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Pre-stroke physical activity is related to good functional outcomes in stroke patients after endovascular thrombectomy.

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Keywords: physical activity; stroke; endovascular thrombectomy; prognosis; functional outcome.

Abstract. Studies have shown that regular physical activity (PA) may reduce the risk of stroke. Nevertheless, the protective effect of pre-stroke PA on the post-stroke functional status in patients treated with endovascular thrombectomy (EVT) is still uncertain. For this study, hospitalized patients with acute ischemic stroke were selected, all of whom underwent EVT after occlusion of the large vessels in the anterior circulation. The PA levels before the stroke were assessed by the International Physical Activity Questionnaire, and the outcome indicators (the modified Rankin scale score and the Barthel index) were evaluated. A total of 144 patients were included in this study. Among the patients with high PA levels before the stroke, men were more active than women, and the proportion of patients with smoking and alcohol abuse was high before admission. Also, the patients with a high PA level were more likely to have no history of hypertension and atrial fibrillation, and had lower triglyceride levels at admission. We determined that a high pre-stroke PA level is independently related to a favorable functional outcome at three months. In addition, there was no correlation between a high pre-stroke PA and a good functional outcome at two weeks. A high pre-stroke PA level is independently associated with satisfactory activities of daily living at three months. Regular PA before a stroke is an independent predictor of a favorable functional outcome in patients with anterior circulation strokes who receive EVT, and it has a protective effect on the functional prognosis.

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La actividad física previa al ictus se relaciona con un buen resultado funcional en pacientes con ictus tras una trombectomía endovascular.

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Palabras clave: actividad física; ictus o infarto cerebral; trombectomía indovascular; pronóstico; resultado funcional.

Resumen. Diversos estudios han demostrado que la actividad física regular (AF) antes del ictus puede reducir su riesgo, pero el efecto protector funcional de la AF previa al ictus sobre el estado funcional posterior al ictus, aún no está claro en los pacientes tratados con trombectomía endovascular (TEV). Se seleccionaron pacientes hospitalizados con ictus isquémico agudo, a todos los cuales se les realizó TEV por una oclusión de los grandes vasos de la circulación anterior. El nivel de la AF antes del infarto cerebral fue evaluado por el Cuestionario Internacional de Actividad Física y se evaluaron los indicadores de resultado de acuerdo a la puntuación de la escala de Rankin modificada y el índice de Barthel. Un total de 144 pacientes fueron incluidos en este estudio. Entre los pacientes con niveles elevados de AF antes del ictus, los hombres eran más activos que las mujeres, y la proporción de pacientes con hábito tabáquico y abuso de alcohol era alta antes del ingreso. Además, lo más probable es que los pacientes con los niveles elevados de AF no tenían antecedentes de hipertensión y fibrilación auricular, y los niveles de triglicéridos estaban más bajos al momento de su ingreso. Se determinó que un nivel alto de AF previa al ictus se relaciona de forma independiente con un buen resultado funcional a los 3 meses. Además, no hubo correlación entre la AF previa al ictus avanzado y un buen resultado funcional a las 2 semanas. Un nivel alto de AF previa al infarto cerebral se asocia de forma independiente con actividades satisfactorias de la vida diaria a los 3 meses. Conclusión: La AF regular antes del ictus es un predictor independiente de un buen resultado funcional en los pacientes con el ictus de la circulación anterior que reciben TEV, y tiene un efecto protector sobre el pronóstico funcional.

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INTRODUCTION

Stroke is one of the most prevalent clinical diseases in the cerebrovascular system and compromises patients' health and quality of life [1,2]. In this disease, cell death happens because of an unexpected decrease or stop of the local arterial blood flow to the brain tissue. This leads to cell death and damage to some parts of the brain, causing its malfunction. It can cause the following symptoms: paralysis, weakness or sensory changes in one side of the body or face, vertigo, understanding or speech disruption, or low vision on one side [3,4]. Stroke is divided into two types: ischemic stroke, with high morbidity, it can cause disability or death, because of the loss of blood supply and hem-

