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ORIGINAL COMMUNICATION

Low-dose statin pretreatment reduces stroke severity and improves functional outcomes

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Abstract

Objectives Pre-stroke statin use reduces stroke severity and improves functional outcomes; however, whether low-dose statins as a primary preventive measure have similar effects on the Chinese population remains unclear.

Methods Consecutive cases of ischaemic stroke between May 2011 and January 2017 were retrospectively analysed. The primary endpoints were stroke severity on admission and functional outcomes at 90 days. The secondary endpoints were factors related to lower stroke severity on admission. Propensity score matching and logistic regression analyses were performed.

Results Of the 1878 patients, 6.4% and 23.8% were pre-stroke statin users before and after propensity matching, respectively, reducing the National Institutes of Health Stroke Scale (NIHSS) score on admission from 5 (2–9) to 3 (2–4) ($P<0.001$). Patients receiving pretreatment with low-dose statins tended to have a better mRS distribution (median mRS score 2 [1–3] vs. 3 [2–4], $P=0.007$) and a higher likelihood of favourable functional outcomes (FFOs) at 90 days (61 [65.6%] vs. 151 [50.8%], $P=0.005$). The logistic regression analysis showed that low-dose statins taken before stroke (odds ratio [OR] = 0.15, 95% confidence interval [CI] = 0.08–0.27, $P<0.001$) and being male (OR = 0.81, 95% CI = 0.66–0.99, $P=0.035$) were related to a lower stroke severity on admission but not among patients with atrial fibrillation (OR = 1.65, 95% CI = 1.12–2.44, $P=0.012$) or elevated white blood cell (WBC) counts (OR = 1.12, 95% CI = 1.08–1.17, $P<0.001$).

Conclusions Pretreatment with low-dose statins reduced initial stroke severity, improved functional outcomes at 90 days and was independently associated with a lower stroke severity on admission among Chinese patients.

Keywords Low-dose statins · Stroke · Severity · Outcome

Introduction

Stroke has become the leading cause of death and disability in China. Approximately 11 million stroke survivors currently reside in China, with 2.4 million new stroke cases and approximately 1.12 million stroke-related deaths per year, 77.8% of which are due to ischaemic stroke [1]. Elevated blood lipids are closely related to ischaemic stroke. For each 1 mmol/l increase in total cholesterol, the relative risk for stroke increases by 25% [2]. Statin treatment not only reduces lipid levels but also has neuroprotective effects. Previous studies have shown that statin treatment is associated with lower stroke severity and better functional outcomes among both Caucasians [3–6] and Asians [7–11]. Current international guidelines recommend the maximum tolerated dose of statins as primary and secondary preventative measures for stroke [12, 13].

However, cardiovascular studies have shown that low doses of statins also exert anti-inflammatory, cholesterol-lowering, and cardiovascular protective effects [14] and a delayed increase in carotid intima-media thickness (IMT) [15]. Low-dose statins taken before treatment reduce the occurrence [16, 17] and recurrence of ischaemic stroke [10]. In addition, the results from studies of Caucasians have shown that patients who accepted low-to-moderate strength statin treatment before stroke had less severe strokes and better functional outcomes [3–6].

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Furthermore, low doses of statins are preferred among Asian populations given the differences in lifestyle, baseline low-density lipoprotein (LDL) levels, and ethnic differences in the effects of statins on lipid reduction between Asian and Western populations [18–20]. Current Chinese guidelines recommended low-to-moderate doses of statins as an initial therapy, differing from the recommendations in Western countries [21]. A study in Japan provided evidence that Asian patients benefit from low-dose statins before treatment in terms of lower stroke severity, but not in terms of functional outcomes [22]. However, no studies have examined the Chinese population. Moreover, whether low-dose statins taken before stroke reduce the severity of stroke and improve the functional outcomes of patients in China remains unclear.

This study retrospectively analysed the relationships between the pre-stroke use of low-dose statins and the severity of initial stroke, as well as the functional outcomes of a Chinese population, and analysed the factors related to less severe stroke on admission.

