In-hospital prognosis of first-ever noncardiogenic ischemic stroke in patients with and without indication for prestroke antiplatelet therapy: Chinese Stroke Center Alliance

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Background: It is unknown about the influence of prestroke antiplatelet use on early outcomes in patients with and without the indication. We aimed to evaluate the in-hospital prognosis of first-ever noncardiogenic ischemic stroke patients with and without indications of antiplatelet use for primary prevention.

Methods: This was a retrospective, observational study based on a prospective hospital-based registry (Chinese Stroke Center Alliance). Using the data with 436,660 first-ever noncardiogenic acute ischemic strokes recorded from Aug 1, 2015, to July 31, 2019, from 1,453 hospitals in China, we examined the associations between the indication for prestroke antiplatelet use and in-hospital clinical outcomes.

Results: Among 436,660 first-ever noncardiogenic ischemic stroke patients, 42,409 patients (9.7%) had a documented previous vascular indication and 394,251 (90.3%) did not. Compared to those without, patients with the indication were associated with increased prevalence of in-hospital morbid conditions, including stroke severity (OR 2.71; 95% CI: 2.62–2.81; P<0.0001), length of stay >14 days (OR 1.16; 95% CI: 1.13–1.19; P<0.0001), mortality (OR 2.20; 95% CI: 1.96–2.46, P<0.0001), and recurrence of ischemic stroke and transient ischemic attack (TIA) (OR 1.5; 95% CI: 1.43–1.59, P<0.0001). Among patients without indication, prestroke antiplatelet use was associated with lower mortality (OR 0.73, 95% CI: 0.56–0.96; P=0.0221); while among patients with indication, those receiving prestroke antiplatelet had lower odds ratios in stroke severity (P<0.0001) and disability (P=0.0003) than those who not.

Conclusions: Patients with indications of prestroke antiplatelet use were more likely to have unfavorable outcomes than those without. Prestroke antiplatelet might be associated with lower mortality, less disability, and less stroke severity in certain population groups. Future studies to improve risk prediction rules are needed to guide effective primary prevention for ischemic stroke.

Keywords: Antiplatelet therapy; ischemic stroke; prognosis; primary prevention

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Introduction

Stroke is the first leading cause of mortality and disability in China. The stroke burden in China has increased over the past 30 years and remains particularly high in rural areas (1).

Prevention is vital to reduce the disease burden and antiplatelet agents are one of the mainstay therapies for primary and secondary stroke prevention. Although antiplatelet agents play an important role in primary prevention, it remains controversial whether the previous therapy can improve outcomes of acute ischemic stroke. Several previous studies pointed out the fact that prestroke antiplatelet use, especially aspirin, could benefit the vital prognosis of stroke patients (2,3). However, a 2016 meta-analysis of 11 trials that included individual patient level data among 118,445 men and women who were randomly assigned to either aspirin (at doses between 50 and 500 mg daily) or placebo found no significant benefit on nonfatal stroke (relative risk 0.95, 95% CI: 0.85–1.06) (4). According to the guideline, for people with risk factors, the application of aspirin as the primary prevention of cardiovascular disease (CVD) requires careful consideration (5,6).

Therefore, our study aims to (I) describe characteristics of first-ever noncardiogenic ischemic stroke patients by whether an indication of antiplatelet for primary prevention was present or not; (II) examine the difference of in-hospital prognosis of patients with and without indication of previous antiplatelet use; (III) study the in-hospital prognostic value of previous antiplatelet use on stroke severity, mortality, disability, hospital length of stay and in-hospital recurrence of ischemic stroke or transient ischemic attack (TIA).

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-7902).

