scientific reports

OPEN

# No sex difference in the association of pre-stroke physical activity with functional independence after ischemic stroke

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**Whether physical activity is associated with functional outcomes from ischemic stroke remains poorly understood. We aimed to explore the association of pre-stroke physical activity and functional outcomes in patients with acute ischemic stroke according to sex. Pre-stroke physical activity was assessed using a four-level questionnaire named Saltin-Grimby Physical Activity Level Scale (SGPALS). Our primary outcome was functional independence, defined as a modified Rankin Scale (mRS) score of 0–2 three months after stroke onset. The secondary outcome was the shift in the mRS score at 3 and 6 months. A prospective cohort study design was used to estimate the multivariable-adjusted odds of functional independence with pre-stroke physical activity. We analyzed 257 men and 142 women participants, including 230 physically inactive and 169 active ones in the final analysis. Physical active participants were at a higher odds of achieving functional independence at 3 months (adjusted OR 4.14, 95% CI 2.35–7.31; adjusted common odds ratio (cOR) 2.38, 95% CI 1.60–3.56). When stratified by sex adjusted point estimates from logistic regression models indicated that pre-stroke physical activity was significantly associated with 3-month functional independence in both men (adjusted OR 4.75, 95%CI 2.23–10.09; adjusted cOR 2.70, 95% CI 1.63–4.51) and women (adjusted OR 3.64, 95% CI 1.44–9.18; adjusted cOR 2.10, 95% CI 1.01–4.43). This study showed an association between physical activity and functional independence 3 months after ischemic stroke. Moreover, no indication of sex difference in this association were observed.**

**Keywords** Physical activity, Acute ischemic stroke, Sex difference, Functional independence

Identifying healthy lifestyle factors that may reduce stroke morbidity and mortality has become increasingly important. Physical inactivity, a modifiable risk factor for cardiovascular disease, is independently associated with stroke risk[1]. Previous efforts have attempted to examine whether physical activity is associated with stroke severity or functional outcomes from a stroke. A retrospective study showed that pre-stroke physical activity was associated with a less severe stroke and favorable long-term outcome in patients with first-ever stroke[2]. Data from the Ischemic Stroke Genetics Study showed that moderate physical activity was associated with a high Barthel Index score[3]. Consistently, a population-based stroke registry[4] showed that lack of regular pre-stroke physical activity was associated with poor outcomes after first-ever ischemic stroke (odds ratio [OR] 1.70, 95% confidence interval [CI] 1.10–2.50). These findings indicate an association between pre-stroke physical activity and functional advantages after stroke[3]. However, current studies of the relationship between pre-stroke physical activity and stroke outcomes are limited by a retrospective, longitudinal data collection that inevitably introduce recall and selection bias[5].

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Sex differences in stroke outcomes have been reported, where female stroke patients are more prone to have unfavorable outcomes[6]. Previous studies have shown that the relationship of pre-stroke physical activity with stroke risk or initial stroke severity may vary by sex[7]. The Framingham study showed that moderate to intense physical activity was protective against stroke in men but not in women[8]. Moreover, a retrospective, registry-based study showed that women patients had higher odds for physical inactivity in relation to stroke severity[9]. Some clinicians argue that women have a longer lifespan than men and are approximately five years older at stroke onset[10–12], which may be a possible explanation for the sex differences in initial stroke severity. In addition, sex differences in the vascular risk factor profiles may exist[13]. For example, women acute ischemic stroke (AIS) patients predominantly have hypertension and cardioembolic diseases, whereas men AIS patients are more likely to be current smokers[14]. To our knowledge, whether the association of pre-stroke physical activity level with functional outcomes may vary by sex remains unclear. In this prospective study, we aimed to (1) investigate the association of pre-stroke physical activity with the odds of functional independence; and (2) test the hypothesis that the association of physical activity level with stroke outcomes will be similar between men and women.

## Methods

### Study design and participants

This is a retrospective cohort study within a prospective follow-up framework. We analyzed AIS patients from two teaching hospitals between January 2022 and September 2022. Eligibility criteria included age 18 years or older, diagnosis of first-ever AIS confirmed by head computed tomography or magnetic resonance imaging. Patients who were lost to follow-up or without data to assess their physical activity level were excluded. This study protocol was reviewed and approved by Fujian Medical University Union Hospital Ethics Committee (NO.2023KY030), and all methods were performed in accordance with relevant guidelines and regulations. Written informed consent was obtained from participants (or their legal guardians) to participate in the study. This study was conducted in accordance with the Declaration of Helsinki.