Materials and methods

Participants

We included consecutive patients with initial acute ischaemic stroke who were admitted to the West China Hospital of Sichuan University between May 2011 and January 2017. The inclusion criteria were (1) acute ischaemic stroke diagnosed on admission according to the World Health Organization (WHO) criteria and (2) time from onset to admission ≤ 7 days. The exclusion criteria were (1) age < 18 years (2) a history of stroke or transient ischaemic attack (TIA) (3) a pre-onset modified Rankin Scale (mRS) score ≥ 1 (4) thrombolytic therapy or mechanical thrombectomy at administration, and (5) missing data in more than 10% of the cases.

Data collection

General information

Information about patient gender, age, cardiovascular risk factors (i.e., hypertension, diabetes, dyslipidaemia, heart disease, previous stroke and TIA, smoking), and pre-stroke treatment (hypotensive, hypoglycaemic, lipid-lowering, antiplatelet, and anticoagulation therapy) was collected.

Clinical data

Blood chemistry test results on admission (white blood cell [WBC] count, platelets, total cholesterol [TC], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], and the international normalised ratio [INR]), the time from onset to admission, systolic blood pressure (SBP), recanalization therapy, the TOAST subtype, the severity of stroke based on the National Institutes of Health Stroke Scale (NIHSS) score, and the functional outcomes at 90 days after discharge based on the mRS score were recorded.

Definition of risk factors

Cardiovascular risk factors were defined using the 2014 American Heart Association/American Stroke Association (AHA/ASA) Guidelines for the Primary Prevention of Stroke [23]. The stroke subtype was classified as large-artery atherosclerosis (LAA), cardioembolism (CE), small-vessel occlusion (SVO), stroke of other determined aetiology (ODE), or stroke of undetermined aetiology (UDE) according to the TOAST criteria [24]. Based on the results of two statin studies conducted in Asia [7, 8], pre-stroke statin use was defined as statin use at least 1 month before stroke onset. Low-dose statins included atorvastatin (10 mg), rosuvastatin (5 mg), and simvastatin (20–40 mg). Lower severity stroke was defined as an NIHSS score ≤ 4, and a favourable functional outcome (FFO) was defined as an mRS score of 0–2. For the analysis of the overall mRS distribution, we created six levels by collapsing mRS 5 and 6 into a single level that included extreme disability and death.

Follow-up and outcomes

The patients were followed up for 90 days after discharge. The primary outcomes were the NIHSS score on admission, the mRS distribution and the percentage of FFOs 90 days after discharge. The secondary outcomes were factors related to less severe stroke.

Propensity matching

We conducted a logistic regression analysis to obtain a propensity score, where pre-statin treatment was considered as the dependent variable. Next, the statin group was matched with the non-statin group using the proximity matching method, with a matching range of 1–4 and a calliper value of 0.20. The clinical variables of interest used to generate matches were age, gender, hypertension, diabetes mellitus, hypercholesterolemia, coronary arterial disease, atrial fibrillation, infarctions, smoking status, anti-diabetic treatment, antiplatelet treatment, TC, LDL-C, HDL-C, and SBP. An additional stratification analysis was performed for antiplatelet treatment with significant differences after matching.

Data analyses

SPSS 22.0 (SPSS Inc., Chicago, IL, USA) for Windows and GraphPad Prism 5.0 (GraphPad Software, Inc., La Jolla, CA, USA) were used for data analysis and graphical presentation. Normally distributed variables were analysed using *t* tests, categorical variables were compared with Chi-square tests, and the Kruskal–Wallis test was applied when appropriate. For missing data in which more than 10% of all cases were excluded, we used median values to replace the variables for missing data in less than 10% of all cases. To analyse the associated factors with lower stroke severity, logistic regression analysis was conducted for the dichotomised NIHSS scores (0–4 vs. 5–42). Factors associated with $P < 0.10$ in the univariate analysis and covariates considered likely to affect NIHSS scores on admission were incorporated in the regression model. The enter method was used before matching, and the condition method was used after matching for the logistic regression analysis. $P < 0.05$ was considered significant.

