Lower extremity function and subsequent risk of cardiovascular incidence among the elderly in China: evidence from a nationwide survey

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Abstract

Aims

Given that little is known about the effect of lower extremity function (LEF) on cardiovascular disease (CVD) subsequent risk among older adults, the association between LEF and CVD in the older Chinese population was investigated by cross-sectional and longitudinal analysis using the nationally representative data from the China Health and Retirement Longitudinal Study (CHARLS).

Methods

The sample comprised 4636 participants aged at least 60 years from the CHARLS 2011. LEF was defined according to the short physical performance battery (SPPB) scores lower than 8. CVD was defined as the presence of physician-diagnosed heart disease and/or stroke. A total of 4636 participants were recruited from the CHARLS 2011 and were followed up in 2018.

Results

The prevalence of CVD in total populations, good LEF, normal LEF, and poor LEF individuals were 19.07%, 16.97%, 20.72%, 24.77%, respectively. Poor LEF was associated with CVD in total populations. In the longitudinal analysis, individuals with poor LEF were more likely to have incident CVD than good LEF peers, especially stroke. In CVD components, compared to good LEF, individuals with poor LEF had higher risks of heart disease and stroke, and they had higher risks of newly onset stroke but not newly onset heart disease.

Conclusion

The results suggest the potential usefulness of the short physical performance battery for classifying stroke risk in older Chinese adults, which also suggested that preventing and/or improving lower extremity function may be beneficial for reducing stroke incidence and promoting healthy aging for older adults.

Introduction

Advancing age stands out as the most influential risk factor in the development of cardiovascular disease (CVD), which remains a leading cause of mortality among middle-aged and older individuals in China [1]. Globally, in 2016, ischemic heart disease and cerebrovascular disease (stroke) accounted for over 85.1% of all CVD-related deaths [2]. Notably, a study has shown that the association between traditional risk factors like total cholesterol, systolic blood pressure, and diabetes with CVD diminishes with age, specifically in older adults aged 65 and above [3]. This suggests that conventional CVD risk
factors, including lipid levels, may have limited predictive value in older adults [4]. Hence, it becomes crucial to identify nontraditional predictors that are relevant for older adults in assessing their risk of developing CVD.

A growing body of evidence highlights the strong association between lower extremity function (LEF) and various negative outcomes, including falls [5], fractures [6], disability [7], dementia [8], and mortality [9]. Recent studies have also investigated the relationship between physical function and CVD [4, 10]. For instance, a study utilizing data from the atherosclerosis risk in communities (ARIC) reported an independent association between LEF and CVD, separate from other traditional risk factors, among 5,570 individuals aged 65 years and older in the United States [4]. However, there is currently a lack of large population-based or nationwide studies that explore the longitudinal link between LEF and CVD risk specifically among older adults in Asia.

The relationship between LEF and CVD requires further investigation. This study aimed to examine the association between LEF, measured using the Short Physical Performance Battery (SPPB), and the risk of developing composite CVD as well as heart disease and stroke individually. The SPPB, a reliable tool developed by the National Institute on Aging (NIA), assesses physical function in older adults [11–13]. It includes tests for standing balance, repeated chair stands, and short-distance gait speed.

The study utilized nationally representative data from the China Health and Retirement Longitudinal Study (CHARLS) to conduct cross-sectional and longitudinal analyses. The objective was to investigate the relationship between LEF and CVD in the older Chinese population. The hypothesis was that individuals with lower LEF would have a higher risk of future CVD incidence and that LEF would enhance CVD risk prediction beyond traditional risk factors in this population.

**Methods**

**Study population**

The CHARLS is an ongoing longitudinal survey that aims to provide nationally representative data. The survey employs a multistage stratified probability-proportionate-to-size sampling method to select participants. It focuses on individuals aged 45 years and older in China. The survey gathers high-quality data through one-on-one interviews using a structured questionnaire. The questionnaire covers various aspects, including demographic information, lifestyle factors, and health-related information. Standardized methods are used to ensure consistency in data collection across all participants.