### Data extraction

Two authors (S.F. and B.Z.) reviewed the electronic medical records using a digital database, and extracted data regarding base demographics (age, sex, systolic and diastolic blood pressure) and clinical characteristics (tobacco use, regular alcohol use, initial National Institutes of Health Stroke Scale [NIHSS], Stroke subtype), laboratory indicators (D-dimer, baseline blood glucose), comorbidities (hypertension, diabetes, atrial fibrillation, ischemic heart disease, chronic heart failure), prescribed drugs (antithrombotics use before stroke, statin use before stroke), and acute treatment (intravenous thrombolysis, endovascular mechanical thrombectomy using a standard digital sheet. Tobacco users were defined as individuals who consumed any type of tobacco in the previous 12 months and included those who had quit within the past year[15]. Regular alcohol users were defined as those who consumed any dose of alcohol at least one time per week during the past year[16]. Hypertension was defined as documented systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mmHg, or by patients' self-reported diagnosis of hypertension and/or by the treatment of antihypertensives[16]. Diabetes was defined as the current use of antidiabetic agents, having a fasting glucose level > 7 mmol/L, having a non-fasting glucose level > 11.1 mmol/L, or having a history of diabetes. We classified patients as having atrial fibrillation if they had been diagnosed with AF by electrocardiogram at admission or during the hospital stay or had a preadmission history[17]. Ischemic heart disease was defined as a history of myocardial infarction, angina, or coronary artery disease. Chronic heart failure was defined as a documented history or cardiologist's diagnosis[18]. Stroke subtype was categorized based on The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification[19]. Stroke severity at admission was assessed using the National Institutes of Health Stroke Scale (NIHSS; 0–42).

### Assessment of pre-stroke physical activity

Two authors (H.L. and Y.Z) blinded to clinical characteristics assessed physical activity level using a four-level questionnaire (Saltin-Grimby Physical Activity Level Scale) through face-to-face interview within one-week of admission: grade 1: physical inactivity, grade 2: some physical activity for at least 4 h/week (mild physical activity), grade 3: regular physical activity and training for at least 2–3 h/week (moderate physical activity), and grade 4: regular hard physical training for competitive sports several times per week (vigorous physical activity)[20]. As the primary explanatory variable in the current study, the SGPALS score was dichotomized into physically inactivity (grade 1) versus physically activity (grade 2–4) in the regression analyses[21].

### Follow-up and outcome

The modified Rankin Scale (mRS) at 3 and 6 months was assessed by trained raters blinded to baseline characteristics during face-to-face interviews or via telephone conversations with the patients or their caregivers. The mRS is a standard global measure of disability scored from 0 to 6, in which scores of 0 indicating no symptoms, scores of 1 indicating symptoms without clinically significant disability, scores of 2 indicating slight disability, scores of 3 indicating moderate disability, scores of 4 indicating moderately severe disability, scores of 5 indicating severe disability, and scores of 6 indicating death[22]. Our primary outcome was functional independence, defined as a mRS score of 0–2 at 3 months[22]. The secondary outcome was the shift in the mRS score at 3 and 6 months[23].

### Missing data

The missing data were imputed using regression imputation to replace the missing values with predicted values using a linear regression model created from the non-missing data part of the dataset[24]. The variables requiring imputation were baseline blood glucose (64 [15.1%]), serum lipid profiles including total cholesterol (TC), low-density lipoprotein (LDL), and triglyceride (TG, 19 [4.6%]), D-dimer (63 [15.1%]), and body mass index (BMI, 51 [12.2%]).

### Statistical analysis

Continuous variables were tested for normality using the Kolmogorov-Smirnov test, with normal distribution expressed as mean and standard deviation (SD) and non-normal distribution expressed as median and interquartile range (IQR). Categorical variables were expressed as frequencies and percentage, calculated by dividing the number of events by the total number of patients. We used t-tests or Mann-Whitney tests to compare differences in continuous variables and chi-square tests or Fisher exact tests to compare differences in categorical variables. We calculated crude and adjusted odds of functional independence with physical activity in binary logistic regression models. Model 1 was adjusted for age; Model 2 was further accounted for initial NIHSS score; Model 3 was adjusted for all variables that showed an association in the univariate analysis with a $p < 0.1$. We conducted sub-group analsysis stratified by gender. To address the imbalance in the important risk factors between men and women, we conducted 1:1 propensity score matching (PSM) with a match tolerance of 0.02[25]. We did multivariable ordinal logistic regression analysis to assess the association of physical activity with mRS distribution. The common odds ratio (cOR) of improvement one point on the mRS score in the presence of pre-stroke physical activity was calculated with its 95% CI. Multiplicative interaction tests were used to examine whether there was an interaction between sex and physical activity. We performed a sensitivity analysis restricted to patients with a mRS score at 6 months. All statistics were performed using the SPSS software (version 25.0) and R (version 4.5). A p-value of < 0.05 was considered statistically significant.

## Results

We included 399 patients in the final analysis (Fig. 1). The median age was 67 (58–75) years old; and 257 (64.4%) were men. A total of 230 (57.6%) patients were physically inactive (SGPALS grade 1), and 169 (42.4%) were physically active (137 [34.3%] mild, 32 (8.0%) moderate, and 0 vigorous). Table 1 summarizes the baseline demographics and clinical characteristics among physically active and inactive participants. Compared to physically inactive participants, physically active participants were younger (65 [56–73] vs. 68 [59–78], $p < 0.001$), lower proportion of hypertension ($p = 0.022$), lower pre-stroke antithrombotics use ($p = 0.004$), lower pre-stroke statin use ($p = 0.009$), decreasing initial NIHSS score (2 [1–5] vs. 3 [1–6], $p = 0.022$).

Table 2 summarizes the baseline demographics and clinical characteristics among men and women. Compared to women, men participants were younger (65 [56–75] vs. 69 [61–76], $p = 0.008$), more likely to be smokers (141 [54.9%] vs. 6 [4.2%], $p < 0.001$), regular drinkers (121 [47.1%] vs. 9 [6.3%], $p < 0.001$), and physical active individuals (120 [46.7%] vs. 49 [34.5%], $p = 0.024$), had a higher diastolic blood pressure (82mmHg [75–94] vs. 80 [74–89], $p = 0.030$), and less likely to experience a moderate to severe stroke (74 [52.1%] vs. 94 [36.6%], $p = 0.004$). The serum levels of total cholesterol (4.43 mmol/L [3.61–5.10] vs. 4.64 [3.90–5.60], $p = 0.003$) were lower in men than in women.