Results

Sample population

A total of 4840 patients with acute ischaemic stroke were enrolled in our study. A total of 3023 subjects were excluded due to an inclusion/exclusion criteria violation, and the study flow diagram is shown as Fig. 1 in Additional File. As such, 1878 patients were ultimately included. Of these patients, 1052 were men (56%), and the mean age was 63.13 ± 14.25 years old. The median NIHSS score on admission was 4 (interquartile range: 2–9). A total of 121 patients (6.4%) used statins before stroke for the following reasons: 22 patients had hypertriglyceridemia, 90 used statins for the primary and secondary prevention of coronary heart disease, five patients had atherosclerosis with arterial stenosis and occlusion, and four patients had rheumatic heart disease and atrial fibrillation.

Before propensity score matching, the patients who used low-dose statins before stroke were older ($P = 0.020$) and more likely to be men ($P = 0.021$), had hypertension ($P < 0.001$), had coronary heart disease ($P = 0.007$), or had myocardial infarction ($P = 0.005$). These patients also more frequently used medication for hypoglycaemia ($P = 0.021$) and were more likely to accept recanalization therapy ($P = 0.006$) and antiplatelet agents ($P < 0.001$) than those who did not use statins before stroke. After matching, no between-group differences were observed with regard to the baseline data except for pre-stroke antiplatelet therapy ($P < 0.001$) (Table 1). A stratified analysis showed that pre-antiplatelet therapy did not affect the outcomes (Additional File: Table S1).

Primary outcomes

The NIHSS scores on admission, both before and after matching, were significantly lower among patients who received low-dose statins before stroke than in those who did not receive statins (unmatched analysis: 3 [2–4] vs. 4 [2–9], $P < 0.001$; propensity-matched analysis: 3 [2–4] vs. 5 [2–9], $P < 0.001$). In addition, a higher percentage of NIHSS scores ranging from 0 to 4 was observed in the statin group (86.0%) than in the non-statin group (51.2%), $P < 0.001$. This outcome remained significant after propensity matching (86.0% vs. 49.8%, $P < 0.001$) (Table 2).

The patients who received low-dose statins before stroke tended to have a better mRS distribution both in the unmatched and propensity-matched analyses (median mRS score: 2 [1–3] vs. 3 [2–4], $P = 0.008$; 2 [1–3] vs. 3 [2–4], $P = 0.007$; respectively) (Fig. 1). Moreover, the unmatched FFO rate 90 days after discharge was significantly higher among 61.9% patients in low-dose statin than 49.5% non-statin patients, $P = 0.080$. After matching, the rates were 65.6% vs. 50.8% ($P = 0.005$) (Table 2).

To examine the effect of statin initiation and adherence after stroke among patients who did not use statins before stroke, we compared the mRS at 90 days between statin users and statin non-users during their hospital stay and after discharge. We found that statin therapies initiated soon after stroke predicted better functional outcomes among patients than when initiated late after stroke, with FFO percentages of 52.9% vs. 48.3% vs. 41.8% ($P < 0.05$). However, the discontinuation of statins after discharge was associated with poorer functional outcomes in 36.2% of patients compared with the 52.9% patients receiving statin treatment in the hospital and after discharge, as well as the 41.8% patients who did not initiate statin treatment until after discharge (Additional File: Table S2).

Secondary outcomes

We conducted a regression analysis to explore the possible variables contributing to the initial NIHSS score and examine the factors related to lower stroke severity (Table 3). The results of the univariable analysis revealed that being male ($P = 0.010$), receiving antiplatelet treatment ($P = 0.002$) and receiving statin pretreatment ($P < 0.001$) reduced stroke severity. However, having a history of atrial fibrillation ($P = 0.017$), valvular heart disease ($P = 0.017$), other heart disease ($P = 0.019$), extended INR value ($P = 0.019$), or an elevated WBC count on admission ($P < 0.001$) were associated with greater stroke severity.

