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# The association between fatigue and physical activity in patients hospitalized with subacute stroke

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## ABSTRACT

**Background:** Little is known about the association between fatigue and physical activity in patients hospitalized with subacute stroke.

**Objectives:** The aim of this study was to investigate the association between fatigue and physical activity in patients hospitalized with subacute stroke.

**Methods:** This cross-sectional study enrolled 244 consecutive patients with stroke who were admitted to a subacute rehabilitation ward at our hospital. We assessed fatigue with the Fatigue Assessment Scale (FAS) and used an accelerometer (Active style Pro HJA750-C, OMRON) to record the mean duration of sedentary behavior, light-intensity physical activity (LIPA) and moderate-to-vigorous-intensity physical activity (MVPA). We assessed all factors at 1 month after stroke. Multivariate linear regression analysis revealed the associations between FAS score and objectively measured physical activity.

**Results:** In total, we analyzed 85 patients. The duration of sedentary behavior was significantly associated with the FAS score ($\beta$ = 1.46, p = 0.037), and the Functional Balance Scale score ($\beta$ = -1.35, p = 0.045). The LIPA time was significantly associated only with FBS score ($\beta$ = 1.38, p = 0.045), whereas MVPA was not associated with any variable.

**Conclusions:** This study showed that the FAS score was significantly associated with

the duration of sedentary behavior. The more fatigued the patients with subacute stroke felt, the longer they spent in sedentary behavior, suggesting that fatigue management may be necessary to reduce sedentary behavior in these patients.

**KEYWORDS:** Cross-sectional study; Subacute stroke; Fatigue; Fatigue Assessment Scale; Physical activity

# The association between fatigue and physical activity in patients hospitalized with subacute stroke

## Introduction

Fatigue is a common complaint in patients with stroke.[1] At admission to a subacute rehabilitation ward, 56 of 156 patients (35.9%) assessed had fatigue.[2] Being older, female, unmarried,[3] having psychological factors such as depression and anxiety, and sleep disorders[4] have been reported to be associated with fatigue after stroke. It is also an independent risk factor of not being able to resume paid work,[5] poorer health-related quality of life,[6] dependence in activities of daily living, and higher fatality rate.[7]

After stroke, there is often a reduction in physical activity as a result, for example, of neurological impairment. Patients with subacute stroke admitted to rehabilitation hospitals spent most of their waking hours in sitting or lying.[8] Their physical activity will relate to physical function in the future,[9,10] and thus, it is important to identify the factors that influence their reduction in physical activity and to manage them.

In clinical practice, a variety of factors affect the reduction of physical activity in patients, and fatigue is one of them.[11–13] However, the relationship is still controversial. In previous research on patients with chronic stroke, fatigue was associated with

19 balance ability and fear of falling but not with physical activity.[14] Another study found
20 that fatigue was associated with steps per day but not time per day sitting and lying at 1
21 month after stroke.[11] As these two studies included patients in community, the
22 association between fatigue and physical activity in hospitalized patients with subacute
23 stroke remains unknown.
24 Therefore, we hypothesized that in patients hospitalized with subacute stroke, fatigue
25 would cause a decrease of physical activity, and if this association were clarified, it
26 might suggest the importance of managing fatigue to increase physical activity. Thus,
27 the purpose of this study was to clarify the association between fatigue and physical
28 activity in patients hospitalized with subacute stroke.
29
30 **Methods**
31 *Study design and patients*
32 This was a single-center, cross-sectional study for which we obtained informed
33 consent from all patients. From July 2021 to May 2023, 244 consecutive patients
34 diagnosed as having cerebral infarction or cerebral hemorrhage who were admitted to a
35 subacute rehabilitation ward at our hospital were enrolled in the study. Exclusion
36 criteria were those with a modified Rankin Scale (mRS) >3 before hospitalization, those

admitted more than one month after stroke, those discharged within 1 month of stroke, patients with dementia or aphasia as evaluated by their primary care physician, those with severe cardiopulmonary disease or psychiatric disease such as depression based on evaluation of the patient's medical records by a physical therapist, and those who did not agree to participate in this study. All participants underwent a standard rehabilitation program every day of the week that included physical therapy, occupational therapy, and speech therapy for a maximum of 180 minutes each day. Rehabilitation was of the same intensity and duration on weekends/holidays as on weekdays. Outside of rehabilitation time, based on the nurse's or therapist's evaluation of the patient's motor and cognitive abilities, the patients could move around the ward or within their own room. We conducted this study on the basis of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[15]