Baseline characteristics among patients with and without 3-month functional independence are shown in Table 3. The variables associated with 3-month functional independence in the univariate analysis were younger age ($p < 0.001$), pre-stroke Antithrombotics use ($p = 0.004$), pre-stroke statin use ($p < 0.001$), physical activity ($p < 0.001$), lower proportion of atrial fibrillation ($p = 0.037$), decreasing initial NIHSS score ($p < 0.001$), lower serum level of D-dimer ($p < 0.001$) and blood glucose ($p = 0.001$). Similar findings were obtained among patients with and without 6-month functional independence (Supplemental Table 1).

Baseline characteristics among patients with and without 3-month functional independence in men and women are shown in Table 4. In comparison, in men, the variables associated with 3-month functional independence in the univariate analysis were younger age ($p < 0.001$), pre-stroke statin use ($p = 0.026$), physical activity ($p < 0.001$), lower proportion of atrial fibrillation ($p = 0.037$), decreasing initial NIHSS score ($p < 0.001$), lower serum level of D-dimer (< 0.001) and blood glucose ($p = 0.014$). In comparison, in women, the variables associated with 3-month functional independence in the univariate analysis were younger age ($p = 0.007$), pre-stroke statin use ($p = 0.003$), physical activity ($p = 0.063$), decreasing initial NIHSS score ($p < 0.001$), lower systolic blood pressure ($p = 0.004$) and blood glucose ($p = 0.033$). The stroke subtypes among patients with and without 3-month functional independence were significantly different in both men and women ($p < 0.05$, respectively). Similar findings were obtained among patients with and without 6-month functional independence in men and women (Supplemental Table 2).

Table 5 shows the association of pre-stroke physical activity with functional independence (mRS 0–2) at 3-month. Physical active participants were at a higher odds of achieving functional independence at 3 months (unadjusted OR 3.16, 95%CI 2.01–4.97). After adjustment for confounding variables, pre-stroke physical activity remained associated with a higher odds of achieving functional independence at 3 months (adjusted OR 4.14, 95%CI 2.35–7.31). A sensitivity analysis restricted to patients with a mRS score of 0–2 at 6 months yielded similar results to the primary analyses (Supplemental Table 3).

When stratified by sex, univariable regression analysis showed that pre-stroke physical activity was associated with a higher odds of achieving functional independence at 3 months in men (OR 3.78, 95%CI 2.12–6.75, $p < 0.001$) and in women (OR 2.15, 95%CI 1.02–4.52, $p = 0.043$). This association remained after adjustment for age and NIHSS score in men (OR 3.88, 95%CI 1.93–7.80, $p < 0.001$) but was lost in women (OR 1.92, 95%CI 0.88–4.18, $p = 0.102$). Multivariable regression analysis showed that pre-stroke physical activity was associated with a higher odds of achieving functional independence at 3 months in men (adjusted OR 4.75, 95%CI 2.23–10.09) and in women (adjusted OR 3.64, 95%CI 1.44–9.18, Table 5). A sensitivity analysis restricted to patients with a mRS score of 0–2 at 6 months yielded similar results to the primary analyses (Supplemental Table 3).

The demographics, clinical characteristics, comorbidities, laboratory indicators, prescribed drugs, and acute treatments showed a balance between men and women in the matched pairs after 1:1 PSM (Supplemental

