
	Isolated low muscle mass	1.295 (1.071–1.580)
	Isolated low grip strength	1.056 (0.770–1.450)
	Sarcopenia phenotype	0.875 (0.609–1.270)
Moderate-intensity activity	Normal muscle phenotype	Reference
	Isolated low muscle mass	1.013 (0.834–1.226)
	Isolated low grip strength	0.592 (0.443–0.765)
	Sarcopenia phenotype	0.707 (0.529–0.960)
Walking	Normal muscle phenotype	Reference
	Isolated low muscle mass	0.885 (0.708–1.118)
	Isolated low grip strength	0.633 (0.457–0.869)
	Sarcopenia phenotype	0.636 (0.468–0.878)

Normal muscle phenotype was the reference group. Values are Model 5 RRRs and 95% CIs from multinomial logistic regression.

Model 5 adjusted for age, sex, residence, region, education, marital status, employment status, smoking, alcohol consumption, sleep duration and number of chronic diseases.

3.3 Longitudinal Associations of 2011 Physical Activity With Newly Observed Muscle Abnormalities in 2015

Outcome-specific risk sets free of the corresponding muscle abnormality at baseline were constructed. During 2011–2015 follow-up, 172 newly observed sarcopenia-phenotype events, 401 newly observed low-grip-strength events and 175 newly observed low-muscle-mass events were identified. Vigorous physical activity, moderate-intensity physical activity and walking in 2011 were not consistently associated with these newly observed muscle abnormalities in 2015 (Figure 1). Across Models 1–5, from the unadjusted model to models sequentially adjusted for sociodemographic factors, health

behaviours and chronic disease burden, effect estimates were generally stable (Supplementary Table S2). After further use of stabilized IPCW and P1/P99 weight truncation, the directions and magnitudes of the estimates were broadly consistent with complete-case analyses (Supplementary Table S3).

3.4 Longitudinal Associations of 2015 Muscle Phenotypes With Functional Health Outcomes in 2018

In 2015, 3,066 participants had classifiable muscle phenotypes. Outcome-specific analytic samples were constructed according to baseline outcome status, 2018 follow-up and covariate completeness. Finally, 1,966 participants were included in the incident IADL limitation analysis, with 416 events, and 2,678 participants were included in the self-rated health deterioration analysis, with 1,492 events (Supplementary Table S4).

In fully adjusted Model C, 2015 muscle phenotype was significantly associated with incident IADL limitation in 2018 (overall $P = 0.005$). Compared with the normal muscle phenotype, isolated low grip strength was significantly associated with a higher risk of incident IADL limitation ($RR = 1.550$, 95% CI 1.209–1.989), whereas isolated low muscle mass ($RR = 1.246$, 95% CI 0.995–1.559) and the sarcopenia phenotype ($RR = 1.186$, 95% CI 0.864–1.629) did not reach statistical significance (Table 3; Figure 2).

For self-rated health deterioration, the overall association with muscle phenotype was also statistically significant (overall $P = 0.019$). Isolated low grip strength ($RR = 1.115$, 95% CI 1.010–1.231) and the sarcopenia phenotype ($RR = 1.186$, 95% CI 1.053–1.336) were both significantly associated with higher risk of self-rated health deterioration, whereas isolated low muscle mass showed no significant association ($RR = 1.076$, 95% CI 0.981–1.180) (Table 3; Figure 2). From Model A to Model C, after sequential adjustment for sociodemographic characteristics, health behaviours, chronic disease burden and prior physical activity, the main effect directions and magnitudes were generally stable.

After further use of stabilized IPCW and alternative weight handling, the main effect estimates were broadly consistent with complete-case analyses; further adjustment for obesity status also did not materially change the results (Supplementary Table S5). After additional adjustment for baseline self-rated health in 2015, the association with self-rated health deterioration was attenuated for the sarcopenia phenotype ($RR = 1.068$, 95% CI 0.901–1.265) and remained positive for isolated low grip strength ($RR = 1.151$, 95% CI 1.001–1.322) (Supplementary Table S5). In secondary outcome analyses, isolated low grip strength was also associated with higher risks of incident ADL limitation and incident depressive symptoms, and these associations remained statistically significant after FDR correction (Supplementary Table S6).