orrhagic stroke, caused by bleeding, with high mortality, high disability rate and high relapse speed [3,5,6]. Ischemic stroke is the main cause of death and disability. This disease almost always happens in people over 40 years-old. To date, recombinant tissue plasminogen activator (rt-PA), endovascular thrombectomy (EVT) and antiplatelet therapy are the only three well-documented emergency treatment methods for ischemic stroke [7]. For patients with acute ischemic stroke caused by an occlusion of the large vessels in the anterior circulation, EVT has become one of the standard treatment methods when there is an indication for EVT (within a specified time limit, based on the mismatch between regional cerebral perfusion and infarction) [8,9]. Approximately two-thirds of stroke survivors need some help in their daily life [10], so it is very important for them to have a reduced degree of functional impairment.

Fors M *et al*. found that preoperative exercise therapy was moderately correlated with maintaining the postoperative physical activity level of patients with degenerative lumbar diseases [11]. Moran *et al.* found that preoperative exercise rehabilitation training can reduce all kinds of postoperative complications after abdominal surgery [12]. In addition, there is strong evidence that regular physical activity (PA), as a preconditioning stimulus [13], has been consistently shown to be associated with a reduced risk of first stroke and its recurrence [14]. Animal studies have proven the beneficial effects of preischemic exercise training on stroke, and these beneficial effects include a prolonged survival time, a reduction in neurological deficits [15], a decreased infarct volume and an improvement in the sensorimotor function after stroke [13,16]. The mechanism by which exercise provides this protection may involve a combination of highly interactive ways, such as reducing the neurotoxicity through the glutamate system [15], reducing oxidative stress and apoptosis of nerve cells [17], inhibiting the inflammatory injury after cerebral ischemia/reperfusion [18], improving the function of the blood–brain barrier after an ischemic stroke [19], activating endothelial nitric oxide synthase [16] to reduce the vascular injury after stroke, and promoting the expression of heat shock protein in neurons and glia [20]. Therefore, the clinical guidelines for stroke prevention recommends regular PA (2014, Class IIa, Level of Evidence C) [21]. Regular PA is an important recommendation in preventing stroke [22].

In this study, we intend to provide PA advice to the public by investigating the PA level before stroke and determining whether it has a beneficial effect on the poststroke functional status in patients who have had EVT, for a stroke that was caused by an anterior circulation large vessel occlusion.

METHODS

This study is a prospective cohort study that was conducted from September 2018 to May 2020. Patients with acute stroke consecutively admitted to the Department of Neurology of the Affiliated Hangzhou First People's Hospital of Zhejiang University School of Medicine (Hangzhou, China, a first-class tertiary hospital) were included. Stroke was defined according to the World Health Organization (WHO) standard [23]. In addition, according to the diagnosis and treatment standard that was currently used in the respective stroke unit ward of the neurology department, all patients received standardized reperfusion therapy (EVT with or without intravenous rt-PA).

Inclusion and exclusion criteria

The inclusion criteria of this study were as follows: patients with acute ischemic stroke who were at least 18 years old and were hospitalized within 24 hours after symptoms had appeared; patients who had a confirmed occlusion of the anterior circulation large vessels on admission; patients who were treated with emergency EVT; and patients who had a modified Rankin scale

(mRs) score of ≤ 1 before the stroke. The exclusion criteria were as follows: no reliable information about the patient's past physical activities; patients with pre-stroke cognitive impairment; patients who were lost to follow-up; and patients who were missing information on their mRs at three months.

The Medical Ethics Committee of the Affiliated Hangzhou First People's Hospital of Zhejiang University School of Medicine approved this study. After fully informing the patients of the condition assessment and treatment methods in this study, the patients or their legally authorized person signed the informed consent form and participated in the clinical trial. The patient had the right to withdraw from the trial.

Observation and evaluation index

We recorded information including age, sex, height, weight, body mass index, education level, smoking (currently smoking more than ten cigarettes a day), alcohol abuse, on-going antiplatelet therapy, ongoing anticoagulant therapy, hypertension, diabetes, atrial fibrillation (persistent or paroxysmal), the severity of stroke (the National Institute of Health Stroke Scale, NIHSS) at admission, hypertension, vascular occlusion, blood lipids, blood glucose, fibrinogen and the PA level before the stroke.