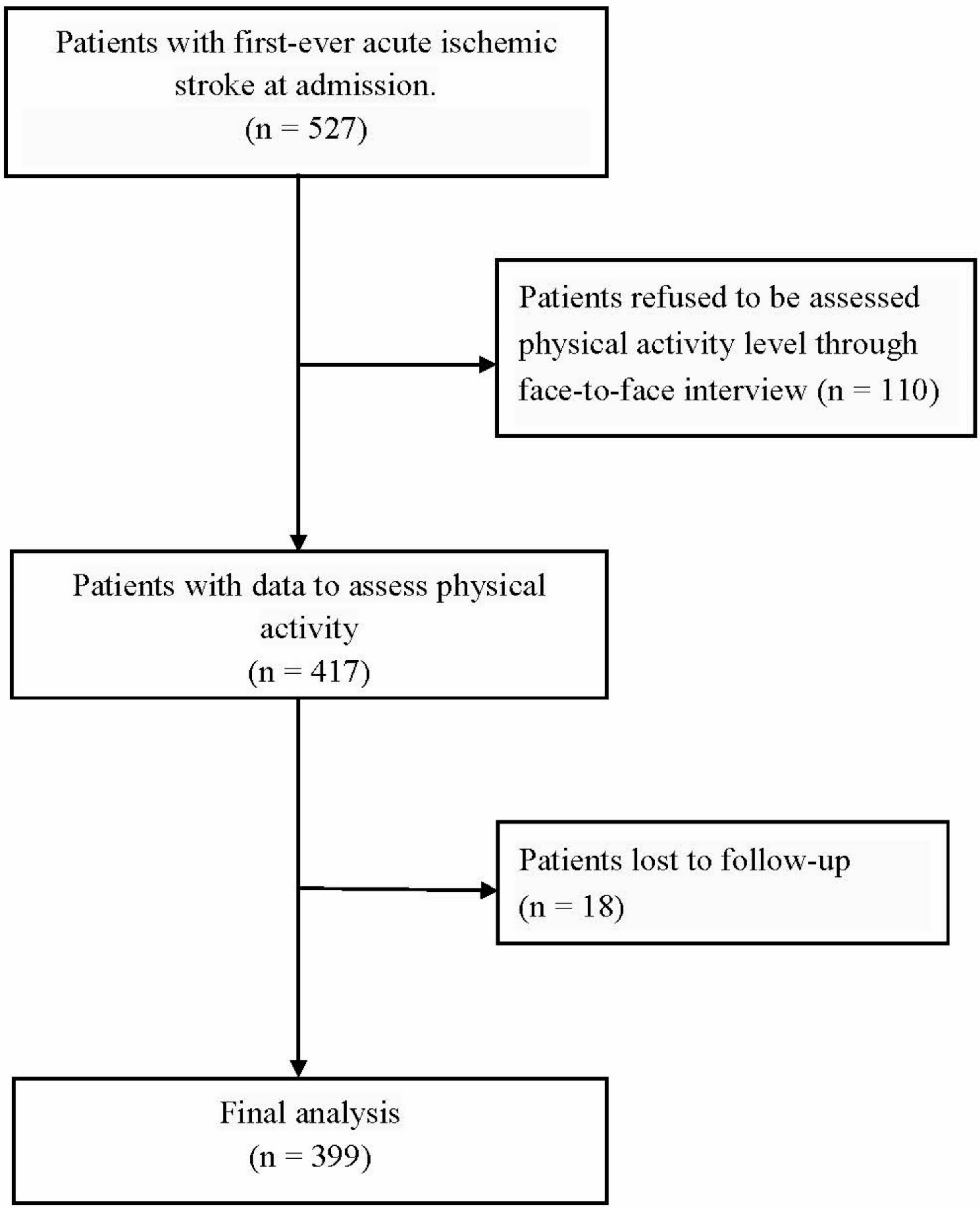


**Fig. 1**. Flow chart.

Table 4). The results showed that those with pre-stroke physical activity were more likely to have functional independence at 3-month (Supplemental Table 5) and 6-month (Supplemental Table 6) in both men and women.

Multivariable ordinal logistic regression analysis showed that pre-stroke physical activities was significantly associated with mRS distribution at 3-month (adjusted cOR of 2.38 95% CI 1.60–3.56) and 6-month (adjusted cOR of 2.35 95% CI 1.58–3.52, Supplemental Table 7). This association remained when stratified by sex in men (at 3-month, adjusted cOR 2.70, 95% CI 1.63–4.51; at 6-month, adjusted cOR 2.43, 95% CI 1.47–4.05) and women (at 3-month, adjusted cOR 2.10, 95% CI 1.01–4.43; at 6-month, adjusted cOR 2.19, 95% CI 1.04–4.67).

| | **Total ($n$ = 399)** | **Physically inactive ($n$ = 230)** | **Physically active ($n$ = 169)** | ***p* value** |
|---|---|---|---|---|
| Age, y (median, IQR) | 67 (58–75) | 68 (59–78) | 65 (56–73) | < 0.001 |
| Sex, n (%) | | | | 0.024 |
| Women | 142 (35.6) | 93 (40.4) | 49 (29.0) | |
| Men | 257 (64.4) | 137 (59.6) | 120 (71.0) | |
| BMI, kg/$m^2$ (median, IQR) | 23.92 (22.04–25.23) | 23.92 (21.98–24.73) | 23.92 (22.04–25.63) | 0.128 |
| Tobacco users, n (%) | 147 (36.8) | 78 (33.9) | 69 (40.8) | 0.190 |
| Regular alcohol users, n (%) | 130 (32.6) | 67 (29.1) | 63 (37.3) | 0.108 |
| Hypertension, n (%) | 307 (76.9) | 187 (81.3) | 120 (71.0) | 0.022 |
| Diabetes, n (%) | 152 (38.1) | 93 (40.4) | 59 (34.9) | 0.309 |
| Atrial fibrillation, n (%) | 74 (18.5) | 46 (20.0) | 28 (16.6) | 0.459 |
| Ischemic heart disease, n (%) | 68 (17.0) | 46 (20.0) | 22 (13.0) | 0.089 |
| Chronic heart failure, n (%) | 17 (4.3) | 14 (6.1) | 3 (1.8) | 0.063 |
| Antithrombotics use before stroke, n (%) | 43 (10.8) | 34 (14.8) | 9 (5.3) | 0.004 |
| Statin use before stroke, n (%) | 41 (10.3) | 32 (13.9) | 9 (5.3) | 0.009 |
| Acute treatment, n (%) | | | | 0.969 |
| IVT | 25 (6.3) | 15 (6.5) | 10 (5.9) | |
| EVT | 24 (6.0) | 14 (6.1) | 10 (5.9) | |
| IVT + EVT | 8 (2.0) | 4 (1.7) | 4 (2.4) | |
| TOAST subtypes, n (%) | | | | 0.005 |
| LAA | 254 (63.7) | 139 (60.4) | 115 (68.0) | |
| CE | 84 (21.1) | 50 (21.7) | 34 (20.1) | |
| SAO | 35 (8.8) | 30 (13.0) | 5 (3.0) | |
| SOE | 13 (3.3) | 5 (2.2) | 8 (4.7) | |
| SUE | 13 (3.3) | 6 (2.6) | 7 (4.1) | |
| Initial NIHSS score, (median, IQR) | 3 (1–6) | 3 (1–6) | 2 (1–5) | 0.022 |
| SBP, (mmHg) | 145.40 ± 21.52 | 146.95 ± 22.41 | 143.30 ± 20.13 | 0.089 |
| DBP, (mmHg) | 81 (75–93) | 81.5 (75–91) | 81 (75–93) | 0.936 |
| D-dimer, (ug/mL) | 0.50 (0.30–0.80) | 0.50 (0.33–0.80) | 0.47 (0.27–0.81) | 0.167 |
| Baseline blood glucose, (mmol/L) | 5.47 (5.00–7.38) | 5.46 (5.00–7.38) | 5.47 (5.10–7.29) | 0.775 |
| LDL-C, (mmol/L) | 2.90 (2.20–3.50) | 2.90 (2.03–3.51) | 2.90 (2.27–3.45) | 0.697 |
| TG, (mmol/L) | 1.10 (0.93–1.30) | 1.29 (0.94–1.64) | 1.39 (1.05–1.78) | 0.095 |
| TC, (mmol/L) | 1.33 (0.97–1.74) | 4.52 (3.67–5.20) | 4.51 (3.73–5.19) | 0.548 |

