

Quality of care for ischemic stroke in China vs India

Findings from national clinical registries

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Abstract

Objective

To understand stroke risk factors, status of stroke care, and opportunities for improvement as China and India develop national strategies to address their disproportionate and growing burden of stroke.

Methods

We compared stroke risk factors, acute management, adherence to quality performance measures, and clinical outcomes among hospitalized ischemic stroke patients using data from the Indo-US Collaborative Stroke Project (IUCSP) and China National Stroke Registry-II (CNSR-II). The IUCSP included 5 academic stroke centers from different geographic regions (n = 2,066). For comparison, the CNSR-II dataset was restricted to 31 academic hospitals among 219 participating sites from 31 provinces (n = 1,973).

Results

Indian patients were significantly younger, had health insurance less often, and had significantly different risk factors (more often diabetes mellitus, dyslipidemia, and coronary heart disease; less often prior stroke, hypertension, atrial fibrillation, and smoking). Hospitalized Indian patients had greater stroke severity (median NIH Stroke Scale score 10 vs 4), higher rates of IV thrombolysis within 3 hours (7.5% vs 2.4%), greater in-hospital mortality (7.9% vs 1.2%), and worse outcome (3-month modified Rankin Scale score 0–2, 49.3% vs 78.1%) (all $p < 0.001$). The poorer clinical outcomes were attributable mainly to greater stroke severity in IUCSP patients. Chinese patients more often received antithrombotics, stroke education, and dysphagia screening during hospitalization.

Conclusion

These data provide insights into the status of ischemic stroke care in academic urban centers within 2 large Asian countries. Further research is needed to determine whether these patterns are representative of care across the countries, to explain differences in observed severity, and to drive improvements.

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Page 643

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Glossary

AHA-GWTG = American Heart Association's Get With The Guidelines; **CI** = confidence interval; **CNSR-II** = China National Stroke Registry-II; **DVT** = deep vein thrombosis; **IUCSP** = Indo-US Collaborative Stroke Project; **mRS** = modified Rankin Scale; **NIHSS** = NIH Stroke Scale; **OR** = odds ratio; **tPA** = tissue plasminogen activator.

Stroke burden is increasing, especially in low- and middle-income countries.¹ China and India, which account for more than one-third of the world's population,² have a major stroke burden.^{3,4} In China, the age-standardized incidence and prevalence rates are 246.8 and 1,114.8 per 100,000 person-years.⁵ In India, the incidence and prevalence rates are estimated to be 117 to 145 and 147 to 922 per 100,000 population.⁴ As China and India develop national strategies to address their growing burden of stroke, it is important to compare stroke risk factors and the status of stroke care and to understand their effect on the process of stroke care and outcomes. We used the data from China National Stroke Registry-II (CNSR-II)⁶ and Indo-US Collaborative Stroke Project (IUCSP)^{7,8} to compare demographics, risk factors, stroke quality performance measures, and clinical outcomes in China and India.

Methods

Standard protocol approvals, registrations, and patient consents

This comparative project was approved by the Ethics Committee of the IUCSP participating hospitals and the Central Institutional Review Board of Beijing Tiantan Hospital. For both registries, trained research coordinators reviewed the medical records daily to identify and enroll consecutive eligible patients at each hospital. Written informed consent was obtained. Data were prospectively entered in a secure web-based electronic platform.

The IUCSP

The IUCSP was a multicenter hospital-based study conducted at 5 high-volume academic tertiary hospitals across India funded by the US NIH and the Indian government's Department of Biotechnology to study the inpatient profile of ischemic stroke, to train a core group of researchers to stimulate stroke infrastructure development, and to lay the foundation for future scientific collaborations.^{7,8} Patients were enrolled consecutively from January 2012 until August 2014 if they met the following criteria: ischemic stroke symptoms of <2 weeks' duration with imaging-confirmed infarction or perfusion deficit by CT or MRI or >70% stenosis in the relevant artery for patients with transient symptoms. Data variables and definitions were consistent with the NIH Stroke Common Data Elements and American Heart Association's Get With The Guidelines (AHA-GWTG)-Stroke datasets, plus risk behaviors or variables relevant to India (e.g., beedi, paan tobacco consumption). Admission NIH Stroke Scale

(NIHSS) scores were obtained by certified physicians or coinvestigators.