Table 3. Associations between muscle phenotypes in 2015 and functional health outcomes in 2018

Outcome	Muscle phenotype	Model A RR (95% CI)	Model B RR (95% CI)	Model C RR (95% CI)	Overall P†
Incident IADL limitation	Normal muscle phenotype	Reference	Reference	Reference	0.005
	Isolated low muscle mass	1.151 (0.924–1.435)	1.232 (0.983–1.543)	1.246 (0.995–1.559)	
	Isolated low grip strength	1.548 (1.204–1.990)	1.544 (1.201–1.985)	1.550 (1.209–1.989)	
	Sarcopenia phenotype	1.127 (0.829–1.533)	1.183 (0.862–1.625)	1.186 (0.864–1.629)	
Self-rated health deterioration	Normal muscle phenotype	Reference	Reference	Reference	0.019
	Isolated low muscle mass	1.043 (0.952–1.143)	1.079 (0.984–1.184)	1.076 (0.981–1.180)	
	Isolated low grip strength	1.135 (1.028–1.254)	1.112 (1.007–1.228)	1.115 (1.010–1.231)	
	Sarcopenia phenotype	1.157 (1.029–1.302)	1.182 (1.050–1.331)	1.186 (1.053–1.336)	

Model A: adjusted for age, sex, education, residence, and marital status.

Model B: additionally adjusted for smoking, alcohol consumption, sleep duration, and number of chronic diseases.

Model C: additionally adjusted for prior physical activity participation breadth in 2011.

Model C included 1,966 participants with 416 incident IADL limitation events and 2,678 participants with 1,492 self-rated health deterioration events.

Normal muscle phenotype was the reference group. Overall P values were obtained from global 3-df Wald tests for muscle phenotype in Model C. Modified Poisson regression with community-clustered HC1 robust standard errors was used.

3.5 Exploratory Joint Associations of Prior Physical Activity and Muscle Abnormalities

Compared with participants with a normal muscle phenotype and broader prior physical activity participation, those with muscle abnormality and limited prior physical activity participation had the highest risk of incident IADL limitation (RR = 1.575, 95% CI 1.216–2.039). However, no clear multiplicative interaction was observed (P for interaction = 0.803), and additive interaction measures were also not statistically significant (RERI = 0.115; AP = 0.073). Analyses of self-rated health deterioration likewise did not show clear evidence of interaction (Supplementary Table S7).

4 Discussion

Using multiple waves of CHARLS data from 2011, 2015 and 2018, this study examined associations among physical activity, muscle health and subsequent functional outcomes. The main findings showed that, in cross-sectional analyses, associations between different physical activity dimensions and muscle health were not identical: moderate-intensity physical activity and walking were relatively consistently associated with low-grip-strength phenotypes, whereas associations with low muscle mass were weaker. In the 2011–2015 longitudinal analyses, baseline physical activity did not stably predict newly observed muscle abnormalities. Further analyses showed that low-grip-strength phenotypes in 2015, especially isolated low grip strength, had clearer prospective associations with IADL limitation and self-rated health deterioration in 2018.

Previous evidence generally supports an association between higher physical activity levels and better muscle health [17]. The cross-sectional results of this study are broadly consistent with this pattern, but the associations were mainly evident for low grip strength. Muscle mass and muscle strength do not necessarily change in parallel, and age-related strength decline is also influenced by motor-unit loss, neuromuscular-junction degeneration, mitochondrial dysfunction and changes in muscle quality [18]. Exercise, especially resistance training, can improve muscle mass, but improvements are often more apparent for grip strength and other muscle-strength indicators [19,20]. The positive association between vigorous physical activity and isolated low muscle mass should not be interpreted causally; vigorous activity in CHARLS may include substantial occupational physical labour, and low muscle mass is strongly influenced by BMI and body size.

