

# TOAST subtypes: its influence upon doctors' decisions of antihypertensive prescription at discharge for ischemic stroke patients

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**Aim:** To investigate the influence of the Trial of Org 10172 in Acute Stroke Treatment (TOAST) subtypes in doctors' decisions to use antihypertensive prescriptions at discharge for ischemic stroke patients in a real-world setting.

**Methods:** Using the China National Stroke Registry, we analyzed data from 12,063 hospitalized patients who had been diagnosed with ischemic stroke. The cause of ischemic stroke was classified according to the TOAST criteria. The information about the prescription of antihypertensive medication at discharge was extracted from medical records. Multivariate logistic regression was used to assess the impact of TOAST subtypes on the prescription of antihypertensive medication at discharge.

**Results:** Multivariate analysis showed that, compared with large artery atherosclerosis patients with moderate (<70%) stenosis, large artery atherosclerosis patients with severe ( $\geq 70\%$ ) stenosis or patients with stroke of undetermined etiology were less likely to be prescribed antihypertensive medication at discharge (odds ratio [OR], 0.72; 95% confidence interval [CI]: 0.59–0.88; OR, 0.71; 95% CI: 0.64–0.79), while patients with small artery occlusion were more likely to be prescribed antihypertensives (OR, 1.50; 95% CI: 1.33–1.69).

**Conclusion:** The TOAST subtype is an important determinant of the prescription of antihypertensive medication for ischemic stroke patients at discharge in normal clinical practice.

**Keywords:** antihypertensive agents, ischemic stroke, TOAST classification

## Introduction

Antihypertensive treatment is recommended for secondary prevention in ischemic stroke patients with or without a documented history of hypertension by current American Heart Association/American Stroke Association guidelines.<sup>1</sup> However, in normal clinical practice, the mechanisms of ischemic stroke may have influenced doctors' decisions to initiate antihypertensive therapies, particularly in patients with severe stenosis or occlusion in intracranial or extracranial arteries, or with nonatherosclerotic mechanisms such as hypercoagulable states, vasculitis, and so on. In this study, we investigated the influence of Trial of Org 10172 in Acute Stroke Treatment (TOAST) subtype on doctors' decisions to use antihypertensive prescriptions at discharge for ischemic stroke patients in a real-world setting.

## Methods

Patient data were obtained from the China National Stroke Registry (CNSR), a nationwide, prospective cohort study aimed at identifying vascular risk factors, and documenting the clinical characteristics, diagnosis, and treatments for patients with acute stroke.

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The detailed protocol of the CNSR has been published elsewhere.<sup>2</sup> Between September 2007 and August 2008, all consecutive stroke patients aged 18 years or older who were admitted to 132 hospitals within 14 days after the onset of symptoms were recruited. The collection of data for the CNSR was approved by ethics committees at the participating hospitals. Written informed consent was obtained from the patient or his/her legally authorized representative.

The cause of ischemic stroke was classified according to the TOAST criteria,<sup>3</sup> including large artery atherosclerosis (LAA); small artery occlusion (SAO); cardioembolism (CE); stroke of other determined etiology (SOE); and stroke of undetermined etiology (SUE). In this study, LAA patients were further divided into two groups: moderate stenosis (<70% stenosis in intracranial or extracranial arteries) and severe stenosis ( $\geq 70\%$ ). The information about the prescription of antihypertensive medication at discharge was extracted from medical records. Classes of antihypertensive medication included angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, diuretics, beta-blockers, and other antihypertensives including centrally acting adrenergics, peripherally acting antiadrenergics, and vasodilators.

## Statistical analysis

Univariate and multivariate logistic regression analyses were used to calculate the crude and adjusted odds ratios (ORs), respectively, for the association between TOAST subtypes and the prescription of antihypertensive medication at discharge. The multivariate models were created using variables associated with antihypertensive medication prescription (gender, age, monthly household income, types of health insurance, hypertension, diabetes mellitus, dyslipidemia, coronary heart disease, atrial fibrillation, history of stroke, previous antihypertensive medication use, and systolic blood pressure at discharge). Effect sizes were expressed as ORs and 95% confidence intervals (CIs). Two-tailed statistical significance was defined as  $P < 0.05$ . All statistical analyses were performed using SAS 9.1.3 (SAS Institute Inc, Cary, NC, USA).