The CNSR-II

The CNSR-II, launched in 2012 by the Ministry of Health of China, is a nationwide database focusing on the delivery of stroke care in clinical practice. Hospitals are classified into 3 grades according to location, bed numbers, staff expertise, and facilities.⁹ Patients were recruited consecutively from 219 hospitals from June 2012 to January 2013 if they met the following criteria: age ≥ 18 years; diagnosis of ischemic stroke, TIA, spontaneous intracerebral hemorrhage, or subarachnoid hemorrhage within 1 week confirmed by CT or MRI; and direct hospital admission from a physician's clinic or emergency department. Detailed methods have been published.⁶

Comparison of registry data

We included all 2,066 patients from the IUCSP. The CNSR-II has a total of 19,604 patients with acute ischemic stroke admitted to 219 hospitals, including 127 (58%) academic hospitals. To allow comparison, we restricted the CNSR-II cohort to the 1,973 ischemic stroke patients admitted to 31 academic (grade III) hospitals¹⁰ (1 from each of 27 provinces and 4 municipalities in Mainland China, with convenience sampling to select target hospitals from provinces having >1 grade III hospital).

Baseline variables common to both registries are listed in table 1. Risk factors such as hypertension, diabetes mellitus, and smoking were considered present if documented in the medical chart or if supported by laboratory values or clinical assessments. In addition, 9 stroke quality performance metrics were compared (table 2): (1) IV tissue plasminogen activator (tPA) therapy; (2) antithrombotic medication by the end of hospital day 2; (3) deep vein thrombosis (DVT) prophylaxis by the end of day 2 for nonambulatory patients; (4) dysphagia screening before any oral intake; (5) antithrombotic medication on discharge; (6) anticoagulation for atrial fibrillation/flutter on discharge; (7) antihypertensive medication; (8) statin treatment; and (9) stroke education. These performance measures were similar but not identical to the AHA-GWTG performance measures because of language and cultural differences (table 2).

In-hospital outcomes included pneumonia and all-cause mortality. Pneumonia was defined as the presence of clinical/laboratory features (fever, cough, auscultatory findings, new purulent sputum, or positive sputum culture) supported by chest x-ray results. Finally, we compared 3-month modified Rankin Scale (mRS) scores, which were obtained during

Table 1 Patient characteristics

Variables	China (n = 1,973)	India (n = 2,066)	p Value
Demographics			
Age, mean ± SD, y	63.9 ± 12.6	58.3 ± 14.7	<0.001
Male, n (%)	1,310 (66.4)	1,389 (67.2)	0.593
Health insurance, n (%)	1,636 (82.9)	813 (39.4)	<0.001
Medical history, n (%)			
Previous stroke/TIA	639 (32.4)	539 (26.1)	<0.001
Diabetes mellitus	456 (23.1)	737 (35.7)	<0.001
Hypertension	1,266 (64.2)	1,257 (60.8)	0.029
Dyslipidemia	229 (11.6)	298 (14.4)	0.009
CHD/previous MI	293 (14.9)	362 (17.5)	0.024
Atrial fibrillation	164 (8.3)	126 (6.1)	0.007
Tobacco use	855 (43.3)	668 (32.2)	<0.001
Alcohol use	559 (28.3)	707 (34.2)	<0.001
Prior ambulatory status, n (%)			
Independent	1741 (88.2)	1,943 (94.0)	
With assistance	196 (9.9)	67 (3.2)	
Unable to ambulate	36 (1.8)	56 (2.7)	<0.001
Admission NIHSS score, median (IQR)	4 (2–8)	10 (5–15)	<0.001

Abbreviations: CHD = coronary heart disease; MI = myocardial infarction; NIHSS = NIH Stroke Scale; IQR = interquartile range.

follow-up visits by clinicians or via telephone by trained and certified research personnel using standardized scripts.

Statistical analysis

Student *t*, χ^2 , Pearson, and Wilcoxon rank-sum tests were used as appropriate. Missing data were excluded from the denominator. Multivariable logistic regression analyses were conducted to identify predictors of favorable 3-month outcome (mRS score ≤ 2), including all variables significant at $p < 0.10$ on univariate testing. A value of $p < 0.05$ was considered statistically significant. Statistical analyses were performed with SAS version 9.3 (SAS Institute Inc, Cary, NC).

Data availability

All data used for analysis are presented in the tables. Data will be shared after ethics approval if requested by other investigators for purposes of replicating the results.