All patients had a CTP (computed tomography-guided perfusion scan), an emergency computed tomography (CT) and/or a magnetic resonance imaging scan. The patient's baseline arterial occlusion was evaluated by two methods: digital subtraction angiography and computed tomography angiography. If the M2-MCA segment (middle cerebral artery, MCA, the second segment of the middle cerebral artery) was noted to be occluded when evaluating the anterior circulation of large vessels, then a distal occlusion was considered. The M1 segment (the first segment of the middle cerebral artery) and intracranial carotid artery, ICA) were considered proximal occlusions (proximal-M1, proximal-ICA).

Our research group conducted quantitative and qualitative interviews with each patient by a questionnaire to determine the patient's regular PA level before the stroke.

When the patient could not answer because of aphasia, memory loss or any other stroke-related reasons, we interviewed the patient's close relatives. In this study, we used a standardized and validated questionnaire, the International Physical Activity Questionnaire (IPAQ) [18], which recorded the PA of the patients during the week before admission. The participants were asked if the activity level of that week actually represented the activities of the previous several weeks. If not, the patients were excluded from the study. The IPAQ quantified the level of PA. The calculation of the total score of the questionnaire was defined as the sum of the daily cumulative time (in minutes) and frequency (days) of all activities with different intensities (low, medium, or intense) in four fields (work, transportation, housework, gardening, and leisure) that were performed in a week. The level of physical activity (MET-min/week) is expressed by the metabolic equivalent (MET).

According to the criteria recommended by the IPAQ working group, the patients were divided into three groups based on their pre-stroke PA levels. The details are as follows:

High PA was defined as meeting any one of the following two standards: (a) the total number of days that the patient engaged in various types of vigorous-intensity physical activity was ≥3 d/w, and the overall level of physical activity was ≥1500 MET-min/week; (b) the total number of days that the patient engaged in physical activity at three intensities was >5 d/w, and the overall level of physical activity was ≥3000 MET-min/week.

Moderate PA was defined as meeting any one of the following three standards: (a) engaging in all kinds of vigorous physical activity for at least 20 min every day that totaled ≥3 d/w; (b) engaging in all kinds of moderate intensity and/or walking activities for at least 30 minutes every day that totaled ≥ 5

d/w; (c) the total number of days of that the patient engaged in physical activity at 3 intensities was ≥ 5 d/w, and the overall level of physical activity was ≥ 600 MET-min/week.

Low PA was defined as no activity had been reported, or if there was some activity, it was lower than 600 MET-min/week [19].

We used the mRS to evaluate the functional results and the Barthel Index to evaluate the activities of daily living (ADL) results, and these data were obtained from in person interviews or communication tools.

Evaluation at admission

Within 48 hours after admission, an interview was conducted by a researcher (Yan Wu) who did not participate in the clinical treatment and was trained on how to conduct the clinical evaluation. The basic information and clinical information of the patients were recorded in the case report form.

Follow-up endpoint

The primary outcome was a good functional outcome defined as an mRs≤ 2 after three months of stroke (90 days (within a window of ±7 days) after entering the study). The secondary outcomes were the mRs score (Good defined as ≤2) two weeks after stroke (14 days and within a window of ±1 day after the study entry) and the ADL l evel (Good defined as a Barthel index score between 95 and 100) three months after admission (90 days within a window of ±7 days after the study entry).

Statistical analysis

Data for continuous variables were reported as the mean ± standard deviation (SD) or median (interquartile range, IQR), depending on whether the variables were normally distributed. Categorical variables are described as percentages. The χ^2 test was used to compare the categorical variables between the groups, and Student's t test or ANOVA (normal distribution variables) and the Kruskal–Wallis test (nonnormal distribution variables) were used to compare the continuous variables between the groups.