Methods

Cohort

We derived data from the Chinese Stroke Center Alliance (CSCA) database. The protocol for case identification and data collection have been previously reported elsewhere (7). Briefly, the CSCA is a national, hospital-based, voluntary, and multifaceted intervention, and also a continuous quality improvement initiative. It provides a unique platform to develop stroke centers and to improve stroke care quality and clinical outcomes. This program is available to all Chinese secondary and tertiary grade hospitals. Hospitals continued to join the program in a staggered manner. Patients were enrolled if they had a primary diagnosis of stroke or TIA and were then confirmed by brain computerized tomography (CT) or magnetic resonance imaging (MRI). Data were collected by trained hospital personnel using a web-based Patient Management Tool (Medicine Innovation Research Center, Beijing, China). The China National Clinical Research Center for Neurological Diseases (NCRCND) serves as the data analysis center and has an agreement to analyze the aggregate deidentified data for care quality feedback and research purposes.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the central Institutional Ethics Board at Beijing Tiantan Hospital (No.: KY 2018-061-02) and individual consent for this retrospective analysis was waived.
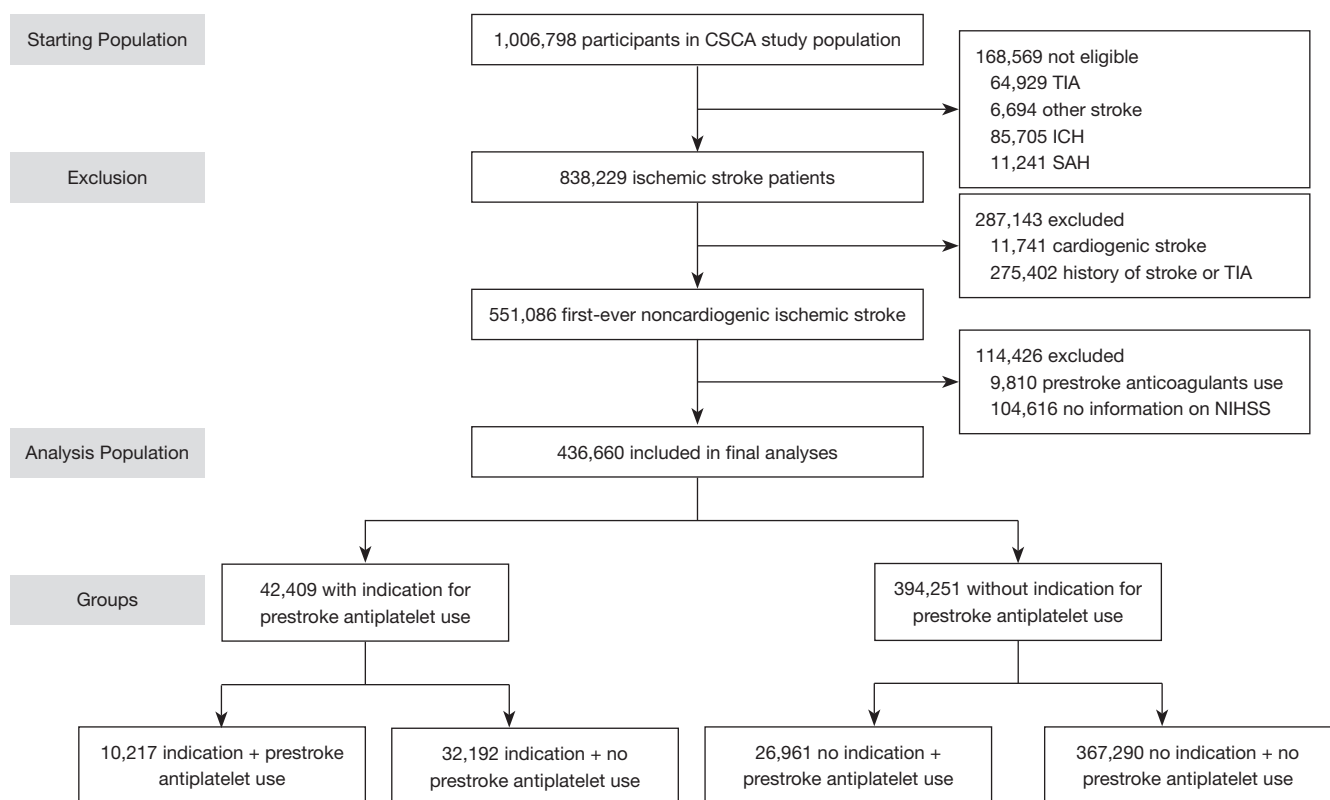
Study population

The population of this study consists of all stroke/TIA patients enrolled from secondary or tertiary hospitals across 31 provinces, autonomous regions, or municipalities in Mainland China participating in the CSCA program from Aug 1, 2015, to July 31, 2019. A total of 838,229 patients were recruited consecutively from all 1,476 hospitals in CSCA if they met the following criteria: (I) age >18 years; (II) diagnosis within 7 days of the index event of ischemic stroke; (III) informed consent provided by the patient or a legally authorized representative. Patients with cardiogenic stroke or with a history of stroke or TIA, patients receiving prestroke anticoagulants, and patients missing information on the National Institute of Health Stroke Scale (NIHSS) score were excluded. After these exclusions, our primary study population consisted of 436,660 patients from 1,453 hospitals in China (Figure 1).