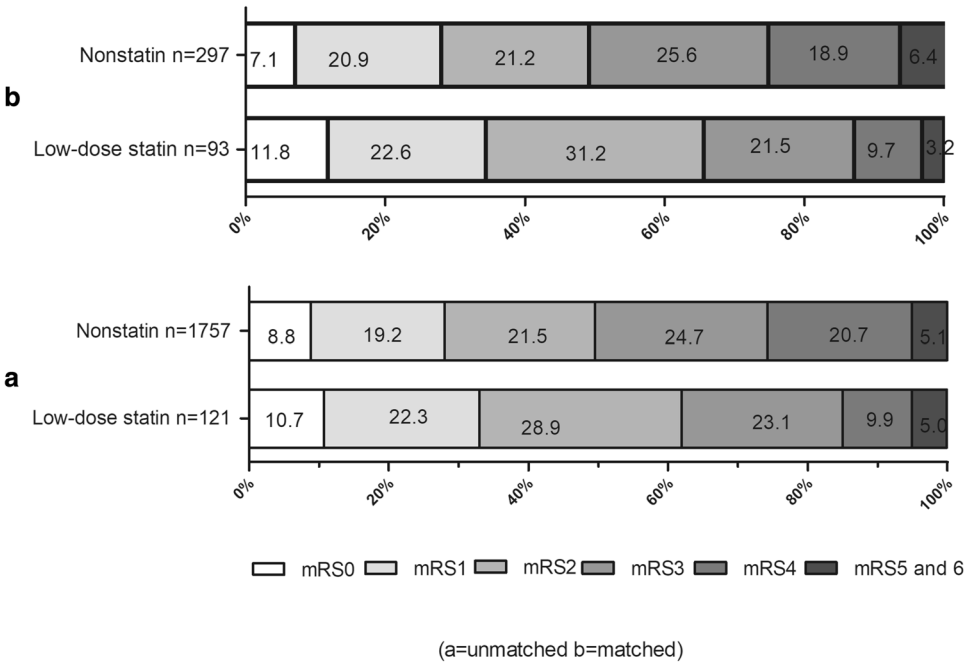

Fig. 1 Distribution of mRS score at discharge 90 days between unmatched and propensity-matched analyses

Next, a multivariate logistic analysis showed that male gender (odds ratio [OR] = 0.81, 95% CI = 0.66–0.99, $P = 0.035$) and pre-stroke statin use (OR = 0.15, 95% CI = 0.08–0.27, $P < 0.001$) were independently associated with stroke severity on admission. Conversely, atrial fibrillation (OR = 1.65, 95% CI = 1.12–2.44, $P = 0.012$) and WBC count (OR = 1.12, 95% CI = 1.08–1.17, $P < 0.001$) were associated with greater stroke severity on admission. (Table 3).

Discussion

Our study showed that low-dose statin administered before treatment reduced stroke severity and was associated with better functional outcomes after 90 days. Furthermore, we found that better functional outcomes might contribute to an initial neuroprotective effect and early stroke recovery among pre-stroke patients receiving statins. These results are consistent with a previous study conducted in Korea [11]. Most earlier work has found that pre-stoke statin use is associated with a lower stroke severity and more favourable outcomes [3, 25]; however, the effect might depend on the dose [26], statin type [27], and treatment received upon admission [3, 6]. However, Sánchez did not find a dose-dependent effect of pre-stroke statin treatment on stroke severity [5]. This null result might have occurred because of the uncertain duration and type of pre-statin use and the lack of a direct comparison of the outcomes between the low-to-moderate and high-dose groups. Previous studies conducted in Japan also support the link between low-dose statin use and milder stroke severity but found no benefit with regard to early functional recovery [9]. Two possible explanations for this result are that both initial and recurrent stroke patients were included, and the duration of statin use prior to treatment was not recorded.

Our study only enrolled initial stroke patients to avoid the effect of the differences in statin use among patients with unique stroke histories. Furthermore, we clearly defined statin dose and pre-statin duration as at least 1 month prior to stroke. As another important consideration, we excluded patients with rt-PA thrombolysis or mechanical thrombectomy who might not have benefitted from pre-statin use with regard to their FFOs at discharge [3].