A comprehensive description of the CHARLS study design has been previously published [14]. For this study, a retrospective analysis was conducted using data from the 2011 to 2018 waves. The inclusion criteria for this study were: (1) individuals aged 60 years or older at baseline, and (2) availability of data on physical function. Exclusion criteria were: (1) missing age information, and (2) lack of data on residence, body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP) at baseline.
The study was divided into two sections. Firstly, in the cross-sectional analysis, data from the baseline were utilized. Out of the 17,708 participants interviewed at baseline, 10,418 individuals were excluded due to being below 60 years of age (n = 10,418), missing data on the Short Physical Performance Battery (SPPB) (n = 2,654), or incomplete information on gender, living status, residence, smoking, drinking, region, or education (n = 2). This resulted in a final sample of 4,636 participants for the cross-sectional analysis and subsequent longitudinal analysis. Secondly, in the sensitivity analysis, an additional 937 subjects with cardiovascular diseases (CVDs) at baseline were excluded. The final analytic sample included 3,699 individuals who did not have CVDs at baseline. A detailed overview of the selection process is presented in Fig. 1.

All participants provided informed consent, and the protocol was approved by the Ethical Review Committee of Peking University (approval number: IRB00001052 – 11,015). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline [15].

**Assessment of lower extremity function**

SPPB, containing chair stands test, standing balance, and gait speed test, was implemented by trained and certified staff[16]. The chair stands test required participants to rise from a chair 5 times with arms folded across their chest. Every individual received a score, according to the time of completion ranging from 0 to 4, higher means better lower body muscle strength. The standing balance for 10 seconds was first examined with the semi-tandem feet position. Once the semi-tandem position was completed, the tandem position was tested. The side-by-side position was assessed only when the semi-tandem balance was not completed. Thus, the total score of standing balance ranged from 0 to 4, higher means better balance ability. In the gait speed test, participants walked 4 m at their usual pace twice, with the result of the faster trial recorded. The score of the gait speed test ranged from 0 to 4. The SPPB total score is the sum of the 3 test scores, ranging from 0 to 12, with higher scores indicating better LEF. For detailed test methods and scoring rules, see Table S1.

**Assessment of CVD events**

The outcomes of interest included the composite and independent outcomes of heart disease and stroke. Briefly, heart disease and stroke events were ascertained through careful evaluation based on self-reported diagnosis and medication [17]. Heart disease was identified by answering 'Yes' to one of the following questions: “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 “Are you now taking any of the following treatments to treat Heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems or its complications? Taking Chinese traditional medicine, taking Western modern medicine, other treatments?”. Stroke was identified by answering 'Yes' to one of the following questions: “Have you been told by a doctor that you have been diagnosed with a stroke?” or “Are you now
taking any of the following treatments to treat stroke or its complications? Taking Chinese traditional medicine, taking Western modern medicine, other treatments?”. CVD events were defined as heart attacks or stroke events occurrence.

**Covariates**

At baseline, demographic variables included age, sex, education (0 years, 1–6 years, and 6 years above), solitary (living alone and with a partner), residence (rural, urban), and region (East, Middle, West, Northeast China). Health-related factors included BMI, smoking, drinking, diabetes, hypertension, self-reported physician-diagnosed dyslipidemia. Diabetes was defined based on the use of insulin, or oral hypoglycemic agents, or plasma glucose ≥ 200 mg/dL, or fasting plasma glucose ≥ 126 mg/dL. Subjects were diagnosed as hypertensive when systolic blood pressure (SBP) was ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg or if antihypertensive medications were currently used. BMI was divided into three groups: underweight (BMI < 18.5 kg/m²), normal weight (BMI = 18.5 kg/m² to 24 kg/m²), and overweight or obesity (BMI ≥ 24 kg/m²). Central obesity was defined as a waist circumference ≥ 85 cm in men and ≥ 80 cm in women. In the cross-sectional analysis, a subgroup of 2988 individuals underwent measurements of plasma biomarkers, including fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), C-reactive protein (CRP), and estimated glomerular filtration rate (eGFR). The eGFR was calculated according to the Chronic Kidney Disease Epidemiology Collaboration’s 2009 creatinine equation[18]. Definitions of covariates were shown in Table S2.