**Table 1**. Baseline characteristics among physically active and inactive participants. NIHSS = National Institutes of Health Stroke Scale; TOAST = Trial of Org 10,172 in Acute Stroke Treatment; IVT = intravenous thrombolysis, EVT = endovascular mechanical thrombectomy; LAA = large-artery atherosclerosis; SE = cardioembolism; SAO = small-artery occlusion; SOE = acute stroke of other determined etiology; SUE = stroke of undetermined etiology; SBP = systolic blood pressure, DBP = diastolic blood pressure; TC = total cholesterol; TG = triglycerides LDL-C = low density lipoprotein cholesterol.

The association of pre-stroke physical activity with 3-month and 6-month mRS distributions after PSM are shown in Supplemental Table 8.

We detected no significant interaction between physical activity and sex regarding the association of pre-stroke physical activity and functional independence at 3 or 6 months (p for interaction = 0.239, and p for interaction = 0.457, respectively).

## Discussion

The current study showed that pre-stroke physical activity was significantly associated with functional independence 3 and 6 months after stroke onset. Moreover, there was no statistically significant sex difference in the association between pre-stroke physical activity and functional independence.

Physical inactivity is a global problem, with one-quarter of the worldwide population being insufficiently physically active[26]. In our cohort, fewer women (49 [34.5%]) than men (120 [46.7%]) were physically active before stroke onset. The higher age among women could explain the lower level of physical activity. Moreover, a cross-sectional study showed that socioeconomic status may explain the sex difference in physical activity. The low educational level in women could have led to less odds of being effectively educated about the importance and proper methods of exercise[27].

Although the relationships of physical activity level with stroke risk and severity have been well established, fewer studies have investigated the relationship between physical activity and functional outcomes after ischemic

| | Men (*n* = 257) | Women (*n* = 142) | *p* value |
|---|---|---|---|
| Age, y (median, IQR) | 65 (56–75) | 69 (61–76) | 0.008 |
| BMI, kg/m$^2$ (median, IQR) | 23.88 (21.74–25.61) | 23.44 (21.48–25.30) | 0.301 |
| Tobacco users, n (%) | 141 (54.9) | 6 (4.2) | < 0.001 |
| Regular alcohol users, n (%) | 121 (47.1) | 9 (6.3) | < 0.001 |
| Physical activity, n (%) | 120 (46.7) | 49 (34.5) | 0.024 |
| Hypertension, n (%) | 191 (74.3) | 116 (81.7) | 0.121 |
| Diabetes, n (%) | 96 (37.4) | 56 (39.4) | 0.762 |
| Atrial fibrillation, n (%) | 51 (19.8) | 23 (16.2) | 0.446 |
| Ischemic heart disease, n (%) | 51 (19.8) | 17 (12.0) | 0.062 |
| Chronic heart failure, n (%) | 10 (3.9) | 7 (4.9) | 0.816 |
| Antithrombotics use before stroke, n (%) | 24 (9.3) | 19 (13.4) | 0.281 |
| Statin use before stroke, n (%) | 27 (10.5) | 14 (9.9) | 0.975 |
| Acute treatment, n (%) | | | 0.444 |
| IVT | 14 (5.4) | 11 (7.7) | |
| EVT | 18 (7.0) | 6 (4.2) | |
| IVT + EVT | 4 (1.6) | 4 (2.8) | |
| TOAST subtypes, n (%) | | | 0.186 |
| LAA | 166 (64.6) | 88 (62.0) | |
| CE | 54 (21.0) | 30 (21.1) | |
| SAO | 17 (6.6) | 18 (12.7) | |
| SOE | 11 (4.3) | 2 (1.4) | |
| SUE | 9 (3.5) | 4 (2.8) | |
| Initial NIHSS score, (median, IQR) | 3 (1–6) | 4 (1–6) | 0.099 |
| Stroke severity, n (%) | | | 0.004 |
| Minor to mild, n (%) | 163 (63.4) | 68 (47.9) | |
| Moderate to severe, n (%) | 94 (36.6) | 74 (52.1) | |
| SBP, (mmHg) | 145.44 ± 21.91 | 145.33 ± 20.88 | 0.961 |
| DBP, (mmHg) | 82 (75–94) | 80 (74–89) | 0.030 |
| D-dimer, (ug/mL) | 0.50 (0.28–0.76) | 0.50 (0.34–0.89) | 0.038 |
| Baseline blood glucose, (mmol/L) | 5.50 (5.03–7.40) | 5.40 (5.00-7.10) | 0.593 |
| LDL-C, (mmol/L) | 2.90 (2.18–3.45) | 2.91 (2.26–3.62) | 0.303 |
| TG, (mmol/L) | 1.30 (0.94–1.69) | 1.43 (1.03–1.85) | 0.131 |
| TC, (mmol/L) | 4.43 (3.61–5.10) | 4.64 (3.90–5.60) | 0.003 |