Results

Table 1 shows baseline characteristics. Patients in the IUCSP were significantly younger by an average of 5 years; the sex distribution was similar. The IUCSP patients had health insurance less often, although both populations were predominantly covered by government insurance. The vascular

risk profile was significantly different between groups, with IUSCP patients having significantly greater rates of diabetes mellitus, dyslipidemia, coronary heart disease, and alcohol use and the CSNR-II patients having significantly higher rates of prior stroke, hypertension, atrial fibrillation, and tobacco use (in the IUSCP, tobacco use included consumption of beedi, paan, hukka, and other indigenous products).

In Indian academic centers, hospitalized patients had greater stroke severity (median NIHSS score 10 vs 4, $p < 0.001$). Among patients presenting to IUCSP hospitals, the rate of IV tPA administered within 3 hours was 7.5% vs 2.4% in CSNR-II ($p < 0.001$).

In India, tPA is approved for use up to 4.5 hours and endovascular treatment is available. An additional 84 patients received IV tPA either at the transferring hospital or between 3 and 4.5 hours (including 30 who underwent bridging with intra-arterial lysis) for an overall IV tPA rate of 11.5%; in addition, endovascular treatment alone was administered to 29 (1.4%) patients.

Table 3 shows performance on in-hospital and discharge quality measures. The CSNR-II data reflected greater

Table 2 Performance measures

Measure	Definition
Acute performance measures^a	
IV tPA	IV tPA initiated <3 h of last known well time
Early antithrombotics	Antiplatelet or anticoagulant therapy administered within 48 h of hospitalization
Dysphagia screening	Dysphagia screening before any oral intake
DVT prophylaxis	DVT prophylaxis by end of hospital day 2 for nonambulatory patients, including pneumatic compression, warfarin sodium, or heparin sodium
Discharge performance measures^b	
Antithrombotic therapy	Discharged on antiplatelet or anticoagulant therapy
Anticoagulation for atrial fibrillation/flutter	Patients with known or newly diagnosed atrial fibrillation/flutter discharged on anticoagulants
Statin therapy	Discharged on statin medication
Antihypertensive therapy	Patient with known or newly diagnosed hypertension discharged on antihypertensive medication
Stroke education	Stroke education provided to patient or caregiver on discharge concerning weight loss, dietary modification, physical activity, stroke warning signs

Abbreviations: DVT = deep vein thrombosis; tPA = tissue plasminogen activator.

^a Denominator included all patients.

^b In-hospital deaths were excluded.

adherence to guideline-recommended stroke quality performance, e.g., significantly higher rates of antithrombotics within 48 hours of admission, dysphagia screening, antithrombotics on discharge, and stroke education concerning weight loss, physical activity, and dietary modification on discharge. IUCSP patients received significantly more stroke

preventive medications, including statins, anticoagulants for atrial fibrillation, and antihypertensives.

Outcomes

On univariate testing, CSNR-II patients had lower rates of in-hospital pneumonia (8.3% vs 12.7%, $p < 0.001$) and in-

Table 3 Adherence to performance measures

Performance measure	China (n = 1,973), n/N (%)	India (n = 2,066), n/N (%)	p Value
Acute/in-hospital measures			
Intravenous tPA within 3 hours	47/1,924 (2.4)	155/2,066 (7.5)	<0.001
Early antithrombotics	1,812/1,924 (94.2)	1,909/2,066 (92.4)	0.027
DVT prophylaxis ^a	359/620 (57.9)	789/1,374 (58.6)	0.76
Dysphagia screening	1,617/1,952 (82.8)	1,555/2,066 (75.3)	<0.001
Discharge measures^b			
Antithrombotics	1,647/1,653 (99.6)	1,831/1,875 (97.7)	<0.001
Statin	981/1,949 (50.3)	1,535/1,903 (80.7)	<0.001
Anticoagulation for AF ^a	52/170 (30.6)	176/212 (83.0)	<0.001
Antihypertensive ^a	857/1,249 (68.6)	843/1,155 (73.0)	0.02
Stroke education			
Weight loss/physical activity	1,469/1,949 (75.4)	662/1,903 (34.8)	<0.001
Diet or equivalent	1,825/1,949 (93.6)	1,051/1,903 (55.3)	<0.001

Abbreviations: AF = atrial fibrillation; DVT = deep vein thrombosis; tPA = tissue plasminogen activator.

^a Eligible patients only.

^b Deaths excluded. Missing data were excluded from the denominator.

hospital mortality (1.2% vs 7.9%) and more favorable outcomes (78.1% vs 49.3% with mRS score 0–2, $p < 0.001$). After adjustment for baseline variables shown in table 1, patients in the CSNR-II showed significantly lower odds of pneumonia (odds ratio [OR] 0.50, 95% confidence interval [CI] 0.39–0.65), in-hospital mortality (OR 0.11, 95% CI 0.07–0.19), and better 3-month outcome (mRS score 0–2, OR 3.11, 95% CI 2.47–3.92).