**Statistical analysis**

The characteristics of the participants were described using mean values with standard deviations (SD) for continuous variables and frequency with percentages for categorical variables. The baseline characteristics of participants in the cross-sectional and longitudinal analytical samples were summarized and compared based on their SPPB scores. Statistical tests such as the chi-squared test, analysis of variance, Tukey's test, or the Kruskal-Wallis test were employed as appropriate for comparisons.

Logistic regression analysis was used to assess the associations between SPPB levels and CVD as well as its individual components in the cross-sectional analysis. Incidence rates of CVD per 1000 person-years in the CHARLS 2011 dataset were calculated in the longitudinal analysis. Follow-up time was measured from the date of the last interview to either the date of CVD diagnosis or the most recent interview the individual participated in. To examine the relationship between baseline SPPB levels and incident CVD, Cox proportional hazards models were employed to calculate hazard ratios (HRs) with corresponding 95% CIs. The association between different test parts (chair stands test, standing balance, and gait speed test) of the SPPB and CVD, stratified by sex, was also evaluated.

In both the cross-sectional and longitudinal analyses, three models were estimated: model 1 adjusted for age and sex, model 2 adjusted for age, sex, solitary, residence, region, education, smoking, drinking, waist, and BMI, and model 3 adjusted as model 2 with further inclusion of SBP, DBP, diabetes, hypertension, and dyslipidemia. Additionally, biomarker-adjusted models were used for participants who
underwent plasma examinations (2988 participants in the cross-sectional analysis and 2997 participants in the longitudinal analysis). All statistical analysis was performed retrospectively with Stata MP 17.0, and R version 4.2.1. In all cases, $P < 0.05$ was considered statistically significant.

**Results**

**Characteristics of participants in the cross-sectional and longitudinal study**

Table 1 displays the characteristics of the participants categorized according to their SPPB level. The study population had the mean (SD) age of 67.07 ± 5.90, and 2308 individuals (49.78%) were females. Among the 4636 older adults included in the analysis, the prevalence of poor LEF was 18.55% (860/4636), while normal LEF was observed in 17.39% (806/4636) of the participants.