*Clinical characteristics*

We collected the following patient characteristics, including age, sex, body mass index (BMI), subtype of stroke (ischemic or hemorrhage stroke), National Institutes of Health Stroke Scale (NIHSS), Functional Independence Measure (FIM), medical history (e.g., hypertension, diabetes, heart disease), and Functional Balance Scale (FBS) from

55 the patients' electronic medical records. We performed the assessment with the NIHSS,
56 FIM, and FBS at one month after stroke. The NIHSS is a quantitative assessment of
57 stroke-related neurologic dysfunction that consists of items to evaluate level of
58 consciousness, gaze, visual fields, facial palsy, motor ability, ataxia, sensation,
59 language, dysarthria, and attention deficit.[16] Item scores are summed to a total score
60 ranging from 0 to 42, with a higher score indicating increased severity of the stroke. The
61 FIM consists of 18 items related to activities of daily living, each scored on a scale of 1
62 (full assistance) to 7 (independence).[17] Item scores are summed to a total score ranging
63 from 18 to 126, with a higher score indicating better levels of independence in ADL.
64 The FBS is a performance-oriented measure of balance[18] that consists of 14 items
65 scored from 0 to 4, with a total score ranging from 0 to 56. Higher scores on the FBS
66 indicate better balancing ability. We selected the FBS for use in this study because it is
67 reported to have good reliability and validity in patients with stroke[19] and to be
68 associated with physical activity in these patients.[14]
69
70 *Assessment of fatigue*
71 We assessed fatigue of the patients using the Fatigue Assessment Scale (FAS)[20] at one
72 month after stroke because this measure is feasible, valid, and reliable in patients who

have had a stroke.[21] The FAS is a self-reported questionnaire consisting of 10 questions scored 1–5 (1, never; 2, sometimes; 3, regularly; 4, often; 5, always). A higher score implies greater fatigue.[22]

*Physical activity measurement*

We measured physical activity using an activity monitor with a triaxial accelerometer (Active style Pro HJA750-C, OMRON, Kyoto, Japan).[23] Activity monitoring distinguishes between ambulant and other activities using a gravity-removal physical activity algorithm to calculate extremely accurate estimates of metabolic equivalents (METs) for a variety of body motions in daily activities.[24] In patients with subacute stroke, its validity and reliability have been shown throughout sitting, standing, and walking activities.[25] All patients wore the accelerometer belted to their waist between 8:00 am and 5:00 pm including during rehabilitation time, except while bathing, for 6 consecutive days. MET data were recorded every 60 s and processed using the manufacturer's software (HMS-HJA-IC01J, OMRON). We classified the MET data into three categories based on intensity: sedentary behavior, ≤1.5 METs; light-intensity physical activity (LIPA), 1.6–2.9 METs; and moderate-to-vigorous physical activity (MVPA), ≥3 METs. We calculated the average duration of sedentary behavior

(min/day), LIPA (min/day), and MVPA (min/day) and measured physical activity at one month after stroke.

*Statistical analysis*

The results are expressed as the median (interquartile range [IQR]) for continuous variables or number (%) for categorical variables. We performed multivariate linear regression analysis to determine the associations between FAS score and objectively measured physical activity (sedentary behavior, Model 1; LIPA, Model 2; and MVPA, Model 3). From the clinical point of view and previous studies on functional outcomes, the covariates selected to adjust bias were age, sex, BMI,[26] type of stroke, NIHSS, FIM-total,[27] and FBS score.[28] We considered a p-value of $<0.05$ to indicate statistical significance and performed all statistical analyses with EZR version 1.55 (Saitama Medical Center, Jichi Medical University, Saitama, Japan).