The research results can be explained in two ways. On one hand, the characteristics of our study cohort might have partially contributed to the positive effect of low-dose statin therapy before stroke. For instance, the higher proportion of LAA stroke subtype patients in our study might benefit more from statin use than those with other subtypes [28]. Moreover, most of the patients included in our study were at low risk for cardiovascular disease. The proportion of stroke risk factors such as hypertension, diabetes, dyslipidaemia, and atrial fibrillation in the pre-stroke statin group was lower than that in previous studies. On the other hand, studies have shown the benefits of low-dose statin therapy. First, several previous studies have demonstrated that low-dose statin therapy provided similar benefits to higher-dose statin therapy in Asian and Caucasian populations [17, 20]. Second, both low- and high-dose statin treatment not only improved the collateral circulation to reduce the infarction volume in atrial fibrillation-related stroke but also reduced plaque enhancement and stabilized the plaques in patients

Table 1 Baseline characteristic

Variable	Total patients $N=1878$	Unmatched			Propensity-matched		
		Low-dose statins $N=121$	Non-statins $N=1757$	P	Low-dose statins $N=93$	Non-statins $N=297$	P*
Age†, years, mean (SD)	63.14 (14.25)	67.56 (12.86)	62.83 (14.30)	0.020	66.72 (13.34)	65.94 (13.11)	0.617
Men†, %	1052 (56.0)	80 (66.1)	972 (55.3)	0.021	61 (65.6)	178 (59.9)	0.328
Hypertension†, %	900 (47.9)	80 (66.1)	820 (46.7)	<0.001	57 (61.3)	190 (60.4)	0.639
Diabetes mellitus†, %	534 (28.4)	38 (31.4)	496 (28.2)	0.454	29 (31.2)	85 (28.6)	0.635
Hypercholesterolemia†, %	351 (18.7)	19 (15.7)	332 (18.9)	0.383	14 (15.1)	49 (16.5)	0.741
Coronary arterial disease†, %	157 (8.4)	18 (14.9)	139 (7.9)	0.007	10 (10.8)	29 (9.8)	0.782
Atrial fibrillation†, %	162 (8.6)	14 (11.6)	148 (8.4)	0.233	11 (11.8)	27 (9.1)	0.437
Infarctions†, %	15 (1.3)	5 (4.1)	20 (1.1)	0.005	3 (3.2)	5 (1.7)	0.360
Smoking†, %	567 (30.2)	30 (24.8)	537(30.6)	0.181	23 (24.7)	99 (33.3)	0.118
Anti-hypertension treatment, %	154 (8.2)	13 (10.7)	141 (8.0)	0.292	11 (11.8)	37 (12.5)	0.872
Anti-diabetic treatment†, %	58 (3.1)	8 (6.6)	50 (2.8)	0.021	7 (7.5)	11 (3.7)	0.125
Antiplatelet treatment†, %	134 (7.1)	61 (50.4)	73 (4.2)	<0.001	33 (35.5)	53 (17.8)	<0.001
Anticoagulant treatment, %	53 (2.8)	3 (2.5)	50 (2.8)	0.814	2 (2.2)	11 (3.7)	0.467
TC†, mmol/l	4.35 (1.12)	3.80 (0.87)	4.39 (1.13)	<0.001	3.83 (0.92)	3.96 (0.95)	0.260
LDL-C†, mmol/l	2.54 (0.95)	2.03 (0.72)	1.28 (0.43)	<0.001	2.07 (0.74)	2.18 (0.82)	0.236
HDL-C†, mmol/l	1.27 (0.42)	1.19 (0.31)	2.57 (0.95)	0.005	1.20 (0.31)	1.23 (0.39)	0.569
SBP†, mmHg, Med (IQR)	148 (126–171)	127 (120–154)	149 (128–172)	<0.001	139.42 (40.03)	143.51 (48.03)	0.456

Table 1 (continued)