Compared to the population with good LEF, individuals with poor LEF were generally older (mean age: 71.41 vs. 65.45 years) and more likely to be female (67.44% vs. 42.73%). They also had a higher proportion of individuals living alone (31.78% vs. 14.62%) and a higher prevalence of non-smokers (69.65% vs. 55.93%) and non-drinkers (68.60% vs. 53.97%). Additionally, the group with poor LEF exhibited higher systolic blood pressure (140.59 vs. 131.51), higher diastolic blood pressure (76.07 vs. 74.05), and higher prevalence of diabetes (16.75% vs. 12.61%), hypertension (68.03% vs. 49.21%), and cardiovascular disease (25.21% vs. 17.14%) (all $P < 0.001$). For more detailed information, please refer to Table 1. Table S3 presents the baseline characteristics of the 3699 participants without cardiovascular disease (CVD) in the longitudinal study, stratified by SPPB level.
Table 1
Baseline characteristics of all participants by SPPB level.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Low SPPB (n = 860)</th>
<th>Moderate SPPB (n = 806)</th>
<th>High SPPB (n = 2970)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>71.41 ± 6.81</td>
<td>68.43 ± 6.02</td>
<td>65.45 ± 4.74</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female</td>
<td>580 (67.44)</td>
<td>459 (56.95)</td>
<td>1269 (42.73)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Solitary</td>
<td>273 (31.78)</td>
<td>201 (24.94)</td>
<td>434 (14.62)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rural</td>
<td>583 (67.79)</td>
<td>547 (67.87)</td>
<td>1926 (64.85)</td>
<td>0.122</td>
</tr>
<tr>
<td>Smoking</td>
<td>261 (30.35)</td>
<td>306 (37.97)</td>
<td>1309 (44.07)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Drinking</td>
<td>270 (31.40)</td>
<td>309 (38.34)</td>
<td>1367 (46.03)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Region,</td>
<td></td>
<td></td>
<td></td>
<td>0.113</td>
</tr>
<tr>
<td>East</td>
<td>268 (31.16)</td>
<td>235 (29.16)</td>
<td>903 (30.40)</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>252 (29.30)</td>
<td>227 (28.16)</td>
<td>928 (31.25)</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>286 (33.26)</td>
<td>283 (35.11)</td>
<td>976 (32.86)</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>54 (6.28)</td>
<td>61 (7.57)</td>
<td>163 (5.49)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>0 year</td>
<td>507 (58.95)</td>
<td>347 (43.05)</td>
<td>809 (27.24)</td>
<td></td>
</tr>
<tr>
<td>0–6 years</td>
<td>288 (33.49)</td>
<td>365 (45.29)</td>
<td>1525 (51.35)</td>
<td></td>
</tr>
<tr>
<td>Over 6 years</td>
<td>65 (7.56)</td>
<td>94 (11.66)</td>
<td>636 (21.41)</td>
<td></td>
</tr>
<tr>
<td>Waist, cm</td>
<td>85.64 ± 12.92</td>
<td>84.13 ± 12.66</td>
<td>84.04 ± 11.83</td>
<td>0.007</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>25.24 ± 61.70</td>
<td>22.92 ± 4.23</td>
<td>23.57 ± 17.13</td>
<td>0.288</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>140.59 ± 23.59</td>
<td>134.21 ± 22.15</td>
<td>131.51 ± 21.37</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>76.07 ± 12.03</td>
<td>74.16 ± 12.05</td>
<td>74.05 ± 11.48</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Metabolic biomarkers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FPG, mg/dL</td>
<td>5.35 ± 0.90</td>
<td>5.33 ± 0.86</td>
<td>5.26 ± 0.73</td>
<td>0.162</td>
</tr>
<tr>
<td>HbA1c, mg/dL</td>
<td>3.12 ± 6.88</td>
<td>3.08 ± 7.84</td>
<td>2.77 ± 7.32</td>
<td>0.018</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>82.43 ± 15.00</td>
<td>84.23 ± 13.74</td>
<td>86.55 ± 13.19</td>
<td>0.447</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73 m²</td>
<td>111.80 ± 29.38</td>
<td>111.04 ± 34.80</td>
<td>109.27 ± 30.53</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Note: Values were described in mean ± SD for continuous variables or frequency (percentages) for categorical variables.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Low SPPB (n = 860)</th>
<th>Moderate SPPB (n = 806)</th>
<th>High SPPB (n = 2970)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>142 (16.75)</td>
<td>119 (14.93)</td>
<td>371 (12.61)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypertension</td>
<td>534 (68.03)</td>
<td>420 (56.91)</td>
<td>1331 (49.21)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>104 (12.50)</td>
<td>97 (12.34)</td>
<td>353 (12.13)</td>
<td>0.954</td>
</tr>
<tr>
<td>History of CVDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalent CVD</td>
<td>213 (25.21)</td>
<td>167 (20.93)</td>
<td>504 (17.14)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Prevalent heart disease</td>
<td>57 (6.72)</td>
<td>27 (3.37)</td>
<td>66 (2.24)</td>
<td>0.002</td>
</tr>
<tr>
<td>Prevalent stroke</td>
<td>173 (20.43)</td>
<td>147 (18.42)</td>
<td>458 (15.58)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Note: Values were described in mean ± SD for continuous variables or frequency (percentages) for categorical variables.