**Table 2**. Baseline characteristics among men and women. NIHSS = National Institutes of Health Stroke Scale; TOAST = Trial of Org 10,172 in Acute Stroke Treatment; IVT = intravenous thrombolysis, EVT = endovascular mechanical thrombectomy; LAA = large-artery atherosclerosis; SE = cardioembolism; SAO = small-artery occlusion; SOE = acute stroke of other determined etiology; SUE = stroke of undetermined etiology; SBP = systolic blood pressure, DBP = diastolic blood pressure; TC = total cholesterol; TG = triglycerides LDL-C = low density lipoprotein cholesterol.

stroke[28,29], with conflicting and controversial conclusions. A longitudinal study from three Swedish registries suggests that physical inactivity before stroke is associated with dependency in basic Adult Daily Living 3 months after stroke (adjusted OR 2.30, 95CI 1.89–2.80][30]. A population-based stroke registry[4] showed that lack of regular pre-stroke physical activity was associated with poor outcomes after first-ever ischemic stroke (OR 1.70, 95%CI 1.10–2.50). Moderate to heavy physical activity showed some association with better functional outcomes 90 days after discharge, but not all of these associations were significant[3].

To our knowledge, whether the association of physical activity level with functional independence from ischemic stroke may vary by sex remains poorly understood. Our study built on the above-mentioned studies by showing a significant association between pre-stroke physical activity and functional independence in both men and women. In a recent meta-analysis[31], of 10 studies that included data on ischemic stroke in men and women, five (50%) suggested similar effects in both sexes, four (40%) indicated a significant effect in women but not in men, and only one (10%) showed an effect in men but not women. A prospective analysis of the Physician's Health Study showed that men who exercise vigorously ≥ 5 times/week had a lower risk (OR 0.84, 95%CI 0.61–1.14) for stroke with perfect functional outcome defined as a mRS 0–1, and (OR 0.85, 95%CI 0.67–1.08) for functional independence defined as a mRS score 2 to 3 [32]. However, other levels of physical activity failed to show a significant impact on the functional outcomes after cerebral vascular events. To what extent pre-stroke physical

| | mRS 3–6 (*n* = 139) | mRS 0–2 (*n* = 260) | *p* value |
|---|---|---|---|
| Age, y (median, IQR) | 72 (64–79) | 64 (55–73) | < 0.001 |
| Sex, n (%) | 82 (59.0) | 175 (67.3) | 0.123 |
| Women | 57 (41.0) | 85 (32.7) | |
| Men | 82 (59.0) | 175 (67.3) | |
| BMI, kg/m$^2$ (median, IQR) | 23.92 (22.49–24.43) | 23.92 (21.78–25.36) | 0.721 |
| Tobacco users, n (%) | 51 (36.7) | 96 (36.9) | 1.000 |
| Regular alcohol users, n (%) | 43 (30.9) | 87 (33.5) | 0.688 |
| Physical activity, n (%) | 35 (25.2) | 134 (51.5) | < 0.001 |
| Hypertension, n (%) | 112 (80.6) | 195 (75.0) | 0.256 |
| Diabetes, n (%) | 60 (43.2) | 92 (35.4) | 0.157 |
| Atrial fibrillation, n (%) | 34 (24.5) | 40 (15.4) | 0.037 |
| Ischemic heart disease, n (%) | 25 (18.0) | 43 (16.5) | 0.821 |
| Chronic heart failure, n (%) | 4 (2.9) | 13 (5.0) | 0.459 |
| Antithrombotics use before stroke, n (%) | 6 (4.3) | 37 (14.2) | 0.004 |
| Statin use before stroke, n (%) | 3 (2.2) | 38 (14.6) | < 0.001 |
| Acute treatment, n (%) | | | 0.131 |
| IVT | 9 (6.5) | 16 (6.2) | |
| EVT | 12 (8.6) | 12 (4.6) | |
| IVT + EVT | 5 (3.6) | 3 (1.2) | |
| TOAST subtypes, n (%) | | | < 0.001 |
| LAA | 95 (68.3) | 159 (61.2) | |
| CE | 37 (26.6) | 47 (18.1) | |
| SAO | 1 (0.7) | 34 (13.1) | |
| SOE | 2 (1.4) | 11 (4.2) | |
| SUE | 4 (2.9) | 9 (3.5) | |
| Initial NIHSS score, (median, IQR) | 6 (3–10) | 2 (1–4) | < 0.001 |
| SBP, (mmHg) | 147.99 ± 22.84 | 144.02 ± 20.70 | 0.088 |
| DBP, (mmHg) | 80 (71–91) | 82 (76–93) | 0.063 |
| D-dimer, (ug/mL) | 0.60 (0.35–1.29) | 0.50 (0.27–0.64) | < 0.001 |
| Baseline blood glucose, (mmol/L) | 6.04 (5.32–7.98) | 5.40 (5.00–6.67) | 0.001 |