## Results

*Patients and clinical characteristics*

Participant flow through this study is shown in Figure 1. Of the 244 patients with stroke, we excluded 159 patients because of mRS >3 before hospitalization (n = 22),

admission more than 1 month after stroke (n = 51), discharge within 1 month of stroke (n = 9), dementia or aphasia (n = 34), severe complications (n = 9), refusal to participate in this study (n = 21), transfer to another hospital (n = 1), measurement failure of physical activity (n = 2), and suspension from the study due to the impact of the COVID-19 pandemic (n = 10). Finally, we enrolled 85 patients in the analysis, and their clinical characteristics are shown in Table 1. Their median age was 72.0 (IQR 65.0–79.0) years, and the number of males was 44 (51.8%). The median NIHSS score was 4.0 (IQR 2.0–7.0), and stroke severity in most patients was mild to moderate.[29] The median FAS score of 19.0 (IQR 14.0–26.0) for the participants in this study indicated that they were more mildly fatigued than those in a previous study.[11]

*FAS score and physical activity*

The results of the multivariate linear regression analysis are shown in Table 2. The sedentary behavior time in Model 1 was significantly associated with the FAS score ($\beta = 1.46$, $p = 0.037$) and the FBS score ($\beta = -1.35$, $p = 0.045$). The LIPA time in Model 2 was significantly associated only with FBS score ($\beta = 1.38$, $p = 0.045$). The MVPA time in Model 3 was not associated with any of the variables.

## Discussion

In this study, we investigated the association between fatigue and physical activity in in patients hospitalized with subacute stroke. To our knowledge, this is the first study to examine the associations between fatigue and objectively measured physical activity in these patients using multivariate analysis. The results indicated that there was an association between the duration of sedentary behavior and the FAS score in patients hospitalized with subacute stroke. A previous study reported that the FAS score was not associated with the duration of sedentary behavior 1 month after stroke by univariate analysis[11]; however, the result of the present study suggested that a higher FAS score was associated with longer sedentary time. Our result might differ from that of the previous study because we only included patients hospitalized with subacute stroke, and multiple linear regression analysis was used with adjustment for confounding factors.

In patients with chronic stroke, the higher the level of fatigue, the lower the self-efficacy for exercise and consequently the lower the participation in physical activity.[30] Although we did not examine self-efficacy in this study, in the patients with subacute stroke participating in the present study, those who were more fatigued may also have had lower self-efficacy for exercise, which might have resulted in reduced participation in physical activity, and as the duration of LIPA and MVPA decreased, it was replaced

by an increase in the duration of sedentary behavior. Increased physical activity may be able to reduce feelings of fatigue through improved cerebral blood flow,[31] aerobic fitness,[32] and muscle strength[33,34]; however, in the present research, those who felt more fatigued were found to be less physically active. It has also been reported that fatigue in patients with stroke responds well to rest[35] and that patients often respond to fatigue by resting,[36] but our study participants became increasingly fatigued the longer they rested by sitting or lying on their bed. Although the present study cannot prove a causal relationship between fatigue and the duration of sedentary behavior, in patients hospitalized with subacute stroke, increasing rest time by sitting or lying on a bed as a response to fatigue may not lead to improvement of fatigue.

The result of the present study suggested that fatigue management may be necessary to reduce the duration of sedentary behavior. It has been reported that participation in exercise is associated with good sleep, which may improve fatigue in patients with chronic stroke.[37] Interventional studies are needed to examine whether a similar effect exists in patients hospitalized with subacute stroke. In addition, because both physical activity and fatigue are related to prognosis,[9,10] and the relationship between the two may change over time, longitudinal studies are needed to clarify the long-term association between the two factors and their impact on prognosis in patients

with stroke.

## Limitations

This study has several limitations. First, this was a single-center, cross-sectional study consisting of a relatively small number of patients; thus, the results should be interpreted with caution. Second, there is potential selection bias as patients who were admitted more than one month after stroke or discharged within one month of stroke were excluded. Third, stroke lesion location may also influence fatigue,[38] but this was not considered in this study. Fourth, as the FAS is a questionnaire, patients with aphasia or dementia were excluded because their responses may be less reliable. Fifth, self-efficacy may also be associated with fatigue, but this was not considered in the present study. Finally, depression and sleep disorder, which are closely related to fatigue,[4] were not investigated.