We used a multivariate logistic regression model to evaluate the correlation between the PA level before stroke and the functional outcome. In the logistic regression model, the pre-stroke PA was evaluated in two different ways as an independent variable: (1) as a categorical variable, it was compared with the high, moderate and low PA groups; (2) as a binary variable, we used the receiver operating curve (ROC) to determine the predictive value of the IPAQ score for predicting a good functional outcome in order to find the best cutoff point for the total IPAQ score for the prediction of a good functional outcome. The weekly exercise time corresponding to the IPAQ cutoff point can be calculated by IPAQ score/(days * METs assigned by different intensity activities). The cutoff point was used to divide the patients with different pre-stroke PA levels into two groups, high and low PA, and the differences between the two groups were compared. The results are expressed as the adjusted odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs).

All statistical analyses were conducted using SPSS 20.0 for Windows (IBM Corp). A two-sided P value of < 0.05 was considered to be statistically significant.

RESULTS

Clinical characteristics of the population

During the trial, 945 patients with ischemic stroke were admitted to the researcher's hospital. Patients who did not meet the inclusion criteria were excluded: six patients whose PA in the last week before admission did not represent the patient's activity in the weeks prior to stroke and four patients who lacked reliable information on their previous physical activity. No patients were lost to follow-up. A total of 144 patients were finally included in this study (Fig. 1). Table 1 summarizes the baseline characteristics of the cohort and the three groups of patients with different PA levels, and this data included the patients' basic data and clinical information.

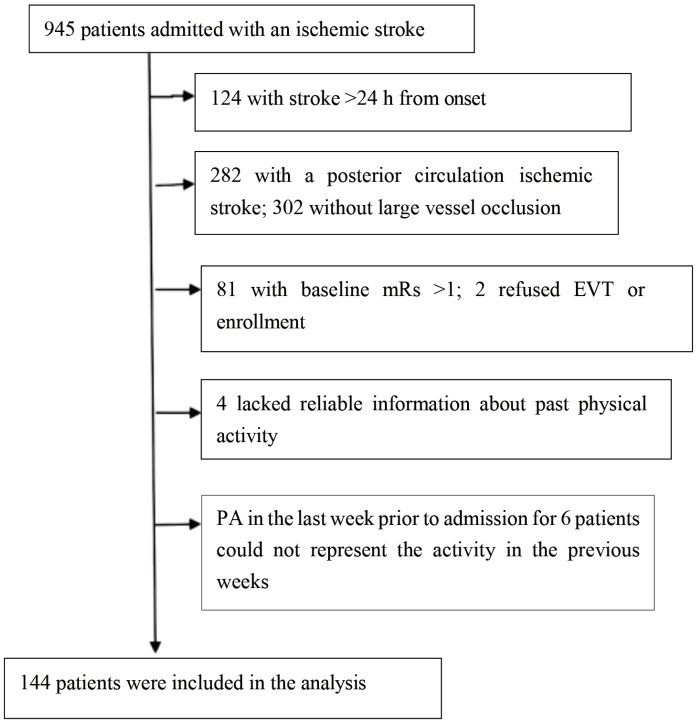

Fig. 1. Flow diagram of patients' selection for the study (PA= Physical activity. EVT= Endovascular thrombectomy; mRs = modified Rankin scale.

Table 1
Socio-demographic of the patient.

Variables		Total population (n=144)	Low PA (n=35)	Moderate PA (n=65)	High PA (n=44)	p
Sex (males)		88(61.1%)	17(48.6%)	36(55.4%)	35(79.5%)	0.009
Age, years		69.6±11.3	69.3±13.0	71.0 ±10.3	67.9±11.3	0.375
Educa tion level	Primary school and below	98(68.1%)	24(68.6%)	43(66.2%)	31(70.5%)	
	Junior middle school	32(22.2%)	7(20.0%)	16(24.6%)	9(20.5%)	0.972
	Senior high school or above	14(9.7%)	4(11.4%)	6(9.2%)	4(9.1%)	
Smoking habit		45(31.2%)	12(34.3%)	13(20.0%)	20(45.5%)	0.017
Alcohol abuse		37(25.7%)	5(14.3%)	14(21.5%)	18(40.9%)	0.016
BMI, kg/m^2		23.4±3.5	23.7±4.1	23.1±3.5	23.5±2.9	0.389
NIHSS at admission		16 [13-20.75]	17 [12.5-21.5]	16 [12.25-21]	16 [13-20]	0.894

Notes: Data are expressed as n (%), mean ± standard deviation or the median [interquartile ranges].