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP diastolic blood pressure; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; CVD, cardiovascular disease.

Missing data: 2 for living status, 623 for waist, 649 for BMI, 650 for SBP, 1472 for FPG, 1101 for HbA1c, 1125 for CRP, 1130 for eGFR, 50 for diabetes, 408 for hypertension, 107 for dyslipidemia, 51 for CVD, 34 for heart disease, 51 for stroke.

The mean values and percentages in different quintiles were compared using ANOVA analysis and χ² tests.

**Cross-sectional associations of SPPB level with cardiovascular disease**

In the cross-sectional study, the prevalence of cardiovascular disease (CVD) was 19.07% (884/4636) in the total population, 16.97% (504/2970) in individuals with good lower extremity function (LEF), 20.72% (167/806) in individuals with normal LEF, and 24.77% (213/860) in individuals with poor LEF (as shown in Table 1 and Table S4). After adjusting for demographic characteristics and health-related factors, individuals with low Short Physical Performance Battery (SPPB) scores had a significantly higher risk of CVD [odds ratio (OR) (95% CI): 1.62 (1.27−2.05), P<0.001] (Figure 2 and Table S4). The cross-sectional association between SPPB level and CVD did not change significantly after further adjusting for plasma biomarkers in the subgroup of 2988 participants (Table S5).

The associations between SPPB level and different components of CVD are presented in Table S4 and Figure 2. After adjusting for covariates, individuals with low SPPB scores were found to have a higher
risk of heart disease [1.35 (1.05−1.74), P<0.05] and stroke [3.09 (1.92−4.96), P<0.05] compared to those with high SPPB scores (Table S4). Similar results were observed among the subgroup of 2988 participants with completed plasma biomarkers measurements, where individuals with low SPPB scores remained significantly associated with stroke [2.85 (1.68−4.84), P<0.001] after further adjusting for metabolic biomarkers (Table S5).

**Longitudinal association between baseline SPPB level and incident cardiovascular disease at follow-up, 2011–2018**

During the 8-year follow-up period, a total of 1354 cases (29.54%) with incident cardiovascular disease (CVD) events were identified. In the longitudinal analysis, the incidence rate of CVD was 33.33 per 1000 person-years among individuals with high SPPB level, 28.77 per 1000 person-years among those with moderate SPPB level, and 45.35 per 1000 person-years among participants with low SPPB level. Table 2 presents the relationship between baseline SPPB level and incident CVD. After adjusting for covariates in Models 1-3, individuals with low SPPB level had a higher likelihood of experiencing CVD incidence [hazard ratio (HR) (95% CI): 1.11 (1.01−1.23)] compared to those with high SPPB level (P<0.05, Figure 3).

Regarding CVD components, individuals with low SPPB level had higher risks of heart disease [1.21 (1.00−1.45), P<0.05] and stroke [1.98 (1.47−2.67), P<0.001] (Table 2 and Figure 3). The longitudinal associations between low SPPB level and CVD were significantly affected after further adjusting for metabolic biomarkers among the subpopulation of 2997 subjects with plasma biomarkers measurements (Table S6). Individuals with low SPPB level had an 11.0% increased risk of incident CVD compared to those with high SPPB level [1.11 (0.99−1.24), P<0.1]. After further adjusting for metabolic biomarkers, individuals with low SPPB level had a higher likelihood of experiencing incident stroke [2.02 (1.46−2.78), P<0.001] compared to those with high SPPB level (Table S6).