Variable	Total patients $N=1878$	Unmatched			Propensity-matched		
		Low-dose statins $N=121$	Non-statins $N=1757$	P	Low-dose statins $N=93$	Non-statins $N=297$	P*
Stroke subtype, %							
LAA	1217 (64.8)	83 (68.6)	1134 (64.5)	0.126	63 (67.7)	183 (61.6)	0.591
CE	208 (11.1)	17 (14.0)	191 (10.9)	0.386	11 (11.8)	36 (12.1)	0.949
SVO	145 (7.7)	9 (7.4)	136 (7.7)	0.938	9 (9.7)	22 (7.4)	0.578
ODE	87 (4.6)	3 (2.5)	84 (4.8)	0.394	2 (2.2)	15 (5.1)	0.283
UDE	221 (11.8)	9 (7.4)	212 (12.1)	0.287	8 (8.6)	41 (13.8)	0.272
Recanalization therapy	27 (1.4)	6 (5.0)	21 (1.2)	0.006	5 (5.4)	2 (0.7)	0.057

Recanalization therapy only refers to the patients who underwent carotid stent angioplasty (CAS), not includes patients with thrombectomy. *P* is calculated by *t* test, Chi-square test, or Kruskal–Wallis test as appropriate.

SD standard distance, *Mean* mean value, *Med* median value, *IQR* interquartile range

†Represents the propensity-matched variables

*P** is calculated by conditional logistic regression

with intracranial atherosclerosis stroke [7, 28–30]. Third, a study in Taiwan found that low-dose statin use was associated with lower platelet activity in patients with acute non-cardioembolic ischaemic stroke [7].

Moreover, we found that pre-stroke statin use and male gender were protective factors for mild stroke on admission. The benefits of pretreatment statin use can be explained by the aforementioned pleiotropic neuroprotective effect. Sex differences exist in the severity of stroke, where women present with more severe ischaemic stroke than men. This finding might be partially explained by the differences in risk factors before stroke [31]. Nevertheless, the history of atrial fibrillation and an elevated WBC count aggravated the severity of stroke on admission, which is consistent with reports in the literature [32–35]. Patients with atrial fibrillation-associated stroke often have underlying heart disease and are less tolerant of ischaemia. Furthermore, they show more severe hypoperfusion, infarct growth, and haemorrhagic transformation when a stroke occurs, resulting in a more severe stroke and a higher mortality rate [35]. Peripheral leukocytes were associated with larger early cerebral infarcts in patients with ischaemic stroke [36]. WBC count was consistently defined as an independent predictor of more severe stroke and worse functional outcomes, accounting for poor prognoses after stroke [32–34].

This study has numerous limitations. First, retrospective studies have inevitable selection and recall biases, and additional studies are required. This study only suggests a base from which to generate hypotheses and does not provide a definitive clinical practice. Second, mRS scores of 5 and 6 were combined because of the low death rate among our sample population. The main causes for this low death rate were that majority of patients included had lower NIHSS scores and briefer follow-up times after discharge, and many deaths were excluded because of recurrent stroke or endovascular treatment on admission. However, we conducted another analysis comparing the inclusion and exclusion of deaths and found no effect on the outcomes. Third, the statin rate was unusually low compared with that in other studies, also reflecting the pessimistic primary prevention situation in our country. In addition, the patients in our study had lower NIHSS scores, the reasons for which were shorter times from onset to admission within 24 h (41.2%) and within 72 h (72.0%), as well as the low proportion of patients with cardiogenic stroke (11.0%). Another possible reason is that we excluded patients receiving thrombolytic or mechanical thrombectomy who were more likely to present with severe stroke. However, a lower NIHSS score would not have influenced the main results. Finally, the effect on stroke outcome might differ depending on stroke subtype, statin type and compliance. However, we cannot perform a sub-analysis on the low statin rates, and we did not record the reasons for statin withdrawal. More research on the