Data on BMI were missing for four patients (1 in the low PA group, and 3 in the mderate PA group) Data on NIHSS at admission were missing for 4 patients (2 in the low PA group, 1 in the moderate PA group, and 1 in the high PA group).

The average age of the enrolled population was 69.6±11.3 years old, 61.1% of the patients were male, and their average baseline NIHSS was 16 (quartile 13, 20.75). Cardiogenic stroke was the most common subtype of stroke (46.50%). The median total IPAQ score was 1680 MET-min/week (quartile range 661.5, 3659.25). According to the IPAQ grouping criteria, there were 44 (30.56%) patients with high PA levels, 65 (45.14%) patients with moderate levels, and 35 (24.31%) patients with low activity levels.

The differences between the groups (patients classified according to the PA levels before the stroke) are shown in Table 1 and Table 2. When the patients with high pre-stroke PA levels were compared with the patients with low and moderate PA levels, men were more active than women, and the proportion of patients with smoking and alcohol abuse was high before admission. The patients with high pre-stroke PA levels were more likely to have no history of hypertension or atrial fibrillation and had lower triglyceride levels at admission. The baseline NIHSS scores did not differ among the three groups of patients (p = 0.894).

Comparison of the primary neurological outcomes

Seventy patients (48.61%) showed good functional outcomes at three months (Table 3). The proportion of functionally-independent patients at three months was significantly higher in the patients with high PA levels (Table 3). The logistic regression analysis showed that high pre-stroke PA levels were independently associated with good functional outcomes (OR=3.19, 95% CI: 1.07-9.47, p=0.037, Table 4, Model A).

Model A: PA of the patients during the week before admission and Model B: High PA was defined as meeting any one of the following two standards: (a) the total number of days that the patient engaged in various types of vigorous-intensity physical activity was ≥3 d/w, and the overall level of physical activity was ≥1500 MET-min/week; (b) the total number of days that the patient engaged in physical activity at three intensities was >5 d/w, and the overall level of physical activity was ≥3000 MET-min/week.

Analysis of the ROC curve analysis showed that the total IPAQ cutoff point score of 3859.5 MET-min/week (the area under the curve is 0.688, 95% CI 0.586-0.789) has the highest predictive value of functional independence, with a sensitivity of 74.8% and a specificity of 68.8% (p=0.001). Regarding the ROC curve, it is necessary to mention that due to the sensitivity of 68.8% and specificity of 74.8%, and subsequently high false negative and false positive values (FN= 25.2%; FP: 21.84%), this test has limitations as a good indicator to distinguish PA groups (Fig. 2).

The logistic regression analysis showed that the pre-stroke high PA level group, which was above the cutoff point (IPAQ > 3859.5 MET-min/week), was also independently associated with good functional outcomes (OR = 3.3, 95% CI: 1.25-8.71, p = 0.016, Table 4, model B).

Comparison of the secondary neurological outcomes

Thirty-nine patients (27.08%) showed good functionality at two weeks (Table 3). The logistic regression analysis showed no correlation between a high pre-stroke PA and a good functional outcome at two weeks (Table 4, Models A and B). Regarding the Barthel index, 71 patients (49.30%) showed satisfactory activities in daily living at three months (Table 3). The proportion of patients with acceptable activities of daily living at three months was significantly higher in the patients with high levels of PA (Table 3). The logistic regression analysis showed that a high pre-stroke PA was correlated independently with good ADL (p <0.05, Table 4, Models A and B). Pre-stroke PA is an independent predictor of good ADL.

Table 2
Characteristics of the patients at baseline.

