

International Comparison of Patient Characteristics and Quality of Care for Ischemic Stroke: Analysis of the China National Stroke Registry and the American Heart Association Get With The Guidelines—Stroke Program

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Background—Adherence to evidence-based guidelines is an important quality indicator; yet, there is lack of assessment of adherence to performance measures in acute ischemic stroke for most world regions.

Methods and Results—We analyzed 19 604 patients with acute ischemic stroke in the China National Stroke Registry and 194 876 patients in the Get With The Guidelines—Stroke registry in the United States from June 2012 to January 2013. Compared with their US counterparts, Chinese patients were younger, had a lower prevalence of comorbidities, and had similar median, lower mean, and less variability in National Institutes of Health Stroke Scale (median 4 [25th percentile–75th percentile, 2–7], mean 5.4 ± 5.6 versus median 4 [1–10], mean 6.8 ± 7.7). Chinese patients were more likely to experience delays from last known well to hospital arrival (median 1318 [330–3209] versus 644 [142–2055] minutes), less likely to receive thrombolytic therapy (2.5% versus 8.1%), and more likely to experience treatment delays (door-to-needle time median 95 [72–112] versus 62 [49–85] minutes). Adherence to early and discharge antithrombotics, smoking cessation counseling, and dysphagia screening were relatively high (eg >80%) in both countries. Large gaps existed between China and the United States with regard to the administration of thrombolytics within 3 hours (18.3% versus 83.6%), door-to-needle time ≤ 60 minutes (14.6% versus 48.0%), deep venous thrombosis prophylaxis (65.0% versus 97.8%), anticoagulation for atrial fibrillation (21.0% versus 94.4%), lipid treatment (66.3% versus 95.8%), and rehabilitation assessment (58.8% versus 97.4%).

Conclusions—We found significant differences in clinical characteristics and gaps in adherence for certain performance measures between China and the United States. Additional efforts are needed for continued improvements in acute stroke care and secondary prevention in both nations, especially China. (*J Am Heart Assoc.* 2018;7:e010623. DOI: 10.1161/JAHA.118.010623)

Key Words: international comparison • patient characteristics • performance measures • quality of care • stroke

Stroke is the second leading cause of death worldwide. More than 6 million people died of stroke in 2015, with nearly 90% of these deaths in low- and middle-income countries.^{1,2} According to the World Health Organization, these numbers are expected to rise without proper intervention. The stroke burden in China has increased over the past 3 decades and has now become the leading

cause of mortality, resulting in 1.6 million deaths per year.^{3,4} In contrast, the stroke burden and mortality rates have declined in many high-income countries.⁵ For instance, stroke recently declined from the third to the fifth leading cause of death in the United States, largely attributable to improved prevention and acute stroke care.⁶ In an effort to overcome the global stroke

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Clinical Perspective

What Is New?

- Adherence to evidence-based guidelines is an important indicator of hospital stroke care quality.
- This international comparison study found significant differences in adherence to stroke performance measures between China and the United States with regard to stroke thrombolytic therapy, deep venous thrombosis prophylaxis, anticoagulation for atrial fibrillation, lipid treatment, and rehabilitation assessment.

What Are the Clinical Implications?

- We identified suboptimal care in acute stroke treatment and secondary prevention in China, representing potential targets for quality improvement.
- National efforts are needed to improve evidence-based stroke care and outcomes.

pandemic, the World Health Organization and United Nations declaration has called for a 25% relative reduction in premature mortality from noncommunicable diseases including stroke by the year 2025.^{7,8} Given the high mortality rates and chance of stroke recurrence, there is an urgent need to improve both acute stroke care and secondary prevention efforts. This should include measures to ensure adherence to evidence-based stroke care at both the acute phase and after discharge.

Quality improvement programs such as the American Heart Association/American Stroke Association (AHA/ASA) Get With The Guidelines—Stroke (GWTG-Stroke) have been shown to improve quality of care and outcomes for patients with strokes.^{9,10} However, little is known about standardized quality-of-care measures in other nations, especially in the developing world with different racial/ethnic composition and healthcare systems. Furthermore, international comparisons of disease presentation and adherence to evidence-based quality measures may identify gaps and yield actionable insights to guide changes in policy and clinical practice. Therefore, the objective of this study was to compare patient characteristics and performance measures among patients with acute ischemic stroke in China, the largest middle-income economy, and the United States, the largest high-income economy in the world. Comparison of these 2 countries is facilitated by the presence of harmonized reporting measures in the China National Stroke Registry (CNSR) and the GWTG-Stroke registry.