Table 2 Main outcomes of unmatched and propensity-matched subgroups

Variable	Unmatched			Propensity-matched		
	Low-dose statin $N=121$	Non-statins $N=1757$	*P*	Low-dose statin $N=93$	Non-statins $N=297$	*P**
Admission NIHSS, Med (IQR)	3 (2–4)	4 (2–9)	< 0.001	3 (2–4)	5 (2–9)	< 0.001
Admission NIHSS score 0–4,%	104 (86.0)	899 (51.2)	< 0.001	80 (86.0)	148 (49.8)	< 0.001
Discharged mRS at 90 days, Med (IQR)	2 (1–3)	3 (2–4)	0.008	2 (1–3)	3 (2–4)	0.007
FFO at 90 days,%	75 (61.9)	869 (49.5)	0.080	61 (65.6)	151 (50.8)	0.005

P are calculated by *t* test, Chi-square test, or Kruskal–Wallis test as appropriate

NIHSS NIH Scale Score, *mRS* modified Rankin Scale, *FFO* favorable function outcome

**P* are calculated by univariate linear regression or conditional logistic regression

Table 3 Univariable and multivariable analysis for the stroke severity for unmatched cohort

Variables	Univariable analysis		Multivariable analysis	
	β (95% CI)	*P***	β (95% CI)	*P***
Age‡	1.00 (0.99–1.00)	0.353	1.00 (0.99–1.01)	0.397
Men‡	0.73 (0.61–0.88)	0.001	0.81 (0.66–0.99)	0.035
Hypertension	0.85 (0.71–1.02)	0.074	1.00 (0.82–1.23)	0.997
Diabetes mellitus	1.03 (0.85–1.26)	0.743	–	–
Hypercholesterolemia	0.83 (0.65–1.04)	0.108	–	–
Coronary arterial disease	1.02 (0.74–1.42)	0.887	–	–
Atrial fibrillation‡	2.07 (1.49–2.89)	< 0.001	1.65 (1.12–2.44)	0.012
Infarctions	0.54 (0.23–1.25)	0.147	–	–
Other heart disease‡	1.66 (1.09–2.53)	0.019	1.46 (0.93–2.29)	0.102
Smoking	0.96 (0.78–1.17)	0.674	–	–
Antiplatelet treatment‡	0.56 (0.38–0.80)	0.002	0.82 (0.52–1.31)	0.824
Anticoagulant treatment‡	1.11 (0.64–1.91)	0.715	0.59 (0.30–1.14)	0.116
WBC‡	1.13 (1.09–1.17)	< 0.001	1.12 (1.08–1.17)	< 0.001
Platelet count	1.00 (1.99–1.00)	0.405	–	–
TC ‡	0.97 (0.89–1.05)	0.382	0.93 (0.85–1.01)	0.091
INR‡	1.91 (1.11–3.29)	0.019	1.29 (0.71–2.35)	0.400
Time to admission	0.96 (0.91–1.00)	0.059	0.96 (0.9–1.01)	0.129
SBP‡	1.00 (0.99–1.01)	0.007	0.99 (0.98–1.00)	0.007
Stroke subtype‡				
LAA	Ref	Ref	Ref	Ref
CE	1.60 (1.18–2.15)	0.002	1.18(0.82–1.69)	0.367
SVO	0.29 (0.19–0.44)	< 0.001	0.30 (0.12–0.46)	< 0.001
ODE	0.84 (0.54–1.30)	< 0.001	0.74 (0.47–1.18)	0.207
Statin pretreatment‡	0.17 (0.10–0.29)	< 0.001	0.15 (0.08–0.27)	< 0.001

Dependent variable: NIHSS 0–4 versus 5–42

CI confidence interval

‡Values were analyzed in the multivariable model

***P* value was analysed by the enter method of logistic regression analysis

dose-effect of pre-statin treatment on stroke must be conducted in the future.

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Author contributions SD and JG revised and drafted the manuscript. JF was responsible for the manuscript revision. YH and SC collected data and followed up with the patients. LH conceived and designed the study.

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Data availability The data collected for this study are available from the corresponding author upon reasonable request.

Compliance with ethical standards

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval All human-participant procedures in the above studies were performed in accordance with the ethical standards of the institutional and/or national research committee, as well as with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of West China Hospital.

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