Compared with the cross-sectional findings, this study did not observe a stable predictive association between physical activity in 2011 and newly observed muscle abnormalities in 2015. Recent CHARLS studies have reported inconsistent findings on physical activity in relation to incident sarcopenia and its components [21,22], which may reflect differences in outcome definitions, risk sets, age ranges, physical activity classification and covariate adjustment. In addition, physical activity is a time-varying exposure, and activity among middle-aged and older adults may follow different trajectories with retirement and follow-up time [23,24]. Therefore, using a single baseline physical activity measurement to predict muscle status 4 years later may lead to exposure misclassification and regression dilution.

The clearest finding of this study concerns the association between 2015 muscle phenotypes and later functional health outcomes. Previous studies have shown that low grip strength, possible sarcopenia

and sarcopenia are associated with increased subsequent risks of ADL/IADL disability [25-28]. This study further indicates that isolated low grip strength, even without concurrent equation-estimated low muscle mass, was prospectively associated with incident IADL limitation and self-rated health deterioration, whereas isolated low muscle mass provided relatively weaker risk information. Associations with self-rated health deterioration were less robust after further adjustment for baseline self-rated health and should therefore be interpreted more cautiously than the association with incident IADL limitation. These findings support the utility of grip strength as a simple marker of elevated functional risk among middle-aged and older adults.

One finding requiring interpretation is that the point estimate for isolated low grip strength in relation to IADL limitation was higher than that for the sarcopenia phenotype combining low grip strength and low muscle mass. This should not be interpreted as indicating a lower risk for the combined phenotype. The sarcopenia phenotype group had fewer participants and events, resulting in wider confidence intervals, and equation-estimated muscle mass may have introduced phenotype misclassification, attenuating the effect estimate for the combined phenotype toward the null. The joint exposure analysis showed that participants with both muscle abnormality and limited prior physical activity participation had the highest observed risk, but no clear evidence of additive or multiplicative interaction was found; the result is therefore better interpreted as risk accumulation rather than definite synergy.

This study has several strengths. First, CHARLS provides a national sample base, and this study used three survey waves to examine cross-sectional physical activity and muscle health, physical activity and subsequent newly observed muscle abnormalities, and muscle phenotypes and later functional health outcomes. Second, this study separately evaluated low grip strength, equation-estimated low muscle mass and different combined phenotypes, and constructed corresponding risk sets for different incident outcomes, helping to clarify differences among dimensions of muscle health.

Several limitations should also be noted. Physical activity was measured once at baseline using a self-reported questionnaire, and CHARLS records activity in discrete time categories, which may have caused exposure misclassification and regression dilution. AWGS 2025 low-muscle-mass cut-points were originally based on direct body-composition measurement, whereas this study used a prediction equation to estimate ASM; applying DXA reference thresholds to predicted values may have led to phenotype misclassification. Self-rated health deterioration is a subjective outcome and may be influenced by baseline health perception and reporting characteristics in 2015; although an additional sensitivity model adjusted for baseline self-rated health, residual reporting-related confounding may remain. In addition, missing data and loss to follow-up may have caused selection bias, and the observational design cannot exclude unmeasured confounding or reverse causation.

5 Conclusion

In three waves of CHARLS data from 2011, 2015 and 2018, physical activity was more consistently associated with concurrent muscle-strength-related phenotypes, whereas a single baseline physical

activity measure had limited prospective association with later newly observed muscle abnormalities. Compared with equation-estimated low muscle mass, low-grip-strength phenotypes in 2015 showed the clearest prospective association with incident IADL limitation, with weaker evidence for self-rated health deterioration. Future studies should combine repeated physical activity measurements with more precise muscle-mass assessment to further validate the long-term relations among physical activity, muscle structure, muscle function and later functional health.