Data collection and management

Patient information including demographics, risk factors, comorbidities, medications, discharge status, and hospital-level characteristics was systematically collected during hospitalization and at discharge by trained research coordinators at each participating hospital.

Patients were considered to indicate for prestroke antiplatelet therapy if their medical history included coronary artery disease, myocardial infarction, or atrial fibrillation (AF) (8). Patients were categorized as with and without

Figure 1 Study population. Indication for prestrike antiplatelet use: with medical history included coronary artery disease, myocardial infarction, or atrial fibrillation. CSCA, the Chinese Stroke Center Alliance; TIA, transient ischemic attack; ICH, intracranial hemorrhage; SAH, subarachnoid hemorrhage; NIHSS, National Institute of Health Stroke Scale.

indication groups. Prestroke antiplatelet use was defined as using antiplatelet agents (including aspirin, clopidogrel, ticagrelor, etc.) continuously for 2 weeks in recent 6 months. Based on the indication and prestroke antiplatelet use, patients were further divided into 4 subgroups: indication + prestroke antiplatelet use, indication + no prestroke antiplatelet use, no indication + prestroke antiplatelet use, no indication + no prestroke antiplatelet use.

In-hospital outcomes

The National Institute of Health Stroke Scale (NIHSS) score on administration was used as an index of stroke severity and the modified Rankin Scale (mRS) score at discharge as an index of functional outcome. The initial stroke severity was categorized as low (NIHSS ≤15) and high (NIHSS 16–42) levels. Disability at the time of discharge was defined as mRS score ≥2. Our study examined patient-relevant outcomes of NIHSS on administration,

mRS at discharge, hospital length of stay for over 14 days, in-hospital mortality, in-hospital intracranial hemorrhage, and in-hospital recurrence of ischemic stroke and TIA.

Statistical analysis

Categorical variables were reported as absolute numbers with percentages. Means (standard deviations) and medians (25th–75th percentiles) were used to describe the distribution of continuous variables. Multivariable logistic regression analyses investigated the associations between indications for prestroke antiplatelet therapy and each outcome, adjusted for age, gender, medical history, baseline NIHSS, smoking, and poststroke medications. Multivariable logistic regression was used to analyze the difference of outcomes among the four subgroups, with the "no indication + no prestroke antiplatelet use" subgroup selected as the reference. Age, gender, carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, and diabetes mellitus

were introduced in the model.

All P values are 2 sided, with P<0.05 considered statistically significant. All statistical analyses were performed using SAS Version 9.4 software (SAS Institute, Cary, NC, USA). A SAS macro named %ggBaseline was used to analyze and report baseline characteristics automatically (9).

Results

Characteristics at the recruitment of study participants

Among 436,660 first-ever noncardiogenic ischemic stroke patients (*Figure 1*), 42,409 (9.7%) indicated prestroke antiplatelet therapy. 8.5% of patients were not on any antiplatelet therapy before their incident stroke, with 24.1% and 6.8%, respectively, among patients with and without indications. *Table 1* displayed the demographic, clinical, and hospital characteristics according to groups with and without indication for prestroke antiplatelet use. Patients with an indication for prestroke antiplatelet use were more likely to be female (46.2% *vs.* 36.6%) and older (71.3±11.0 *vs.* 64.8±12.3), and had a greater prevalence of cardiovascular risk factors (carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, and diabetes mellitus), and were associated with previous medication (antiplatelets, anti-hypertensives, lipid-lowering medication, and antidiabetics) before the index stroke. After the first-ever stroke, the proportions of patients on treatment among two groups (81.6% *vs.* 86.6%) reflected antiplatelet use for secondary prevention. ASD of all variables above crossed the border of 10%.