Multivariable analyses showed that younger age and lower admission NIHSS scores were associated with 3-month favorable outcome in both China and India (table 4). Prior stroke/TIA, hypertension, and independent ambulatory status were inversely associated with favorable outcome in China but not in India; diabetes mellitus was inversely associated with favorable outcome in India but not in China. Interventions such as IV recombinant tPA treatment, DVT prophylaxis, and dysphagia screening were associated with 3-month favorable outcome in India but not in China.

Discussion

Our results provide important insights into the differences in stroke risk factors, acute and in-hospital management, and outcomes in 2 large cohorts of hospitalized patients with acute ischemic stroke in China and India. Similar to other efforts comparing stroke between countries,^{11,12} this first detailed comparison of stroke demographics, risk factors, and inpatient management in China and India provides data that may improve resource allocation in national stroke prevention and management strategies, evaluate their effect of over time, and foster collaboration. Furthermore, these comparative data are relevant to recent studies showing opportunities for

improvement of stroke prevention guidelines in low- and middle-income countries such as China and India.¹³

While both groups developed stroke at younger ages compared to Western populations,¹⁴ Indian patients were significantly younger than Chinese patients. Stroke was male preponderant in both countries, likely due to a higher incidence and possible cultural biases resulting in men being evaluated and admitted more often than women. There was a relatively high burden of modifiable risk factors in both countries. The rates of hypertension, diabetes mellitus, and dyslipidemia in IUCSP were lower than previously reported in individual Indian hospital-based registries, probably reflecting the larger scope of the IUCSP. The rates in this restricted CSNR-II sample were consistent with rates reported in the overall CSNR-II registry.^{1,4–6,15} The rates of diabetes mellitus and tobacco use were much higher and the rates of hypertension and atrial fibrillation were much lower in China and India compared to AHA-GWTG data from the United States.¹⁴ Strategies such as increasing tobacco taxes, reducing tobacco-product advertisements, labeling foods with sugar, cholesterol, and salt content, and promoting physical exercise are globally important, but some strategies may need greater focus in China (e.g., antitobacco efforts), and diabetes prevention may need more effort in India. Atrial fibrillation, on the other hand, does not appear to be as important in these countries compared to the West. Health insurance was relatively low, especially in India; however, the CSNR-II and IUCSP were conducted in academic government hospitals where insurance status has little or no effect on health care delivery. Nevertheless, these data may be relevant to the future of health insurance in both countries.

There were significant differences in stroke severity and rates of IV tPA administration. These results mainly reflect disparities

Table 4 Multivariable logistic regression: Predictors of mRS score ≤ 2 at 3 months in each registry

Variable	China		India	
	Adjusted OR (95% CI)	<i>p</i> Value	Adjusted OR (95% CI)	<i>p</i> Value
Age, per year	0.95 (0.93–0.96)	<0.001	0.97 (0.96–0.98)	<0.001
Prior stroke/TIA	0.54 (0.37–0.78)	0.001	0.85 (0.62–1.16)	0.305
Hypertension	0.55 (0.32–0.94)	0.028	0.88 (0.56–1.38)	0.584
Diabetes mellitus	0.78 (0.52–1.18)	0.241	0.67 (0.50–0.91)	0.009
Admission NIHSS score per point	0.95 (0.92–0.97)	<0.001	0.88 (0.86–0.91)	<0.001
Prestroke ambulatory status	0.35 (0.20–0.62)	<0.001	0.61 (0.28–1.33)	0.211
Intravenous tPA therapy	0.58 (0.19–1.81)	0.348	2.12 (1.38–3.29)	0.001
DVT prophylaxis	1.51 (0.85–2.66)	0.157	0.65 (0.47–0.91)	0.012
Dysphagia screening	0.78 (0.45–1.35)	0.373	0.67 (0.47–0.95)	0.025
Antithrombotics at discharge	1.49 (0.80–2.80)	0.212	4.23 (1.88–9.53)	<0.001

Abbreviations: CI = confidence interval; DVT = deep vein thrombosis; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; OR = odds ratio; tPA = tissue plasminogen activator.