Variables		Total population (n=144)	Low PA (n=35)	Moderate PA (n=65)	High PA (n=44)	p
Etiology of cerebral infarction	Atherosclerosis	28(19.4%)	7(20.0%)	10(15.4%)	11(25.0%)	0.101
	Cardiogenic	67(46.5%)	15(42.9%)	38(58.5%)	14(31.8%)	
	Undetermined	49(34.0%)	13(37.1%)	17(26.2%)	19(43.2%)	
Site of occlusion	Proximal-ICA	53(36.8%)	13(37.1%)	20(30.8%)	20(45.5%)	0.6
	Proximal-M1	77(53.5%)	18(51.4%)	39(60.0%)	20(45.5%)	
	Distal-M2	14(9.7%)	4(11.4%)	6(9.2%)	4(9.1%)	
Minutes from stroke onset to admission		260 [185.5-363]	292 [169-402]	239 [182-332]	296 [213-403.75]	0.116
Reperfusion therapies	EVT alone	102(70.8%)	26(74.3%)	44(67.7%)	32(72.7%)	0.745
	Combined rt-PA and EVT	42(29.2%)	9(25.7%)	21(32.3%)	12(27.3%)	
On-going antiplatelet therapy		24(16.7%)	9(25.7%)	8(12.3%)	7(15.9%)	0.226
On-going anticoagulant therapy		16(11.1%)	5(14.3%)	7(10.8%)	4(9.1%)	0.761
Hypertension		96(66.7%)	28(80.0%)	46(70.8%)	22(50.0%)	0.012
Diabetes		31(21.5%)	10(28.6%)	13(20.0%)	8(18.2%)	0.494
Glucose, mmol/L		7.2 [6.4-8.5]	7.7 [6.375-9.25]	7.2 [6.4-7.99]	6.985 [6.275-8.125]	0.470
Total cholesterol, mmol/L		3.69 [3.165-4.425]	3.78 [3.25-4.4125]	3.695 [3.1375-4.3025]	3.59 [3.13-4.87]	0.828
HDL cholesterol, mmol/L		1.13 [0.925-1.245]	1.045 [0.8975-1.18]	1.14 [0.955-1.25]	1.16 [0.93-1.25]	0.140
LDL cholesterol, mmol/L		1.97 [1.635-2.565]	2.13 [1.7375-2.4825]	1.99 [1.6325-2.5825]	1.9 [1.56-2.93]	0.902
Triglyceride, mmol/L		1.31 [0.8-1.74]	1.435 [1.1575-2.0525]	1.365 [0.8-2.2175]	1.01 [0.63-1.54]	0.018
Fibrinogen,g/L		2.57 [2.28-2.99]	2.65 [2.45-3.09]	2.45 [2.1425-2.99]	2.595 [2.2875-2.94]	0.269
Atrial fibrillation		79(54.9%)	20(57.1%)	42(64.6%)	17(38.6%)	0.027
CAD		15(10.4%)	4(11.4%)	6(9.2%)	5(11.4%)	0.915

Notes: Data are expressed as n (%), mean ± standard deviation or the median [interquartile ranges].

Proximal-ICA= Proximal- intracranial carotid artery; Proximal-M1= Proximal- the first segment of middle cerebral artery; Distal-M2= Distal- the second segment of the middle cerebral artery; rt-PA = recombinant tissue plasminogen activator; EVT= Endovascular thrombectomy; HDL= High density lipoprotein; LDL=Low density lipoprotein; CAD= Coronary heart disease; PA= Physical activity.

Data on glucose was missing for 1 patient (in the low PA group)

Data on total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride were missing for 3 patients respectively (1 in the low PA group, 1 in the moderate PA group, and 1 in the high PA group), Data on fibrinogen was missing for 1 patient (in the moderate PA group.

Table 3
Comparison of primary and secondary neurological outcomes in different groups.