Methods

The authors declare that all supporting data are available within the article.

GWTG-Stroke and CNSR Phase II

The GWTG-Stroke program is an ongoing, voluntary, national stroke registry sponsored by the AHA/ASA. Details of the design and conduct of the GWTG-Stroke program have been previously reported.^{9,11} Trained hospital personnel use a web-based patient management tool to collect information on consecutive patients with ischemic stroke admitted to the hospital. Standardized data collection includes patient demographics, medical history, diagnostic testing, brain imaging, in-hospital treatment, and outcomes. Importantly, the program includes a set of performance measures to quantify the quality of stroke care and use the results of those measures to guide the quality improvement efforts at participating centers. Each participating hospital received either human research approval to enroll consecutive patients without individual patient consent under the Common Rule or a waiver of authorization and exemption from subsequent review by their institutional review board. Since its inception in 2003, the GWTG-Stroke program has enrolled more than 5 million stroke cases from over 1900 hospitals, representing nearly 70% of ischemic stroke hospitalizations in the United States in recent years.

CNSR phase II, launched in 2012, is a nationwide voluntary hospital-based stroke registry sponsored by the Ministry of Science and Technology and Ministry of Health of the People's Republic of China. Details of CNSR phase II have been reported.^{12,13} A total of 219 hospitals from 27 provinces and 4 municipalities in Mainland China joined CNSR phase II and consecutively enrolled patients presenting with acute stroke or transient ischemic attack within 7 days of symptom onset. Because of a lack of research infrastructure and anticipated low volumes, community hospitals with fewer than 100 beds and rural hospitals did not participate in the registry. Research coordinators at each CNSR phase II hospital were trained to review the medical notes daily and identify, obtain informed consent from, and enroll consecutive patients with stroke. Data were collected using an internet-based patient data management tool for each eligible hospitalized case. Because many data elements in CNSR phase II were developed and adapted from the GWTG-Stroke registry, the overlap reporting systems allow a head-to-head comparison of characteristics, disease presentation, and patterns of stroke care between US and Chinese patients.

Quality-of-Care Definitions

The GWTG-Stroke program developed a set of process-based measures to quantify the quality of care for patients with stroke. These include 7 evidence-based performance measures (3 acute and 4 discharge measures) and 4 quality measures and exclude patients with documented contraindications or other exceptions to treatment eligibility.

Acute performance measures

1. Intravenous tissue plasminogen activator in patients who arrive within 2 hours after symptom onset and are treated within 3 hours of symptom onset (intravenous tissue plasminogen activator <2 hours).
2. Antithrombotic medication (antiplatelet or anticoagulant agents) administered by the end of hospital day 2 (“early antithrombotics”).
3. Deep venous thrombosis prophylaxis (warfarin, heparin, low-molecular-weight heparin, other anticoagulants, or pneumatic compression devices) administered by the end of hospital day 2 in nonambulatory patients.

Discharge performance measures

1. Antithrombotic medication (antiplatelet or anticoagulant) prescribed at discharge (“discharge antithrombotics”).
2. Anticoagulation prescribed at discharge in patients with documented atrial fibrillation (“anticoagulation for atrial fibrillation”).
3. Lipid-lowering medication prescribed at discharge to patients with low-density lipoprotein >100 mg/dL, or those treated with lipid-lowering agents before admission, or in whom low-density lipoprotein was not documented (“low-density lipoprotein 100”).
4. Smoking cessation intervention (counseling or medication) at or before discharge for patients who are current smokers (“smoking cessation”).

Other quality measures

1. Door-to-computed tomography time ≤25 minutes.
2. Door-to-needle time ≤60 minutes in patients treated with intravenous tissue plasminogen activator.
3. Dysphagia screening before any oral intake.
4. Stroke rehabilitation assessment.