**Table 3**. Baseline characteristics among patients with and without 3-month functional independence. NIHSS = National Institutes of Health Stroke Scale; TOAST = Trial of Org 10,172 in Acute Stroke Treatment; IVT = intravenous thrombolysis, EVT = endovascular mechanical thrombectomy; LAA = large-artery atherosclerosis; SE = cardioembolism; SAO = small-artery occlusion; SOE = acute stroke of other determined etiology; SUE = stroke of undetermined etiology; SBP = systolic blood pressure, DBP = diastolic blood pressure.

activity may have a beneficial impact on functional outcomes after ischemic stroke needs to be addressed in future large cohort studies.

An advantage of using the mRS as our measure of functional outcomes from stroke is that it is widely used for stroke studies with good interrater reliability and validity[22,33]. Notably, women in our cohort were four years older than men at stroke onset, which is comparable with the national stroke registries[34]. Thus, our findings may have considerable generalizability within a similar context.

Nevertheless, our findings should be interpreted with caution, as there are some limitations. First, self-reported physical activity may inevitably introduce recall bias. However, the SGPALS has good predictive validity and has been widely applied in stroke patients[20]. Second, this is a retrospective cohort study within a prospective follow-up framework, with considerable imbalance in the demographic and baseline clinical characteristics between men and women. However, our matched data after performing PSM yielded consistent findings to the primary analysis. Third, although we included several confounding variables in our analyses, the impact of pre-stroke neurological function status and socioeconomic status (such as education level, marital status, region, household income, and health insurance) were not analyzed in the current study due to unavailable data. Future studies are needed to address this knowledge gap on this point. Forth, we only included the Chinese stroke population; therefore, our findings are not generalizable to other ethnic stroke populations. Lastly, all analyses in the present study are secondary and should be considered hypothesis-generating only.

## Conclusion

Pre-stroke physical activity was associated with functional independence after ischemic stroke in both men and women. Our findings suggest that physical activity should be encouraged in the healthcare and public health sectors.

| | Men ($n=257$) | | | Women ($n=142$) | | |
|---|---|---|---|---|---|---|
| | mRS 3–6 ($n=82$) | mRS 0–2 ($n=175$) | p value | mRS 3–6 ($n=57$) | mRS 0–2 ($n=85$) | *p* value |
| Age, y (median, IQR) | 73 (62–78) | 62 (52–72) | < 0.001 | 71 (65–80) | 67 (59–74) | 0.007 |
| BMI, kg/m$^2$ (median, IQR) | 23.66 (21.76–25.51) | 24.05 (21.74–25.65) | 0.485 | 23.44 (21.48–24.97) | 23.44 (21.48–25.30) | 0.775 |
| Tobacco users, n (%) | 49 (59.8) | 92 (52.6) | 0.345 | 2 (3.5) | 4 (4.7) | 0.988 |
| Regular alcohol users, n (%) | 41 (50.0) | 80 (45.7) | 0.612 | 2 (3.5) | 7 (8.2) | 0.434 |
| Antithrombotics use before stroke, n (%) | 3 (3.7) | 21 (12.0) | 0.056 | 3 (5.3) | 16 (18.8) | 0.038 |
| Statin use before stroke, n (%) | 3 (3.7) | 24 (13.7) | 0.026 | 0 (0) | 14 (16.5) | 0.003 |
| Physical activity, n (%) | 21 (25.6) | 99 (56.5) | < 0.001 | 14 (24.6) | 35 (41.2) | 0.063 |
| Hypertension, n (%) | 62 (75.6) | 129 (73.7) | 0.864 | 50 (87.7) | 66 (77.6) | 0.194 |
| Diabetes, n (%) | 32 (39.0) | 64 (36.6) | 0.810 | 28 (49.1) | 28 (32.9) | 0.079 |
| Atrial fibrillation, n (%) | 23 (28.0) | 28 (16.0) | 0.037 | 11 (19.3) | 12 (14.1) | 0.556 |
| Ischemic heart disease, n (%) | 18 (22.0) | 33 (18.9) | 0.680 | 7 (12.3) | 10 (11.8) | > 0.999 |
| Chronic heart failure, n (%) | 3 (3.7) | 7 (4.0) | 0.998 | 1 (1.8) | 6 (7.1) | 0.300 |
| Acute treatment, n (%) | | | 0.085 | | | 0.892 |
| IVT | 4 (4.9) | 10 (5.7) | | 5 (8.8) | 6 (7.1) | |
| EVT | 9 (11.0) | 9 (5.1) | | 3 (5.3) | 3 (3.5) | |
| IVT + EVT | 3 (3.7) | 1 (0.6) | | 2 (3.5) | 2 (2.4) | |
| TOAST subtypes, n (%) | | | 0.007 | | | 0.035 |
| LAA | 56 (68.3) | 110 (62.9) | | 39 (68.4) | 49 (57.6) | |
| CE | 23 (28.0) | 31 (17.7) | | 14 (24.6) | 16 (18.8) | |
| SAO | 0 (0) | 17 (9.7) | | 1 (1.8) | 17 (20.0) | |
| SOE | 1 (1.2) | 10 (5.7) | | 1 (1.8) | 1 (1.2) | |
| SUE | 2 (2.4) | 7 (4.0) | | 2 (3.5) | 2 (2.4) | |
| Initial NIHSS score, (median, IQR) | 7 (3–13) | 2 (1–3) | < 0.001 | 5 (3–8) | 3 (1–5) | < 0.001 |
| SBP, (mmHg) | 148 (132–165) | 144 (131–160) | 0.788 | 152 (138–166) | 140 (130–152) | 0.004 |
| DBP, (mmHg) | 81 (71–91) | 84 (77–95) | 0.131 | 80 (71–90) | 80 (76–88) | 0.462 |
| D-dimer, (ug/mL) | 0.62 (0.40–1.31) | 0.43 (0.24–0.52) | < 0.001 | 0.59 (0.33–1.08) | 0.50 (0.34–0.81) | 0.164 |
| Baseline blood glucose, (mmol/L) | 5.97 (5.38–7.98) | 5.40 (5.00-6.75) | 0.014 | 6.14 (5.16–7.81) | 5.40 (5.00-6.30) | 0.033 |