Table 2 Incidence of CVD according to baseline SPPB level among all participants, 2011–2018.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cases, n</th>
<th>Incidence Rate, per 1000 Person-Years</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Model 1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>CVDs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High SPPB</td>
<td>792</td>
<td>33.33</td>
<td>Reference</td>
</tr>
<tr>
<td>Moderate SPPB</td>
<td>250</td>
<td>28.77</td>
<td>1.05 (0.97, 1.14)</td>
</tr>
<tr>
<td>Low SPPB</td>
<td>312</td>
<td>45.35</td>
<td>1.13 (1.04, 1.23) **</td>
</tr>
<tr>
<td>Heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High SPPB</td>
<td>681</td>
<td>28.66</td>
<td>Reference</td>
</tr>
<tr>
<td>Moderate SPPB</td>
<td>200</td>
<td>31.02</td>
<td>1.08 (0.92, 1.27)</td>
</tr>
<tr>
<td>Low SPPB</td>
<td>243</td>
<td>35.32</td>
<td>1.26 (1.07, 1.48) **</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High SPPB</td>
<td>192</td>
<td>8.08</td>
<td>Reference</td>
</tr>
<tr>
<td>Moderate SPPB</td>
<td>78</td>
<td>12.10</td>
<td>1.64 (1.25, 2.15) ***</td>
</tr>
<tr>
<td>Low SPPB</td>
<td>104</td>
<td>15.17</td>
<td>2.25 (1.72, 2.93) ***</td>
</tr>
</tbody>
</table>

Note: Abbreviation: HR, hazard ratio; CVD, cardiovascular disease.

<sup>a</sup> Model 1 was adjusted for age, gender.

<sup>b</sup> Model 2 was adjusted for age, gender, living status, residence, smoking, drinking, region, education, waist, and body mass index.

<sup>c</sup> Model 3 was adjusted as model 2 with further adjustment for systolic blood pressure, diastolic blood pressure, and history of diabetes, hypertension, and dyslipidemia.

Significant at †P<0.1, *P<0.05, **P<0.01 and ***P<0.001 compared to high SPPB group.

**Longitudinal association between baseline SPPB level with newly onset incident cardiovascular disease at follow-up (sensitivity**
After excluding 937 subjects with a history of CVDs at baseline, the longitudinal analysis included 3699 participants. During the 8-year follow-up, 811 cases (21.92%) of newly onset incident CVD events were identified. The incidence rate of CVD was 25.30 per 1000 person-years among individuals with high SPPB level, 27.34 per 1000 person-years among those with moderate SPPB level, and 35.60 per 1000 person-years among participants with low SPPB level.

Table S7 presents the relationship between baseline SPPB level and newly onset incident CVD. After adjusting for covariates in Models 1-3, individuals with low SPPB level did not show a significantly higher likelihood of developing newly onset CVD compared to those with high SPPB level [hazard ratio (HR) (95% CI): 1.10 (0.98−1.23)] (Table S7). The longitudinal associations between low SPPB level and CVD were not significantly affected after further adjusting for metabolic biomarkers among the subpopulations of 3699 subjects with plasma biomarkers measurements (Table S8).

Regarding CVD components, individuals with low SPPB level had a higher risk of newly onset stroke [1.67 (1.22–2.30), P<0.001], but not newly onset heart disease (Table S7). After further adjusting for metabolic biomarkers, individuals with low SPPB level were more likely to have incident stroke [1.69 (1.20−2.40), P<0.001] compared to those with high SPPB level (Table S8).

**Discussion**

In this study, the findings showed that poor lower extremity function (LEF), as assessed by the Short Physical Performance Battery (SPPB), was independently and positively associated with cardiovascular disease (CVD) in the longitudinal analysis. Specifically, individuals with poor LEF, whether they had a history of CVD or not, were found to be at a higher risk of incident stroke among older adults in China. However, there was no significant association observed between poor LEF and incident heart disease. These results suggest that lower extremity function, as measured by the SPPB, may serve as an important predictor of stroke risk in the older Chinese population.