These measures have been adopted in CNSR phase II using the same definitions. While not as comprehensive as the World Stroke Organization stroke quality indicators, these parameters are also covered by the World Stroke Organization guidelines and represent the core elements of stroke care from hyperacute phase, acute inpatient care, to secondary prevention and rehabilitation.⁷

Statistical Analysis

Baseline characteristics and performance measures were compared between Chinese and US patients with stroke using standardized difference. Unlike *t* and chi-square tests, the standardized difference is not dependent on sample size. Importantly, only aggregated data such as mean, variance, and percent are used for standardized difference

calculation without the need for individual-level data sharing.

For binary variables:

$$d = \frac{100 \times (P_{CN} - P_{US})}{\sqrt{\frac{P_{CN}(1-P_{CN}) + P_{US}(1-P_{US})}{2}}}$$

For continuous variables:

$$d = \frac{100 \times (\bar{x}_{CN} - \bar{x}_{US})}{\sqrt{\frac{S_{CN}^2 + S_{US}^2}{2}}}$$

where \bar{x} , S^2 , and P denote mean and variance of a continuous variable and prevalence of a binary variable. A standardized difference <0.1 (10%) and >−0.1 (−10%) indicates a negligible difference in the mean or prevalence of a variable, while ≥ 0.1 (10%) or ≤ -0.1 (−10%) indicate an important imbalance between 2 study groups.¹⁴ There were relatively low rates of missing (<2.5%) for all variables except for last known well to arrival time (0.4% in China and 23.6% in the United States), arrival mode (14.9% in the United States), and National Institutes of Health Stroke Scale (25.7% in the United States). Standardized differences were also used to quantify the quality-of-care measures between China and the United States. No risk adjustment was performed because performance and quality measures apply to eligible patients only.

This study was approved by the institutional review board of Duke University and the Clinical Research Center and Beijing Tiantan Hospital, Capital Medical University. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc).

Results

Baseline Characteristics and In-Hospital Treatment

A total of 19 604 patients with acute ischemic stroke from 219 participating centers in CNSR phase II and 194 876 patients from 1548 sites in the GWTG-Stroke registry between June 2012 and January 2013 were included in this analysis. Compared with US hospitals, the median hospital bed size (1000 versus 367) and stroke volume (447 versus 217) were higher in China (Table 1). Nearly 60% of patients were cared for in academic centers in both China and the United States. Divided by regions in China, the East (59.8%) had the largest number of patients, followed by Central (22.8%), and West (17.4%), which was consistent with the country’s uneven population distribution.

Table 1. Baseline Characteristics and In-Hospital Treatment of Acute Ischemic Stroke in Patients in China and the United States

	CNSR Phase II (n=19 604)	GWTC-Stroke (n=194 876)	Standardized Difference
Patient characteristics			
Age, median (p25–p75), y	65 (57–74)	72 (60–82)	–42.7
Women, %	36.6	51.0	–29.5
Last known well to arrival, median (p25–p75), min	1318 (330–3209)	644 (142–2055)	+38.6
Arrival by EMS, %	13.4	49.4	–131.3
Arrival by private transport/taxi/other from home/scene, %	70.3	35.0	+131.3
NIHSS, median (p25–p75)	4 (2–7)	4 (1–10)	–21.2
Mean	5.4±5.6	6.8±7.7	
Body mass index, median (p25–p75)	24.1 (22.0–25.7)	27.2 (23.7–31.6)	–74.8
Health insurance, %			
Medicare	37.5	...	
Medicaid	10.8	...	
Private insurance	44.1	0.4	
Self-pay	6.9	9.0	
Universal basic medical insurance system	...	51.1	
New rural cooperative medical system	...	39.5	
Medical history, %			
AF	7.1	18.3	–34.5
Previous stroke or TIA	35.6	30.8	+10.2
Hypertension	64.8	76.2	–25.3
Dyslipidemia	12.1	44.3	–76.6
Diabetes mellitus	20.7	33.4	–29.0
Smoking	29.7	18.5	+26.4
Medication before admission, %			
Anticoagulant among patients with AF	7.3	33.8	–69.4
Antiplatelet among patients with AF	31.4	47.9	–34.2
Antihypertensive among patients with hypertension	69.1	82.7	–32.1
Cholesterol reducer among patients with dyslipidemia	57.0	70.9	–29.3
Diabetic medication among patients with diabetes mellitus	76.7	75.2	+3.6
Hospital characteristics			
Bed size, median (p25–p75)	1000 (600–1500)	367 (245–555)	+122.3
Annual ischemic stroke volume	447 (320–804)	217 (145–335)	+122.3
Academic center, %	57.7	60.1	–4.8
Primary stroke center, %	...	48.8	...
Stroke unit admission, %	13.3	71.8	–146.7
Region, %			
US Northeast	...	24.6	...
US South	...	35.7	...
US Midwest	...	20.2	...
US west	...	19.4	...
China East	59.8