Indications for prestroke antiplatelet use and post-stroke outcomes

The number and rates of in-hospital mortality, stroke recurrence, and other outcomes were listed in *Table 2* according to groups with and without indication. Overall rates of in-hospital severe stroke (NIHSS 16–42), hospital stay >14 d, stroke or TIA recurrence, hemorrhagic stroke and mortality were 4.3% (N=18,919), 19.5% (N=85,126), 2.5% (N=11,028), 0.8% (N=3,516), and 0.4% (N=1,597), respectively. After adjusting for potential confounders, we found that patients with an indication were associated with increased prevalence of many morbid conditions including initial stroke severity (NIHSS 16–42) (OR 2.71; 95% CI: 2.62–2.81; P<0.0001), the length of stay >14 d (OR 1.16;

95% CI: 1.13–1.19; P<0.0001), mortality (OR 2.2; 95% CI: 1.96–2.46, P<0.0001), and in-hospital recurrence of ischemic stroke and TIA (OR 1.5; 95% CI: 1.43–1.59, P<0.0001).

Prestroke antiplatelet use and poststroke outcomes

Table 3 showed the regression model results respectively, by prestroke antiplatelet use and indication. Among patients without indication, prestroke antiplatelet use was associated with lower mortality (OR 0.73, 95% CI: 0.56–0.96; P=0.0221), but longer hospital stay (OR 1.03, 95% CI: 1–1.07; P=0.0327), and more recurrence of ischemic stroke and TIA (OR 1.59, 95% CI: 1.48–1.70; P<0.0001); while among patients with indication, there was a marginally significant inverse association of prestroke antiplatelet use with NIHSS ≥16 (P<0.0001) and mRS ≥2 (P=0.0003), and prestroke antiplatelet use was not associated with length of hospital stay, recurrence of ischemic stroke and TIA, or mortality.

Discussion

This national hospital-based study including over 1 million stroke patients across China indicated that, in China, more than 90% of the stroke patients occurred among those without any indication for antiplatelet use based on the current primary prevention guideline; among those who met the indication, only a quarter of the patients were on treatment. Furthermore, in this study, patients with indications were more likely to have unfavorable outcomes than those without, probably due to the high baseline risk for CVD. Prestroke antiplatelet use was, however, only associated with NIHSS and mRS score in the high-risk group. With the large sample size of well-phenotyped stroke patients included, and comprehensive prognostic characteristics recorded, our study may have important clinical implications.

First, in China, 90.3% of patients were classified as non-indication but finally developed ischemic stroke. The paradox of high risk of stroke with low risk of CVD could be observed in Asian and other populations. Previous studies inferred that it was not due to atherosclerosis in the major cerebral arteries but lesions in the small intracerebral arteries (10). Risk factors that enhanced thrombosis and reduced fibrinolysis were also capable of explaining the paradoxical occurrence of the incidence of coronary heart disease and stroke in certain populations (11).

Table 1 Baseline characteristics

Variables	Total (N=436,660)	Indication for antiplatelet use, N=42,409 (9.7%)	No indication for antiplatelet use, N=394,251 (90.3%)	ASD/HL estimator
Age, yrs	65.4±12.4	71.3±11.0	64.8±12.3	55.7
Sex, female, No. (%)	163,822 (37.5)	19,614 (46.2)	144,208 (36.6)	19.6
BMI, kg/m²	23.9±4.0	23.9±4.0	23.9±4.0	0.0
Medical history, No. (%)				
Coronary heart disease or myocardial infarction	30,581 (7.0)	30,581 (72.1)	0	
Heart failure	3,204 (0.7)	2,033 (4.8)	1,171 (0.3)	28.8
Atrial fibrillation	15,752 (3.6)	15,752 (37.1)	0	
Carotid stenosis	3,981 (0.9)	477 (1.1)	3,504 (0.9)	2.0
Peripheral vascular disease	4,016 (0.9)	877 (2.1)	3,139 (0.8)	10.9
Hypertension	321,981 (73.7)	31,729 (74.8)	290,252 (73.6)	2.7
Dyslipidemia	17,983 (4.1)	2,456 (5.8)	15,527 (3.9)	8.9
Diabetes mellitus	113,613 (26.0)	11,695 (27.6)	101,918 (25.9)	3.8
Smoking, No. (%)	166,091 (38.0)	13,073 (30.8)	153,018 (38.8)	16.9
Missing	9,561 (2.2)	780 (1.8)	8,781 (2.2)	2.9
Prestroke medications, No. (%)				
Antiplatelet	37,178 (8.5)	10,217 (24.1)	26,961 (6.8)	49.3
Lipid-lowering therapy	25,511 (5.8)	5,880 (13.9)	19,631 (5.0)	30.8
Antihypertensives	179,794 (41.2)	21,516 (50.7)	158,278 (40.1)	21.4
Antidiabetic agents	63,975 (14.7)	7,446 (17.6)	56,529 (14.3)	9.0
Post stroke medications, No. (%)				
Antiplatelet	375,884 (86.1)	34,606 (81.6)	341,278 (86.6)	13.7
Lipid-lowering therapy	31,942 (7.3)	915 (2.2)	31,027 (7.9)	26.3
Outcomes, No. (%)				
NIHSS 16–42	18,919 (4.3)	4,611 (10.9)	14,308 (3.6)	28.4
Length of stay >14 d	85,126 (19.5)	10,449 (24.6)	74,677 (18.9)	13.8
Missing	6,782 (1.6)	755 (1.8)	6,027 (1.5)	2.4
Death	1,597 (0.4)	544 (1.3)	1,053 (0.3)	11.2
Recurrence of ischemic stroke	9,534 (2.2)	1,827 (4.3)	7,707 (2.0)	13.2
Recurrence of ischemic stroke and TIA	11,028 (2.5)	1,989 (4.7)	9,039 (2.3)	13.1
Hemorrhagic stroke	3,516 (0.8)	1,034 (2.4)	2,482 (0.6)	14.8
mRS 2–6	175,160 (40.1)	12,643 (29.8)	162,517 (41.2)	24.0
Missing	205,636 (47.1)	26,680 (62.9)	178,956 (45.4)	35.7