in resource availability and the systems of care between the 2 countries. In China, all patients with ischemic stroke are admitted and offered IV tPA from 0 to 3 hours if eligible; the tPA delivery rate, however, is relatively low due to patient factors such as affordability, risk aversion, and lesser stroke severity.¹⁶ In India, as a result of limited inpatient bed availability at hospitals like those participating in the registry, patients with severe stroke and thrombolysis are preferentially admitted, and others are sent to lower-level hospitals or home. The relatively high rate of tPA in IUCSP is also attributable to the 24/7 coverage by experienced physicians in enrolling hospitals, the subsidized cost of tPA in India, and government financial support to hospitals offering tPA. These data do not reflect the national rates of tPA use in India. More efforts are still needed to improve acute stroke care, including prehospital notification, prompt access to emergency departments with urgent head CT capability, training of key personnel, and wider availability of thrombolysis in both countries.

Lower stroke severity on admission contributes to the lower rates of in-hospital pneumonia and mortality and better 3-month clinical outcome observed in Chinese patients compared with those in India. However, systems of care may be more advanced in China, contributing to better outcomes. For example, CSNR-II showed higher rates of early antithrombotics, dysphagia screening, and stroke education at discharge. Of note, the number of patients eligible for DVT prophylaxis was lower in China, presumably due to preserved ambulation and consistent with the lower stroke severity of admitted patients; however, the rate of DVT prophylaxis was similar in both countries. Statins and anticoagulant medications were less frequently prescribed at discharge in China as a result of multiple barriers to care, including the limited availability of regular international normalized ratio testing, the cost of medications, and patient and physician concerns about adverse effects. Compared to data from AHA-GWTG–Stroke,¹⁴ the rates of DVT prophylaxis, dysphagia screening, and discharge medications and education were substantially lower in China and India than in the United States, suggesting opportunities to develop national quality improvement programs. Education and training of health care personnel should be a key component of such programs, especially given the relatively low number of neurologists and stroke-trained physicians in these countries.¹⁷

Substantial differences were observed in the adjusted OR for many variables associated with good outcomes between the 2 countries. The reasons for this are not apparent, and there are no data within the registries to address this question. These differences may be due to differences in hospital- or patient-level unmeasured confounders, to differences in post-discharge care and adherence to prescribed interventions, or to patient-level factors such as stroke mechanism, genetics, or unhealthy behaviors.

Because the IUCSP and selected CSNR-II hospitals are urban tertiary centers with stroke experts, our data likely do not

reflect nationwide risk factor prevalence or quality of care in China and India. Therefore, the results of our study have limited generalizability to academic hospital practice. However, these registries provide the best available and reliable evidence for tertiary stroke care in both countries, and the hospital locations were geographically diverse in both countries. The CSNR-II data presented here are consistent with the overall CSNR-II data.⁶ A major strength is that both projects enrolled consecutive patients and achieved a relatively high rate of data acquisition until the 90-day follow-up. Unlike the AHA-GWTG dataset, we did not capture reasons for noncompliance with quality performance measures such as patient refusal or medication contraindications, which may underestimate the quality of care. In CNSR II, 69.8% were assessed for rehabilitation, which is one of the core performance metrics in AHA-GWTG. Given the paucity of post-acute rehabilitation facilities in India, the IUCSP did not collect data on assessment for rehabilitation. Differences in stroke rehabilitation may account for some of the disparity in long-term outcomes of hospitalized stroke patients and may be a target for resource use in India and China. The multivariate analysis did not include some variables that are known to be associated with outcome, e.g., stroke mechanism or infarct volume, because imaging data were not captured in CSNR-II. Lastly, requirements for informed consent may have biased the enrolled cohort to less severe strokes, and this been shown to limit generalizability in other published reports.¹⁸

Vascular risk factors, acute and inpatient management as assessed by quality performance measures, and clinical outcomes in acute ischemic stroke vary in India and China. National strategies should be tailored per regional differences to improve resource use and to ultimately reduce stroke burden in China, India, and other developing countries.

Author contributions

Zixiao Li: analyzed and interpreted the data, drafted the manuscript, performed statistical analysis. Yilong Wang, Xingquan Zhao, and Liping Liu: conceived and designed the research. Chunjuan Wang: acquired the data. Yongjun Wang: conceived and designed the research. Jeyaraj Pandian, P.N. Sylaja, Dheeraj Khurana, M.V. Padma Srivastava, Subhash Kaul, and Deepti Arora: acquired the data. Lee H. Schwamm: conceived and designed the research. Aneesh B. Singhal: conceived and designed the research, analyzed and interpreted the data, and drafted the manuscript.

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Disclosure

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