Several studies suggest that the presence of poor LEF was correlated with higher odds of heart disease and stroke. Windham et al. [19] found that late-life SPPB score was positively associated with midlife cardiovascular health, which suggested that better cardiovascular health during midlife may lead to better LEF in older age. Bellettiere et al. [10] reported that the SPPB may provide a measure of cardiovascular health among older postmenopausal women in the United States beyond that captured by traditional risk factors. And the other study [4] indicated that reduced LEF was independently associated with the risk of composite and individual CVD outcomes and improved their risk prediction beyond traditional risk factors in American community-dwelling older adults. But previous study population included only white and black adults, but in which participation among people from diverse racial and ethnic backgrounds was limited. Further, there is no research on the longitudinal association between LEF and CVD events among the older general population in Asia. These findings indicate that
the assessment of LEF through community-based health check-ups and routine clinical practice might facilitate the identification of those at greatest risk of incident CVD, who would benefit most from early intervention. The underlying mechanisms of the relation between LEF and CVD are multifactorial, involving several pathophysiological changes in poor LEF people, including mitochondrial dysfunction, oxidative stress, chronic inflammation, neurodegeneration, and cellular senescence [20,21]. And lifestyles, such as malnutrition and insufficient physical activity may be also important factors [22,23]. In the sensitivity analysis of this study, poor LEF was found to be insignificantly associated with heart disease after adjusting for a history of heart disease. This may be since more detailed subtypes of heart disease, such as myocardial infarction, heart failure, or coronary heart disease, were not investigated in the CHARLS database. Of course, it is also possible that the correlation between LEF and CVD is different in Asian elderly people than in American elderly people. For example, the Framingham model [24] in the United States, the SCORE model [25] in Europe, and the QRISK model [26] in the UK are not applicable to the Chinese population, so China-PAR model [27] was developed to assess the risk of cardiovascular disease in Chinese. Data with more detailed classification of heart disease information may be needed to study and verify the relationship between LEF and heart disease.

The current study also demonstrated interesting findings regarding the effect of poor LEF on stroke. Compared with good LEF participants, the prevalence of stroke was significantly increased in persons with poor LEF. It was found that poor LEF individuals had a 98% higher risk of stroke compared with the good LEF group. This study found that poor LEF individuals had a 67% higher risk of new-onset stroke compared with the good LEF group. As well known, due to nervous system damage, post-stroke patients are likely to experience short-term and long-term lower limb dysfunction. However, our study found that poor lower extremity function may also be a risk factor for stroke. A few previous studies have separately reported the associations between muscle strength and the occurrence of stroke among the general population. A meta-analysis study [28] showed that lower handgrip strength was an independent predictor of stroke by comprising 42 observational studies in community-dwelling populations. A Mendelian randomization study [29] also reported that good handgrip strength was causally related to a lower risk of incident stroke in UK individuals. An epidemiological study [30] found that both possible sarcopenia and sarcopenia were associated with higher stroke risk among middle-aged and older Chinese adults. The reduction of muscle strength or sarcopenia in the elderly will lead to a series of physiological changes, including but not limited to oxidative stress, metabolic abnormalities, etc., and these abnormalities may be the pathophysiological mechanisms leading to stroke [31,32]. The findings supported the value of LEF assessed by the SPPB as a stroke-predictive tool in Asian older people and suggested that maintaining enough LEF could be beneficial for the prevention of stroke for older adults. Meanwhile, lifestyle interventions and exercise of LEF in routine clinical practice should be taken as a factor in fighting against stroke and promoting healthy aging [33–35].

This current study has several strengths. First, this study used a nationally representative cohort, thereby allowing for broad generalizability of findings to the older Chinese general population. Second, unlike previous cross-sectional studies, this is the first study to explore the longitudinal relationships between
LEF, assessed by SPPB, with CVD in Asia. More importantly, the findings suggested that preventing and/or improving LEF may reduce the risk of stroke.