Continued

Table 1. Continued

	CNSR Phase II (n=19 604)	GWTC-Stroke (n=194 876)	Standardized Difference
China Central	22.8
China West	17.4
In-hospital treatment, %			
Intravenous thrombolytic therapy	2.5	8.1	-31.4
t-PA	1.5	8.1	
Urokinase	1.0		
Door-to-needle time, median (p25–p75), min among t-PA–treated patients	95 (72–112)	62 (49–85)	+75.7

Missing rates in Get With The Guidelines—Stroke (GWTC-Stroke): last known well to arrival 23.6%, mode of arrival 14.9%, National Institutes of Health Stroke Scale (NIHSS) 25.7%, body mass index 34.2%, anticoagulant or antiplatelet in atrial fibrillation (AF) 8.4%, antihypertensives 15.6%, and diabetic medication 16.5%. Missing rates in the China National Stroke Registry (CNSR) phase II: tissue-type plasminogen activator (t-PA) 2.1% and urokinase 2.3%. All other variables have a missing rate <1%. EMS indicates emergency medical services; p25–p75, 25th percentile and 75th percentile; TIA, transient ischemic attack.

As compared with their US counterparts, Chinese patients were younger (median 65 [25th percentile–75th percentile 57–74] versus 72 [60–82]) and were more likely male (63.4% versus 49.0%). With the exception of smoking and history of cerebrovascular disease, Chinese patients had better cardiovascular risk profiles compared with US patients with regard to atrial fibrillation, hypertension, dyslipidemia, and diabetes mellitus. However, among those with corresponding conditions, Chinese patients were less likely to take anticoagulants (7.3% versus 33.8%), antiplatelet agents (31.4% versus 47.9%), antihypertensives (69.1% versus 82.7%), or cholesterol reducers (57.0% versus 70.9%) before admission (all standardized differences >10).

Stroke severity as measured by the National Institutes of Health Stroke Scale had a similar median, a slightly lower mean, and less variability in Chinese patients (median 4 [2–7], mean 5.4 ± 5.6 versus median 4 [1–10], mean 6.8 ± 7.7 , standardized differences -21.2). Chinese patients were less likely to use emergency medical services (13.4% versus 49.4%) and were more likely to have delays from last known well to hospital arrival (median 1318 minutes [330–3209] versus 644 minutes [142–2055]). There was no approved stroke center accreditation or certification agency in China during our study period. In contrast, 48.8% of patients with ischemic stroke were admitted to primary stroke centers in the United States. Only 13.3% of patients with ischemic stroke in China were cared for in a stroke unit, compared with over 70% in the United States. Overall, use of intravenous thrombolytic therapy was 2.5% in China (tissue-type plasminogen activator 1.5% and urokinase 1.0%) and 8.1% in the United States (tissue-type plasminogen activator) among all patients presenting with acute ischemic stroke. In addition, Chinese patients were more likely to experience delays in treatment (median door-to-needle time 95 minutes [72–112] versus 62 minutes [49–85]).

Performance and Quality Measures

Adherence to each individual performance and quality measure is shown in Table 2. Early and discharge antithrombotics, smoking cessation counseling, and dysphagia screening were fairly high (>80%) in both countries, although slightly lower in China than in the United States. Substantial gaps existed between China and the United States, respectively, with regard to administration of tissue-type plasminogen activator in patients arriving within 2 hours of symptom onset (18.3% versus 83.6%), deep venous thrombosis prophylaxis (65.0% versus 97.8%), anticoagulation for atrial fibrillation (21.0% versus 94.4%), lipid-lowering treatment (66.3% versus 95.8%), door-to-needle time ≤ 60 minutes (14.6% versus 48.0%), and rehabilitation assessment (58.8% versus 97.4%). In contrast, door-to-computed tomography time ≤ 25 minutes was relatively low in both countries (China versus the United States, 26.4% versus 27.9%, respectively).