## Conclusions

The present study showed that the FAS score was significantly associated with the duration of sedentary behavior. The more fatigued a patient with subacute stroke felt, the longer was the time spent in sedentary behavior.

## Funding

This research received no external funding.

## Conflicts of Interest

The authors report that they have no competing interests to declare.

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306 **Figure Legend**

307 **Figure 1.** Flow chart of patients through the study. mRS: modified Rankin Scale.

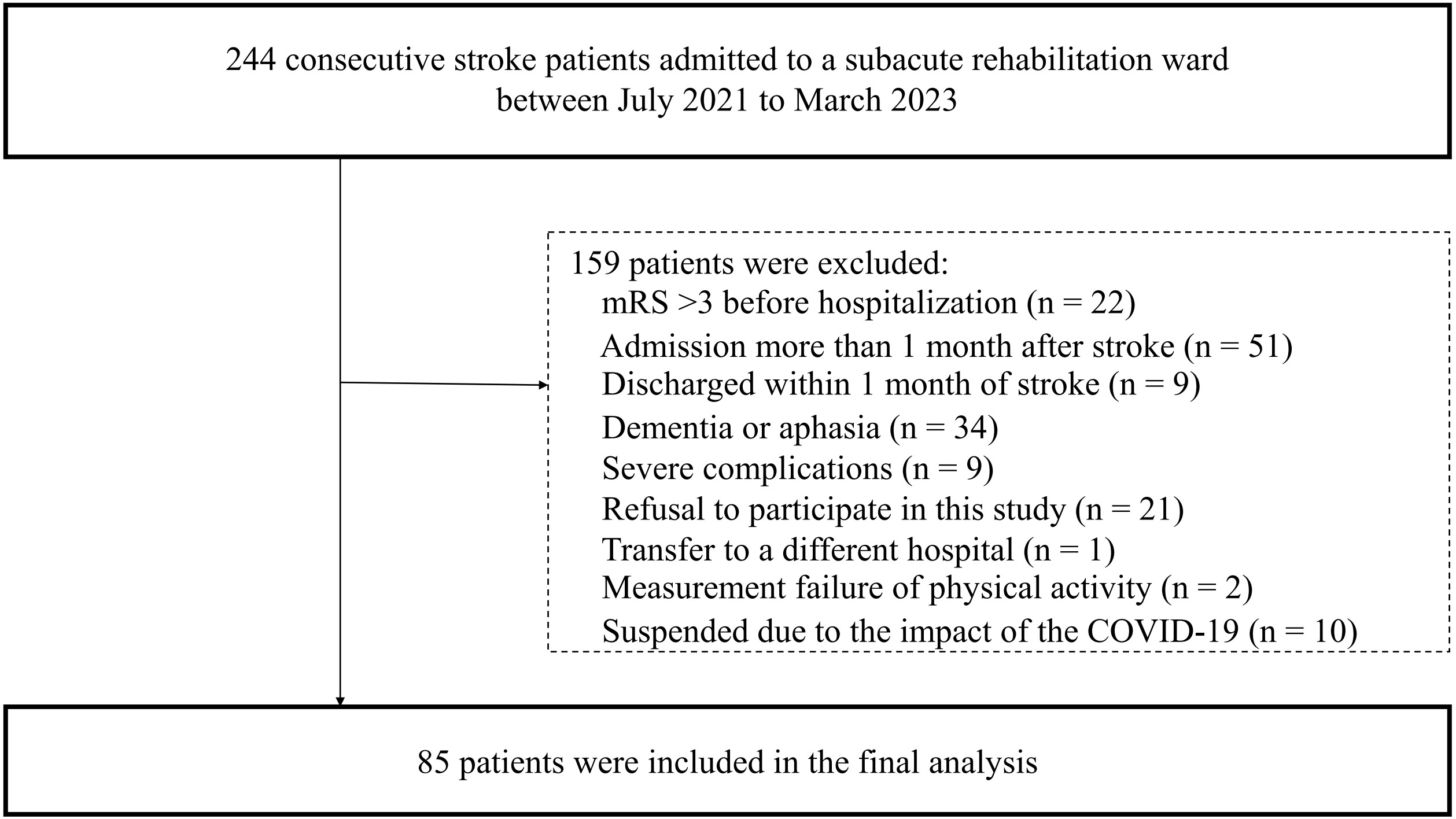
244 consecutive stroke patients admitted to a subacute rehabilitation ward between July 2021 to March 2023
159 patients were excluded:
mRS >3 before hospitalization (n = 22)
Admission more than 1 month after stroke (n = 51)
Discharged within 1 month of stroke (n = 9)
Dementia or aphasia (n = 34)
Severe complications (n = 9)
Refusal to participate in this study (n = 21)
Transfer to a different hospital (n = 1)
Measurement failure of physical activity (n = 2)
Suspended due to the impact of the COVID-19 (n = 10)
85 patients were included in the final analysis