However, there are several limitations in the current study. First, this research was an observational study, which may have a bias of observed relations due to introducing confounding factors. For reducing such bias, the analysis considered as many related factors as possible. However, other potential confounding factors, such as body fat mass and physical inactivity, cannot be ruled out. Second, the diagnosis of CVD was self-reported and physician-diagnosed in CHARLS with no available medical records. Thus, the bias may occur by using self-reported measures of chronic diseases including CVD. However, a study indicated that researchers confirmed 77.5% of self-reported incident coronary heart disease in the English Longitudinal Study of Ageing according to medical records [36]. Third, due to the lack of a detailed classification of CVD, it was not able to analyze the association between LEF and specific stroke subtypes and heart diseases further. Future studies need to pinpoint these critical questions. In addition, it should be considered that some selection biases, such as potential volunteer bias and non-response bias, when interpreting and extrapolating current results. Despite these limitations, this study contributes to extending previous knowledge of the cardiometabolic importance of poor LEF. The findings indicate that the assessment of LEF should introduce in community-based health check-ups and routine clinical practice to reduce the incidence of stroke.

**Conclusion**

In conclusion, lower extremity function, assessed using the short physical performance battery, was associated with higher cardiovascular risk, and poor lower extremity function can independently predict stroke risk among older Chinese adults. The results suggest the potential usefulness of the short physical performance battery for classifying stroke risk in older Chinese adults, which also suggested that preventing and/or improving lower extremity function may be beneficial for reducing stroke incidence and promoting healthy aging for older adults.

**Declarations**

**Ethics approval and consent to participate**

The Biomedical Ethics Review Committee of Peking University approved the ethical application for the collection of human participant data for the CHARLS (IRB00001052-11015). The study data were anonymous. All the respondents provided written informed consent before the survey.

**Consent for publication**

This study is not applicable.

**Data sharing statement**

The datasets generated for this study are available on request to the corresponding author.
Competing interests

The authors declare no competing interests.

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Authors’ Contributions

S.X. FENG, and J.Q. WANG conceived the protocol; H.Y. LI, T.Y. WANG, and J.L. LIU, contributed to analysis and interpretation of data; Y.F. LIANG and Y. WANG contributed to literature search; S.X. FENG and J.Q. WANG grafted the manuscript. J.M. LIU, D.R. HAN and Y.X. LIU critically revised the manuscript. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work and read and approved the final manuscript. The corresponding author had full access to all data in the study and assumed final responsibility for the decision to submit the manuscript for publication.

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References


**Figures**

- CHARLS established in 2011 (n=17708)
- Cross-sectional study in 2011 (n=4636)
- Longitudinal study sample in 2011-2018 (n=4636)
- Excluded individuals with relevant data missing (n=13072)
  - missing data on SPPB (n = 2654);
  - age below 60 years (n=10418);
  - No covariates (n=2)
- Longitudinal newly onset study sample in 2011-2018 (n=3699)
- Excluded subjects with history of CVDs (n=937)
Figure 1

Flow diagram for participants included in the study

Figure 2

ORs and 95% CIs of CVD and its components by SPPB level in the cross-sectional analysis

Forest plots show odds ratios (ORs) and 95%CIs for (A) CVD, (B) heart disease, and (C) stroke adjusted for age, gender, living status, residence, smoking, drinking, region, education, waist, and BMI, SBP, DBP, FPG, HbA1c, CRP and history of diabetes, hypertension, and dyslipidemia.

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP diastolic blood pressure; CVD, cardiovascular disease.
Figure 3


Graph shows hazard ratios (HRs) and 95% CIs for (A) CVD, (B) heart disease, and (C) stroke adjusted for age, gender, living status, residence, smoking, drinking, region, education, waist, and BMI, SBP, DBP, FPG, HbA1c, CRP and history of diabetes, hypertension, and dyslipidemia.

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; cardiovascular disease, CVD.

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