Abbreviations

ADL

Activities of daily living

AP

Attributable proportion due to interaction

ASM

Appendicular skeletal muscle mass

ASMI

Appendicular skeletal muscle mass index

AWGS

Asian Working Group for Sarcopenia

BIA

Bioelectrical impedance analysis

BMI

Body mass index

CES-D10

10-item Center for Epidemiologic Studies Depression Scale

CHARLS

China Health and Retirement Longitudinal Study

CI

Confidence interval

DXA

Dual-energy X-ray absorptiometry

FDR

False discovery rate

HC1

Heteroskedasticity-consistent type 1 variance estimator

IADL

Instrumental activities of daily living

IPCW

Inverse probability of censoring weighting

PA

Physical activity

PR

Prevalence ratio

RERI

Relative excess risk due to interaction

RR

Risk ratio

RRR

Relative risk ratio

SD

Standard deviation

Declarations

Ethics Approval and Consent to Participate

CHARLS was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015). Written informed consent was obtained from all participants. The present analysis used publicly available de-identified CHARLS data.

Consent for Publication

Not applicable.

Availability of Data and Materials

The CHARLS datasets are publicly available from the China Health and Retirement Longitudinal Study website upon registration and data use agreement.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

Shiyuan Shao analyzed and interpreted the data and was a major contributor in writing the manuscript. Hongjuan Li provided critical review, commentary, and revision of the manuscript, and supervised the study. Both authors read and approved the final manuscript.

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Figures

Physical activity participation in 2011 and newly observed muscle outcomes in 2015