**Table 1.** Clinical characteristics of the patients.

| | All patients (n = 85) |
|---|---|
| Age (years) | 72.0 (65.0-79.0) |
| Sex (male), n (%) | 44 (51.8) |
| BMI (kg/m$^2$) | 23.0 (20.3-26.0) |
| Stroke type, n (%) | |
| Infarction | 60 (70.6) |
| Hemorrhage | 25 (29.4) |
| Medical history, n (%) | |
| Hypertension | 50 (58.8) |
| Respiratory disease | 6 (7.1) |
| Diabetes | 20 (23.5) |
| Dyslipidemia | 24 (28.2) |
| Stroke | 14 (16.5) |
| Kidney Disease | 3 (3.5) |
| NIHSS | 4.0 (2.0-7.0) |
| FIM | |
| Total | 85.0 (65.0-106.0) |
| Motor | 59.0 (39.0-77.0) |
| Cognitive | 29.0 (24.0-33.0) |
| FBS | 43.0 (26.0-50.0) |
| SB (min/day) | 399.8 (364.3-428.5) |
| LIPA (min/day) | 120.3 (90.5-165.8) |
| MVPA (min/day) | 5.3 (3.3-11.3) |
| FAS total score | 19.0 (14.0-26.0) |

Values are shown as median (interquartile range) for continuous variables or number (%) for categorical variables.

**Abbreviations:** BMI = body mass index; NIHSS = National Institutes of Health Stroke Scale; FIM = Functional Independence Scale; FBS = Functional Balance Scale; SB = sedentary behavior; LIPA = light-intensity physical activity; MVPA = moderate-to-vigorous physical activity; FAS = Fatigue Assessment Scale.

**Table 2.** Multivariate regression analysis for physical activity.

| | SB<br>Model 1<br>(adjusted<br>$R^2 = 0.32$) | | LIPA<br>Model 2<br>(adjusted<br>$R^2 = 0.30$) | | MVPA<br>Model 3<br>(adjusted<br>$R^2 = 0.14$) | |
|---|---|---|---|---|---|---|
| | β | p | *β* | p | *β* | p |
| Age | -0.81 | 0.107 | 0.92 | 0.073 | 0.06 | 0.599 |
| Sex | -6.17 | 0.562 | 8.28 | 0.447 | 3.54 | 0.170 |
| BMI | 1.28 | 0.309 | -1.70 | 0.187 | -0.05 | 0.861 |
| NIHSS | -3.38 | 0.183 | 3.06 | 0.238 | 0.28 | 0.646 |
| FIM-motor | -0.85 | 0.079 | 0.70 | 0.156 | 0.16 | 0.173 |
| FIM-cognitive | -0.09 | 0.926 | 0.58 | 0.566 | -0.05 | 0.823 |
| FBS | -1.35 | 0.045 | 1.38 | 0.045 | 0.16 | 0.324 |
| FAS score | 1.46 | 0.037 | -1.29 | 0.071 | -0.06 | 0.710 |

**Abbreviations:** SB = sedentary behavior; LIPA = light-intensity physical activity; MVPA = moderate-to-vigorous physical activity; BMI = body mass index; NIHSS = National Institutes of Health Stroke Scale; FIM = Functional Independence Scale; FBS = Functional Balance Scale; FAS = Fatigue Assessment Scale.