Discussion

This study is among the first international comparisons of patient characteristics and patterns of adherence with evidence-based performance measures in ischemic stroke. We found clinically significant differences in baseline characteristics among patients presenting with acute ischemic stroke in China and the United States. Importantly, we identified differences in both acute treatment and secondary prevention for ischemic stroke in China among CNSR phase II hospitals compared with the United States among hospitals participating in GWTC-Stroke, representing potential targets for quality improvement.

Our findings suggest that Chinese patients with stroke, on average, are 7 years younger than US patients. Although Chinese patients have a lower prevalence of comorbidities, medical history of previous stroke/transient ischemic attack

Table 2. Performance Measures Between China and the United States

Measure	CNSR Phase II, %	GWTC-Stroke, %	Standardized Difference
Acute performance measure			
Intravenous t-PA arrive by 2 h, treat by 3 h	18.3	83.6	−31.4
Early antithrombotics	84.6	96.9	−43.7
DVT prophylaxis	65.0	97.8	−93.1
Discharge performance measure			
Discharge antithrombotics	90.3	98.5	−35.9
Anticoagulation for AF	21.0	94.4	−221.9
LDL 100 or not documented	66.3	95.8	−81.5
Smoking cessation	85.8	97.2	−41.9
Quality measure			
Door-to-computed tomography time ≤25 min	26.4	27.9	−3.3
Door-to-needle time ≤60 min	14.6	48.0	−77.2
Dysphagia screening	83.3	83.6	−0.7
Rehabilitation assessment	58.8	97.4	−105.6

AF indicates atrial fibrillation; CNSR, China National Stroke Registry; DVT, deep venous thrombosis; GWTC-Stroke, Get With The Guidelines—Stroke; t-PA, tissue plasminogen activator; LDL, low-density lipoprotein.

and cigarette smoking have been reported more often in the Chinese population. Importantly, among those who had atrial fibrillation, hypertension, or dyslipidemia, Chinese patients were less likely to receive treatment for these conditions before stroke. While we are unable to determine the etiology of stroke, these data suggest that high-risk health behaviors and inadequate treatment for both primary and secondary prevention may have partially explained the early onset of stroke in the Chinese population.

In addition, we found that once patients in China experienced symptoms of a stroke, they were less likely to use an ambulance, more likely to arrive by taxi or private vehicle, and have delays in hospital arrival. Potential reasons for this observation include lack of awareness of stroke symptoms, inadequate financial and geographic coverage for an ambulance, traffic condition, or patient preferences. While we cannot determine the exact reasons, public health campaigns may help educate the public about the symptoms of stroke, overcome the reluctance to seek medical attention, and emphasize the importance of getting to a hospital quickly. Regional strategies and policies to improve availability and access to emergency medical services may also be considered.

Importantly, we found significant gaps in use of evidence-based treatment among patients with acute ischemic stroke in China. Part of these differences could be explained by the different availability of stroke unit care (13.3% in China versus 71.8% in the United States). Despite similar (and longer) door-to-computed tomography time in both countries, use of intravenous thrombolytics in China was less than one third of

the treatment rate in the United States (2.5% versus 8.1%). Among those who arrived within 2 hours of symptom onset, <20% Chinese patients received stroke thrombolytic therapy in China as compared with nearly 85% in the United States. Even among Chinese patients who were treated, they experienced significant delays in treatment with a median door-to-needle time of nearly 100 minutes and <15% treated within 60 minutes of hospital arrival. A previous evaluation of CNSR phase I between 2007 and 2008 identified reasons for low thrombolytic use and treatment delays. These included the need for and delays associated with informed consent, delays in laboratory testing, the necessity for patients to buy tissue-type plasminogen activator first, reduced risk tolerance for bleeding complications, medication cost, and distrust of physicians and the healthcare system.^{13,15} Overall, 2.4% of patients in CNSR phase I received thrombolytic treatment with a median door-to-needle time of 116 minutes, as compared with 2.5% and 95 minutes in CNSR phase II 5 years later between 2012 and 2013. Along with the previous reports, these findings suggest that future efforts should focus on reducing delays in patient arrival to increase the portion of patients with ischemic stroke eligible for treatment and reducing in-hospital delay to improve the timeliness of thrombolytic therapy. In addition, policy initiatives and healthcare reform are needed to improve universal healthcare coverage, increase access to certified stroke centers/stroke unit care, and reduce out-of-pocket costs for catastrophic emergency conditions such as stroke.