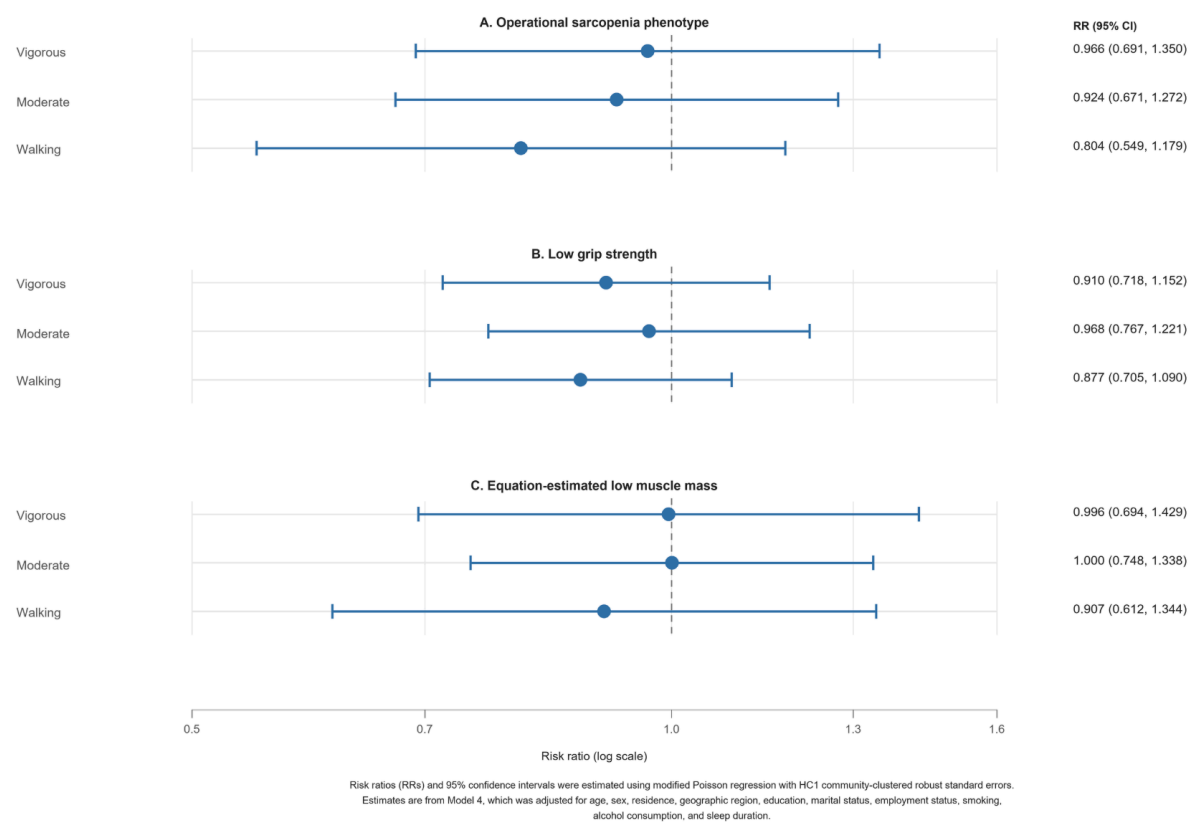


Figure 1

Associations between physical activity participation in 2011 and newly observed muscle abnormalities in 2015. Points and horizontal bars represent risk ratios (RRs) and 95% confidence intervals from Model 4. The dashed vertical line indicates RR = 1.0.

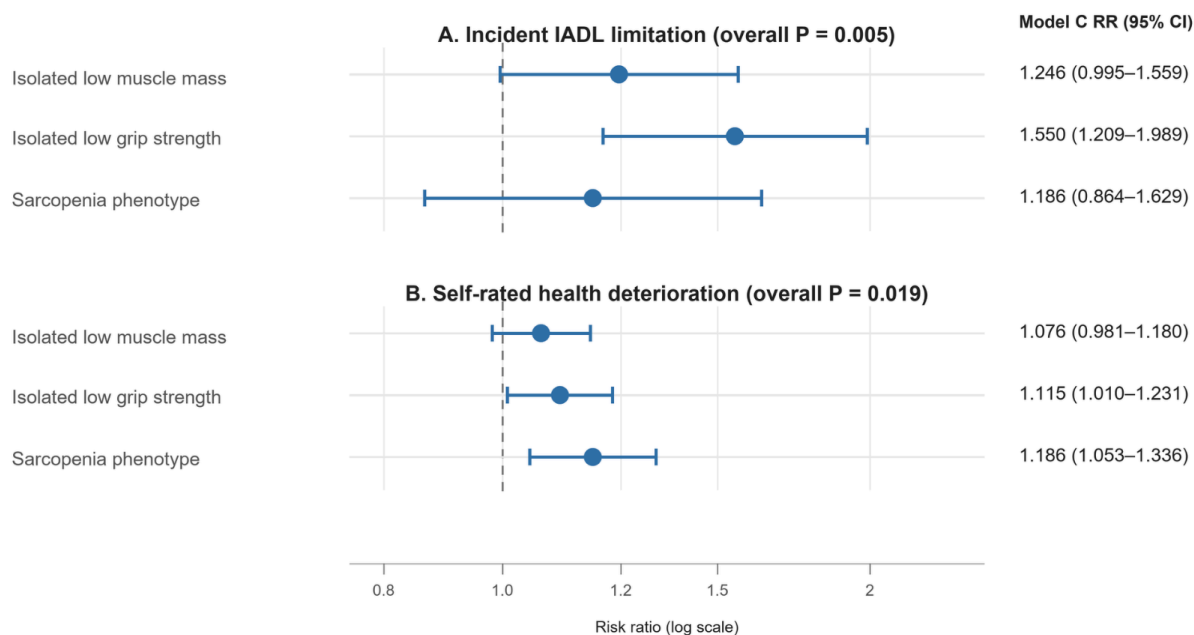


Figure 2

Associations of muscle phenotypes in 2015 with functional health outcomes in 2018. Points and horizontal bars represent risk ratios (RRs) and 95% confidence intervals from Model C. The normal muscle phenotype was the reference group. Model C was adjusted for age, sex, education, residence, marital status, smoking, alcohol consumption, sleep duration, number of chronic diseases, and prior physical activity participation breadth in 2011. Panel A included 1,966 participants with 416 incident IADL limitation events; Panel B included 2,678 participants with 1,492 self-rated health deterioration events. Overall P values were obtained from global 3-df Wald tests for muscle phenotype. The dashed vertical line indicates RR = 1.0.

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- [TableS420152018risksetconstruction4323.xlsx](#)
- [TableS520152018IPCWobesitybaselineSRHsensitivity4323.xlsx](#)
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