BMI, body mass index; TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale.

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Table 2 End points according to indication for prestroke antiplatelet use

Outcomes	Total, N=436,660, n (%)	Indication, N=42,409, n (%)	No Indication, N=394,251, n (%)	Unadjusted		Adjusted*	
				OR (95% CI)	P value	OR (95% CI)	P value
NIHSS 16–42[†]	18,919 (4.3)	4,611 (10.9)	14,308 (3.6)	3.24 (3.13–3.35)	<0.0001	2.68 (2.59–2.78)	<0.0001
Length of stay >14 d	85,126 (19.5)	10,449 (24.6)	74,677 (18.9)	1.41 (1.37–1.44)	<0.0001	1.15 (1.13–1.18)	<0.0001
Death	1,597 (0.4)	544 (1.3)	1,053 (0.3)	4.85 (4.37–5.38)	<0.0001	2.25 (2.01–2.53)	<0.0001
Recurrence of ischemic stroke	9,534 (2.2)	1,827 (4.3)	7,707 (2.0)	2.26 (2.14–2.38)	<0.0001	1.55 (1.46–1.64)	<0.0001
Recurrence of ischemic stroke and TIA	11,028 (2.5)	1,989 (4.7)	9,039 (2.3)	2.1 (2–2.2)	<0.0001	1.51 (1.44–1.6)	<0.0001
Hemorrhagic stroke	3,516 (0.8)	1,034 (2.4)	2,482 (0.6)	3.95 (3.67–4.25)	<0.0001	2.22 (2.05–2.41)	<0.0001
mRS 2–6	175,160 (40.1)	12,643 (29.8)	162,517 (41.2)	1.33 (1.28–1.39)	<0.0001	1 (0.96–1.05)	0.7735

*, adjusted variables: age, sex, carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, diabetes mellitus, prestroke antiplatelet, poststroke antiplatelet, and NIHSS score; [†], adjusted variables: age, sex, carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, diabetes mellitus, prestroke antiplatelet, and poststroke antiplatelet. TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale.