Aside from thrombolytic therapy, our study shows that adherence to other performance and quality measures were

suboptimal in China, although there was still room for improvement in certain measures for both countries. For instance, the largest gaps between China and the United States were seen in anticoagulation for atrial fibrillation (21.0% versus 94.4%), deep venous thrombosis prophylaxis (65.0% versus 97.8%), lipid-lowering treatment (66.3% versus 95.8%), and rehabilitation assessment (58.8% versus 97.4%). Based on these findings, the AHA/ASA and the Chinese Stroke Association launched a quality improvement program “Improve Stroke Care in China” in March 2018. Adapted from the AHA/ASA GWTG-Stroke, the program is designed to improve treatment for, and prevention of, cardiovascular and stroke events by helping hospitals and providers consistently adhere to treatment guidelines. This program aims to address the need for emergency medical services and prehospital caregiver education, reduce door-to-needle times for patients to receive stroke thrombolytic therapy, and increase awareness and application of endovascular reperfusion therapies and secondary stroke prevention in eligible patients.

Study Limitations

Our study has several limitations. First, both CNSR phase II and GWTG-Stroke did not collect specific information regarding the etiology of stroke, such as TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification. Thus, we were unable to classify the subtypes of acute ischemic stroke as small-vessel disease and lacunar infarction, which are more prevalent in Asian patients. Second, despite being the largest stroke registries in both countries, participation in CNSR phase II and GWTG-Stroke are voluntary. There is potential selection bias introduced by the informed consent process in the Chinese stroke registry. The observed findings may not be representative of patients treated in hospitals not participating in the registry or individuals not providing informed consent. Because of the lack of small communities and rural hospitals in the registry, participating centers in CNSR phase II generally had more resources and stroke expertise. It is anticipated that the overall quality of care at the national level may be overestimated based on these high-volume and experienced centers. Nevertheless, the actual gaps in adherence to evidence-based performance measures could be even larger, further highlighting the need for improving quality of stroke care at the national level. Third, we used standardized differences to quantify the differences in characteristics and stroke performance measures. While this method uses aggregate data only without the need of individual patient data sharing, risk adjustment cannot be performed without such information. However, it could be argued that risk adjustment may not be necessary because performance measures only apply to eligible patients. Fourth, the data from both countries are dependent on the quality and accuracy of

the documentation in the medical record and abstraction. Fifth, the data from both countries are 5 years old. The quality of stroke care has likely improved in both countries since 2013. Yet, given the minimum improvement, if any, in stroke thrombolytic therapy between CNSR phases I and II, there is likely room for further improvement, especially in the area of acute stroke treatment and secondary stroke prevention. A related issue is endovascular thrombectomy, although not widely adopted during our study period, endovascular thrombectomy has become the standard of care for large-vessel occlusion.¹⁶ Further study is needed to examine quality of care and outcomes of endovascular thrombectomy in both countries.¹⁷ Finally, although we observed significant gaps in adherence to evidence-based performance measures, the registry did not document potential causes for suboptimal stroke care. To address this limitation, we plan to conduct a nationwide hospital survey in China to understand the common reasons and barriers for underuse of acute and secondary stroke prevention treatment, such as thrombolytics and oral anticoagulation for atrial fibrillation. These data will help us develop quality improvement interventions to improve evidence-based stroke treatment in China.

Conclusions

We found clinically important differences in patient characteristics and adherence to stroke performance measures between China and the United States. National efforts are needed to improve evidence-based stroke care and outcomes in both countries, especially China.

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