Variables	Total population (n = 144)	Low PA (n = 35)	Moderate PA (n = 65)	High PA (n = 44)	p
mRs(≤2) at 3 months	70(48.61%)	10(28.57%)	31(47.69%)	29(65.91%)	0.004
mRs(≤2) at 2 weeks	39(27.08%)	4(11.43%)	18(27.69%)	17(38.64%)	0.026
Barthel index (95~100) at 3 months	71(49.30%)	10(28.57%)	30(46.15%)	31(70.45%)	0.001

Notes: Data are expressed as n (%); PA= Physical activity. mRs= modified Rankin scale

Table 4
Multivariate regression analyses of the association between pre-stroke physical activity level and outcome variables.

Level of PA		mRs 0–2 at 3 months [a] Odds ratio	p-value	mRs ≤2 at 2 weeks [a] Odds ratio	p-value	Barthel Index of 95 or 100 at 3 months [a]	p
Model A	Low	1.0	0.096	1.0	0.163	1.0	0.03
	Moderate	2.34(0.89,6.15)	0.086	3.18(0.92, 11.03)	0.068	2.07(0.81, 5.28)	0.13
	High	3.19(1.07,9.47)	0.037	3.12(0.84, 11.58)	0.089	4.25(1.45,12.41)	0.008
Model B	High PA group: IPAQ≥ cutoff point	3.3(1.25, 8.71)	0.016	1.91(0.77, 4.78)	0.166	3.32 (1.29, 8.56)	0.013

Notes:

In model A, the relationship between pre-stroke PA and prognosis in high, moderate and low level groups was compared.

In model B, the IPAQ cutoff point was 3859.5 MET-min/week.

Patients were divided into high level and low level PA groups with this cutoff point.

The relationship between these two groups and good functional outcomes was compared. PA= Physical activity; IPAQ= International Physical Activity Questionnaire. mRs= modified Rankin scale

a Adjustment for sex, smoking, alcohol abuse, hypertension, atrial fibrillation and triglyceride levels.

DISCUSSION

This prospective study on patients with an acute anterior circulation large vessel occlusion shows that a high level of regular PA before stroke was significantly related to a good functional outcome and better activities of daily living after an EVT.

To the best of our knowledge, there is no report on the influence of the PA on the functional prognosis of stroke in patients who have received an EVT for a stroke caused by an anterior circulation occlusion.

For people who are relatively inactive, such as the elderly (who had an average age of 69 years old in this study), the necessity of physical activity in their daily life and work has been confirmed in this research. As a benefit for the patients themselves and society, PA before a stroke can play a neuroprotective role, which is helpful to improve significantly the outcome of a stroke, reduce the social burden and achieve a healthy and disability-free life.

As shown in Table 1, PA may play a dose-dependent role. The ROC curve indicated a

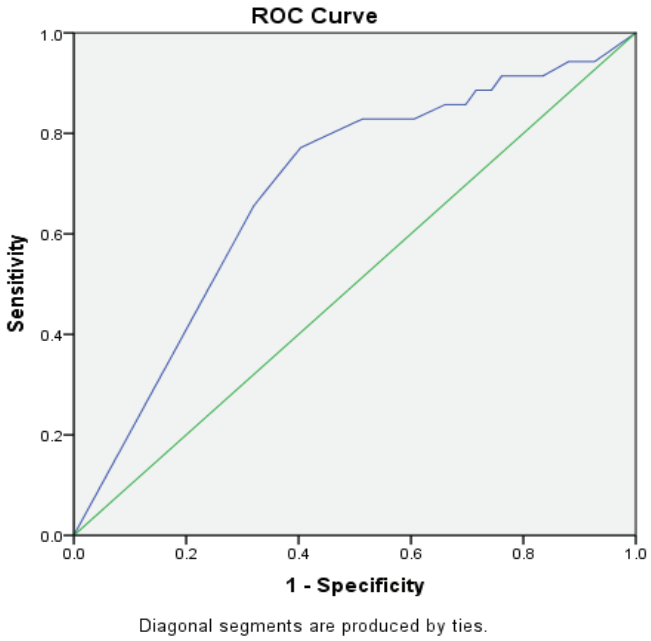

Fig 2. Receiver operating characteristics (ROC) curve analysis for predictive power of International Physical Activity Questionnaire (IPAQ) score on functional outcome in stroke patients who were treated with EVT(= Endovascular thrombectomy). Area under curve (95%CI) =0.688(0.586-0.789).