**Table 4**. Baseline characteristics among patients with and without 3-month functional independence in men and women. NIHSS = National Institutes of Health Stroke Scale; TOAST = Trial of Org 10,172 in Acute Stroke Treatment; IVT = intravenous thrombolysis, EVT = endovascular mechanical thrombectomy; LAA = large-artery atherosclerosis; SE = cardioembolism; SAO = small-artery Occlusion; SOE = acute stroke of other determined etiology; SUE = stroke of undetermined etiology; SBP = systolic blood pressure, DBP = diastolic blood pressure;

| | Unadjusted OR 95%CI | *p*-value | Age -adjusted OR 95%CI | *p*-value | Age + NIHSS -adjusted OR 95%CI | *p*-value | Multivariable OR 95%CI | *p*-value |
|---|---|---|---|---|---|---|---|---|
| Total participants (n = 399) | 3.16 (2.01–4.97) | < 0.001 | 2.75 (1.72–4.40) | < 0.001 | 2.91 (1.74–4.87) | < 0.001 | 4.14 (2.35–7.31) | < 0.001 |
| Stratified by sex | | | | | | | | |
| Men ($n=257$) | | | | | | | | |
| Physical activity | 3.78 (2.12–6.75) | < 0.001 | 3.33 (1.83–6.09) | < 0.001 | 3.88 (1.93–7.80) | < 0.001 | 4.75 (2.23–10.09) | < 0.001 |
| Women (N = 142) | | | | | | | | |
| Physical activity | 2.15 (1.02–4.52) | 0.043 | 1.95 (0.91–4.15) | 0.086 | 1.92 (0.88–4.18) | 0.102 | 3.64 (1.44–9.18) | 0.006 |

**Table 5**. Association of pre-stroke physical activity and 3-month functional independence. In total participants, adjusted for age, antithrombotics use before stroke, statin use before stroke, atrial fibrillation, initial NIHSS, TOAST, SBP, DBP, D-dimer, and baseline blood glucose. In men, adjusted for age, initial NIHSS, antithrombotics use before stroke, statin use before stroke, atrial fibrillation, acute treatment, D-dimer, TOAST, and baseline blood glucose. In women, adjusted for age, initial NIHSS, antithrombotics use before stroke, statin use before stroke, diabetes, TOAST, SBP, and baseline blood glucose.

## Data availability
Persons interested in obtaining access to the data should contact the corresponding author.

Received: 9 May 2024; Accepted: 10 March 2025
Published online: 25 April 2025

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## Acknowledgements
We thank the participants involved in this study.

## Author contributions
Concept and design: S.F and H.D. Acquisition, analysis, or interpretation of data: S.F., B.Z., H.L. (Hanhan Lei), N.L., and H.D. Drafting of the manuscript: S.F, B.Z., H.L. (Hanhan Lei) and H.D. Critical revision of the manuscript for important intellectual content: Y.D., H.L. (Huiying Lin), Q.C., and N.L. Statistical analysis: S.F., H.L. (Hanhan Lei), and H.D., H.D. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors have read and agreed to the published version of the manuscript.

## Funding
This study was supported by the Fujian Provincial Clinical Key Specialty Construction Project (grant number: 05029001) and Sponsored by Longyan City Science and Technology Plan Project (Grant number: 2023LYF17074). The funder (H.H) had no role in the design, data collection, data analysis, and reporting of this study.

## Declarations

## Competing interests
The authors declare no competing interests.

## Ethics approval
This study protocol was reviewed and approved by Fujian Medical University Union Hospital Ethics Committee (NO.2023KY030) and all methods were performed in accordance with relevant guidelines and regulations. Written informed consent was obtained from participants (or their legal guardian) to participate in the study.

## Additional information
**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-93914-5.

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