## Results

### Patients' characteristics

A total of 12,063 ischemic stroke patients were analyzed in this study, with a mean age at entry of  $65.4 \pm 11.6$  years; 38.0% of the patients were women, 33.8% had a history of stroke, 70.8% had hypertension, 28.0% had diabetes, and 55.0% had dyslipidemia (Table 1). Among all ischemic stroke

subjects with or without hypertension, 4742 patients (39.3%) received a prescription at discharge for any antihypertensive, among whom 14 (0.3%) were discharged on four or more antihypertensive agents, 266 (5.6%) were discharged on three, 949 (20.0%) on two, and 3513 (74.1%) on one.

### Influence of TOAST subtype upon antihypertensive prescription at discharge

The multivariate analysis showed that when compared with LAA patients with moderate (<70%) stenosis, the adjusted ORs with 95% CIs were 0.72 (0.59–0.88), 1.50 (1.33–1.69), 0.91 (0.72–1.15), 1.49 (0.95–2.32), and 0.71 (0.64–0.79) in LAA patients with severe ( $\geq 70\%$ ) stenosis, SAO, CE, SOE, and SUE patients, respectively (Table 1).

### Other predictors of antihypertensive prescription at discharge

Multivariate analysis showed that patients with hypertension, diabetes, dyslipidemia, high income, urban employee health insurance, and high systolic blood pressure at discharge were more likely to be prescribed with antihypertensive medication at discharge; however, the elderly were less likely to be prescribed (Table 1).

### Subgroup analyses

We also investigated the influence of the TOAST subtype on antihypertensive prescription at discharge in patients with hypertension. The multivariate analysis showed that when compared with LAA patients with moderate (<70%) stenosis, the adjusted ORs with 95% CI were 0.70 (0.57–0.86), 1.57 (1.38–1.78), 0.89 (0.69–1.14), 1.47 (0.90–2.41), and 0.71 (0.64–0.79) in LAA patients with severe ( $\geq 70\%$ ) stenosis, SAO, CE, SOE, and SUE patients, respectively. This was similar to the group at large.

## Discussion

In normal clinical practice, given the level of concern over stroke recurrence from hypoperfusion, most neurologists tend to hold conservative attitudes toward active antihypertensive treatments for ischemic stroke patients. Our results indicated that the TOAST subtype had an influence on doctors' decisions to use antihypertensive prescriptions at discharge for ischemic stroke patients in real-world settings. Doctors tend to prescribe antihypertensives for SAO patients, but they are very cautious in prescribing them for LAA patients with severe stenosis. Unfortunately, to date there are no guidelines that have given definite recommendations as to how to choose the appropriate antihypertensive treatment for patients with