Table 3 Outcomes by prestroke antiplatelet use and indication

Outcomes	Total	No. of events (%)	Unadjusted		Adjusted	
			OR (95% CI)	P value	OR (95% CI)	P value
NIHSS 16–42						
Indication + prestroke antiplatelet use	10,217	879 (8.6)	2.51 (2.34–2.7)	<0.0001	2.09 (1.95–2.25)	<0.0001
Indication + no prestroke antiplatelet use	32,192	3,732 (11.6)	3.5 (3.37–3.64)	<0.0001	2.87 (2.76–2.98)	<0.0001
No indication + prestroke antiplatelet use	26,961	1,047 (3.9)	1.08 (1.01–1.15)	0.0208	1.06 (1–1.13)	0.0694
No indication + no prestroke antiplatelet use	367,290	13,261 (3.6)	–		–	
Length of stay >14 d						
Indication + prestroke antiplatelet use	10,217	2,590 (25.3)	1.47 (1.4–1.54)	<0.0001	1.34 (1.28–1.4)	<0.0001
Indication + no prestroke antiplatelet use	32,192	7,859 (24.4)	1.4 (1.36–1.44)	<0.0001	1.34 (1.3–1.37)	<0.0001
No indication + prestroke antiplatelet use	26,961	5,484 (20.3)	1.1 (1.07–1.14)	<0.0001	1.03 (1–1.07)	0.0327
No indication + no prestroke antiplatelet use	367,290	69,193 (18.8)	–		–	
Death						
Indication + prestroke antiplatelet use	10,217	136 (1.3)	4.97 (4.15–5.95)	<0.0001	3.5 (2.91–4.21)	<0.0001
Indication + no prestroke antiplatelet use	32,192	408 (1.3)	4.73 (4.21–5.31)	<0.0001	3.45 (3.06–3.88)	<0.0001
No indication + prestroke antiplatelet use	26,961	59 (0.2)	0.81 (0.62–1.05)	0.1124	0.73 (0.56–0.96)	0.0221
No indication + no prestroke antiplatelet use	367,290	994 (0.3)	–		–	
Recurrence of ischemic stroke						
Indication + prestroke antiplatelet use	10,217	489 (4.8)	2.65 (2.41–2.91)	<0.0001	2.37 (2.15–2.6)	<0.0001
Indication + no prestroke antiplatelet use	32,192	1,338 (4.2)	2.28 (2.15–2.42)	<0.0001	2.14 (2.01–2.27)	<0.0001
No indication + prestroke antiplatelet use	26,961	859 (3.2)	1.73 (1.61–1.86)	<0.0001	1.61 (1.5–1.74)	<0.0001
No indication + no prestroke antiplatelet use	367,290	6,848 (1.9)	–		–	

Table 3 (*continued*)

Table 3 (*continued*)

Outcomes	Total	No. of events (%)	Unadjusted		Adjusted	
			OR (95% CI)	P value	OR (95% CI)	P value
Recurrence of ischemic stroke and TIA						
Indication + prestroke antiplatelet use	10,217	531 (5.2)	2.45 (2.24–2.68)	<0.0001	2.24 (2.05–2.46)	<0.0001
Indication + no prestroke antiplatelet use	32,192	1,458 (4.5)	2.12 (2–2.24)	<0.0001	2.02 (1.91–2.15)	<0.0001
No indication + prestroke antiplatelet use	26,961	984 (3.6)	1.69 (1.58–1.81)	<0.0001	1.59 (1.48–1.7)	<0.0001
No indication + no prestroke antiplatelet use	367,290	8,055 (2.2)	–		–	
Hemorrhagic stroke						
Indication + prestroke antiplatelet use	10,217	239 (2.3)	3.78 (3.3–4.33)	<0.0001	3.33 (2.9–3.82)	<0.0001
Indication + no prestroke antiplatelet use	32,192	795 (2.5)	4 (3.68–4.34)	<0.0001	3.57 (3.28–3.88)	<0.0001
No indication + prestroke antiplatelet use	26,961	170 (0.6)	1 (0.86–1.17)	0.983	0.96 (0.82–1.13)	0.6238
No indication + no prestroke antiplatelet use	367,290	2,312 (0.6)	–		–	
mRS 2–6 (missing: 205636)						
Indication + prestroke antiplatelet use	10,217	3,213 (31.4)	1.21 (1.12–1.3)	<0.0001	1.05 (0.97–1.13)	0.2155
Indication + no prestroke antiplatelet use	32,192	9,430 (29.3)	1.39 (1.32–1.45)	<0.0001	1.24 (1.18–1.3)	<0.0001
No indication + prestroke antiplatelet use	26,961	11,394 (42.3)	1.06 (1.02–1.1)	0.0048	0.99 (0.95–1.03)	0.6497
No indication + no prestroke antiplatelet use	367,290	151,123 (41.1)	–		–	

Adjusted variables: age, sex, carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, diabetes mellitus. TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale.