beneficial effect of PA before a stroke on the stroke outcome and that the cutoff point was 3,859.5 MET-min/week. The required PA level can be reached by walking for approximately three hours (180 minutes) every day for seven days or by intense physical activity (such as lifting heavy objects, digging, jogging or fast cycling) for approximately 69 minutes every day. Among the above activities, walking is common, convenient, and cheap. Walking requires the use of large skeletal muscles of the whole body, with almost no side effects; therefore, it is worthy of promotion.

Previous studies that evaluated patients who did not receive rt-PA and EVT [20,21], a study that did not mention thrombolysis [24], and other retrospective observational study that evaluated patients who received rt-PA [25], showed that pre-stroke PA could benefit patients with ischemic stroke in terms of its severity at admission, the final infarct area size reduction and the prognosis. In contrast, other studies that evaluated patients with intravenous rt-PA thrombolytic therapy [26], or only conventional drug therapy [27], showed that PA had no significant effects on the stroke severity and functional outcome.

In this study, we found that there was no significant association between the physical activity level before stroke and the severity of the stroke. However, we found a significant association between the PA level before the stroke and obtaining a satisfactory functional outcome at three months, consistent with some of the abovementioned research results. The inconsistency of the results may be caused by the inclusion population and the research design. The patients in this study had a high degree of stroke (NIHSS score was 16 at admission), which was why they were willing to undergo EVT.

The operation itself may also affect the functional outcome. Another reason may

be that we used the IPAQ to evaluate PA. This questionaire is currently recognized as an effective and worldwide used method for measuring the physical activity levels of adults. It has been used in Chinese population research and has excellent validity and reliability [28,29]. The IPAQ involves asking about the patient's physical activities in various fields of daily life, so the estimated level of the patient's physical activity is higher than the other survey results (in some of above mentioned studies) that simply asked about the patient's physical activity that was undertaken in their leisure time [25,26,30]. The IPAQ will not classify the patients with high-intensity professional sports activities and lack of leisure time for physical activities into the moderate or low PA group. In addition, compared with the effective drugs for treating stroke, the physical activity level is more likely to be only a surrogate marker of the patient's past health status [31].

Our research has some limitations. First, we used a cohort study. The nature of this type of observational study makes us unable to determine the causality. There may also be residual confounding factors, such as the different surgical times and smoothing degrees for each patient, the degree of professional rehabilitation intervention during the postoperative recovery, and psychological factors, such as depression and anxiety symptoms that affect the patient's physical function and stroke prognosis. Second, because the patients entered the study based on their will and compliance with the inclusion criteria, researchers could not select the participants in a targeted way, which resulted in the inconsistency in some of the baseline data levels in the different groups of patients. However, we believe that these inconsistencies are due to the characteristics of the different level of PA groups and the results of the study. Third, the severities of the strokes in the patients enrolled in this study were high. For patients with severe disability and aphasia, most of their PA levels before onset were determined by questioning their families. Moreover, we used self-reports for retrospective registration to assess the level of physical activity before stroke. All these may lead to bias in the results of pre-stroke activity.

In conclusion, this study confirms that regular PA before stroke is an independent predictor of a good functional outcome in patients with an anterior circulation stroke who receive EVT, and PA can play a protective role in the functional prognosis. In future research, we can expand the sample size to determine whether pre-stroke exercise plays a beneficial role in the stroke outcome.

Limitation

According to the cut off obtained from the ROC curve and the values of FN and FP, the test used had limitations for distinguishing groups, and it is necessary and important to pay attention to this point in future studies.

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Competing Interests

The authors declared that they have no competing interests.

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Authors' Contribution

XM, CY, WX, and JL contributed to the conception of the study. XM, HD, and WX performed the experiment. YW contributed significantly to the analysis and manuscript preparation. XM, HD, CY and YW performed the data analyses and wrote the manuscript. JL helped perform the analysis with constructive discussions.

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