**Table 1** Prescription of AH medication at discharge for ischemic stroke patients

Variables	Prescription of AHs at discharge		Crude OR	Adjusted OR
	n	n (%)		
Total	12,063	4742 (39.3)		
TOAST subtype				
LAA (stenosis < 70%)	4885	2098 (43.0)	Reference	Reference
LAA (stenosis ≥ 70%)	583	220 (37.7)	0.81 (0.68–0.96)	0.72 (0.59–0.88)
SAO	2076	1050 (50.6)	1.36 (1.23–1.51)	1.50 (1.33–1.69)
CE	690	226 (32.8)	0.65 (0.55–0.77)	0.91 (0.72–1.15)
SOE	134	55 (41.0)	0.93 (0.65–1.31)	1.49 (0.95–2.32)
SUE	3695	1093 (29.6)	0.56 (0.51–0.61)	0.71 (0.64–0.79)
Sex				
Male	7474	2895 (38.7)	Reference	Reference
Female	4589	1847 (40.3)	1.07 (0.99–1.15)	1.00 (0.91–1.09)
Age				
18–45	773	269 (34.8)	Reference	Reference
46–65	4940	1942 (39.3)	1.21 (1.04–1.42)	0.79 (0.68–1.02)
66–75	3716	1550 (41.7)	1.34 (1.14–1.58)	0.78 (0.70–1.06)
≥76	2634	981 (37.2)	1.11 (0.94–1.32)	0.70 (0.56–0.86)
Monthly household income, yuan				
≤500	1384	503 (36.3)	Reference	Reference
500–1000	2793	1161 (41.6)	1.25 (1.09–1.42)	1.05 (0.90–1.23)
1001–3000	4033	1768 (43.8)	1.37 (1.21–1.55)	1.04 (0.89–1.22)
≥3000	815	402 (49.3)	1.71 (1.43–2.03)	1.27 (1.03–1.57)
Unknown	3038	908 (29.9)	0.75 (0.65–0.85)	0.62 (0.53–0.72)
Types of health insurance				
Own expense	2305	799 (34.7)	Reference	Reference
Urban employee	7293	3077 (42.2)	1.38 (1.24–1.52)	1.21 (1.07–1.36)
Rural cooperative	2075	705 (40.0)	0.97 (0.86–1.10)	1.10 (0.95–1.27)
Commercial and other	390	161 (41.3)	1.36 (1.06–1.65)	1.12 (0.96–1.26)
Hypertension				
No	3520	192 (5.5)	Reference	Reference
Yes	8543	4550 (53.26)	19.75 (16.97–22.98)	16.54 (13.99–19.55)
Diabetes				
No	8682	3211 (37.0)	Reference	Reference
Yes	3381	1531 (45.3)	1.41 (1.30–1.53)	1.10 (1.01–1.20)
Dyslipidemia				
No	5424	1678 (30.9)	Reference	Reference
Yes	6639	3064 (46.2)	1.91 (1.78–2.06)	1.61 (1.48–1.76)
Coronary artery disease				
No	10,357	4015 (38.8)	Reference	Reference
Yes	1706	727 (42.6)	1.17 (1.06–1.30)	0.89 (0.79–1.01)
Atrial fibrillation				
No	10,875	4333 (39.8)	Reference	Reference
Yes	1188	409 (34.4)	0.79 (0.70–0.90)	1.00 (0.83–1.20)
History of stroke				
No	7982	3036 (38.0)	Reference	Reference
Yes	4081	1706 (41.8)	1.17 (1.08–1.26)	0.94 (0.86–1.03)
History of AH medication				
No	6430	1692 (26.3)	Reference	Reference
Yes	5633	3050 (54.2)	3.31 (3.06–3.57)	1.08 (0.98–1.19)
SBP at discharge*				
< 120 mmHg	649	99 (2.1)	Reference	Reference
120–139 mmHg	2558	711 (15.1)	2.14 (1.70–2.69)	1.58 (1.21–2.05)
140–159 mmHg	4538	1727 (36.6)	3.41 (2.73–4.26)	1.87 (1.45–2.41)
≥ 160 mmHg	4265	2176 (46.2)	5.79 (4.63–7.23)	2.65 (2.06–3.42)

**Note:** \*SBP at discharge data was missing for a total of 53 patients.

**Abbreviations:** AH, antihypertensive; n, number; OR, odds ratio; TOAST, Trial of Org 10172 in Acute Stroke Treatment; LAA, large artery atherosclerosis; SAO, small artery occlusion; CE, cardioembolism; SOE, stroke of other determined etiology; SUE, stroke of undetermined etiology; SBP, systolic blood pressure.

different TOAST subtypes. The doctors' decisions are only based on personal experience in clinical practice. Therefore, more evidence from clinical trials and recommendations from guidelines are needed for this decision.

Although current American Heart Association/American Stroke Association guidelines advocate that blood reduction is also reasonable for ischemic stroke patients without hypertension,<sup>1</sup> our study showed that only 5.5% of nonhypertensive ischemic stroke patients were prescribed antihypertensive medications. This finding may reflect the influence of clinical trial results that suggest that nonhypertensive stroke patients may reap benefits from antihypertensive treatments.<sup>4</sup> However, these agents may have been prescribed for other therapeutic reasons, such as using beta-blockers for heart rate control, or angiotensin-converting enzyme inhibitors for heart failure.<sup>5</sup>

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## Disclosure

The authors report no conflicts of interest in this work.

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