Second, the antiplatelet therapy was underused by those at high risk for CVD and overused by those at low risk for CVD. 75.9% of stroke patients in the indication group were not on any preventative antiplatelet medication, indicating that a proportion of them might potentially have benefited from risk stratification to reduce risks of future thrombotic events. This implied gaps in risk prediction rules or in identifying patients at high risk of cardiovascular events. Conversely, treatment with antiplatelet agents in some high vascular risk patients might have been considered inappropriate by the physician due to contra-indications such as gastrointestinal ulcers or hemorrhage or due to the patient's refusal. However, this is unlikely to account for all cases where patients did not receive the appropriate prevention. On the other hand, we found antiplatelet use before stroke in 6.8% of patients in the non-indication group. This might be due to other appropriate indications but could also reflect self-administrative treatment, which would be paid attention because of the potential bleeding hazard (12-14).

Third, our analysis revealed significant differences in rates of negative in-hospital outcomes between the two different groups of patients. Compared with patients without indication, the mortality, hospital length of stay over 14 days and NIHSS score over 16 were higher in patients with indication, which was consistent with previous studies. Besides, patients with indications were likely to suffer both recurrence of stroke or TIA and hemorrhage stroke while hospitalized. In stroke patients receiving antiplatelet therapy, ESSEN Stroke Risk Score and CHA_2DS_2VASc (15) were used to evaluate recurrence of ischemic stroke, and S_2TOP-BLEED, REACH, and B_2LEED_3S (16) were used to predict the baseline risk of major in-hospital bleeding in clinical practice. Because of the shared risk factors in the scales of future risk ischemic and bleeding events, patients with indications for prestroke antiplatelet use were made up of groups with different balances in the risk of ischemic and bleeding events. Our results were consistent with previous reports that about 1/5 patients presenting with acute coronary syndrome were at high ischemic and high bleeding risk, and they were more likely to experience poor clinical outcomes and reduced

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odds of receiving guideline-recommended therapy (17).

Fourth, in contrast to previous studies where the prevalence of antiplatelet use was high (2,8), in this study, prestroke antiplatelet use only had significant protective effects on in-hospital mortality in non-indication group, and on stroke severity and in-hospital disability in the indication group. There were inconsistencies and conflicts about whether prestroke antiplatelet use could benefit patients (2,8,18). Therefore, our study emphasizes the need for better identification of patients at risk, perhaps using emerging novel risk factors (19,20). Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders highlighted that asymptomatic carotid stenosis over 50% and asymptomatic intracranial artery stenosis were considered as high-risk factors and that antiplatelets was recommended as primary prevention (Class IIa, level of evidence C) (21).

The key advantages of our study were the much larger sample size and analysis of diverse relevant and important outcomes for patients. The previous research was limited by relatively small sample size (18) or focused on one or several outcomes alone (22-24).

Our study had several limitations. First, as a hospital-based study, patients and hospitals might not be entirely representative of the Chinese population. Second, the definition of indications for prestroke antiplatelet use might be imperfect. We were unable to gather information about severe stenosis (over 50–70%) of the peripheral artery, carotid artery, and intracranial artery, which were indications as well (21,25). Third, to make a compromise, we regarded AF as an indication. Most AF patients with CHA2DS2-VASc scores of ≥2 were at high risk of atherosclerosis. Antiplatelets could be used as an alternative, although there were debates on whether it would bring benefits (26-29). Besides, for a CHA2DS2-VASc score of 1, aspirin could be considered as the primary prevention (Class IIa, level of evidence C) (30). Forth, we were not able to analyze either the class of antiplatelets, the exact duration of the therapy, and the precise dose, all of which might have effects on the prognosis of ischemic stroke. Fifth, we were unable to evaluate the prognosis in 90 days or longer, because there was no follow-up data after discharge in the CSCA database.

To conclude, for first-ever noncardiogenic ischemic stroke, patients with indications for prestroke antiplatelet therapy were more likely to have unfavorable outcomes than patients without. Prestroke antiplatelet use might be associated with lower mortality, less disability, and less severity of stroke in certain population groups. Future studies to improve risk prediction rules are needed to guide effective primary prevention of ischemic stroke to provide a more individualized approach in the future.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-7902

Data Sharing Statement: Available at http://dx.doi.org/10.21037/atm-20-7902

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-7902). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the central Institutional Ethics Board at Beijing Tiantan Hospital (No.: KY 2018-061-02) and individual consent for this retrospective analysis was waived.

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