Research Article

Impact of macroeconomic status on prehospital management, in-hospital care and functional outcome of acute stroke in China

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Practice Points

- Socioeconomic status is a multidimensional concept that comprises different indicators and is an important predictor of stroke incidence and mortality. Prior studies mainly focused on the potential association between microindicators of socioeconomic status and stroke, such as education, income, occupation, material ownership and area-based deprivation indices, and stroke. There is limited knowledge on the potential impact of macroeconomic status on prehospital management, in-hospital quality of care and functional outcome after stroke.
- This study was based on the largest stroke registry in China, the China National Stroke Registry. Based on the average gross regional product (GRP) per capita in 2008, provinces in China were classified into: developed (GRP per capita above average level) and underdeveloped (GRP per capita below average level) areas. Two variables and ten performance measures were used as quality indicators for prehospital management and in-hospital care, respectively. A summary composite measure was calculated by using an opportunity-based score. Good functional outcome was defined as modified Rankin Scale score ≤2 at discharge.
- It was found that higher GRP per capita was associated with better prehospital management, higher quality of in-hospital care and improved functional outcome at

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discharge after ischemic stroke (acute ischemic stroke/transient ischemic attack). Higher GRP per capita was also associated with better prehospital management and functional outcome at discharge after hemorrhagic stroke (subarachnoid hemorrhage/intracerebral hemorrhage). However, macroeconomic status (GRP per capita) showed less impact on in-hospital quality of care for hemorrhagic stroke.

SUMMARY: Aim: To examine the association between gross regional product (GRP) per capita and prehospital management, in-hospital quality of care and functional outcome after stroke. Methods: The study was based on the China National Stroke Registry between 2007 and 2008. Based on the average GRP per capita in 2008, provinces in China were divided into developed and underdeveloped areas. Two variables and ten performance measures were used as quality indicators for prehospital management and in-hospital care, respectively. Good functional outcome was defined as a modified Rankin Scale score ≤2 at discharge. A summary composite measure was calculated by using an opportunity-based score. A generalized estimation equation was performed to adjust for confounders. Results: For ischemic stroke (acute ischemic stroke/transient ischemic attack), compared with patients in the underdeveloped area (n = 7573), those in the developed area (n = 8516) received better prehospital management (adjusted odds ratio [OR]: 1.03; 95% CI: 1.02–1.04; $p < 0.001$) and a higher quality of in-hospital care (adjusted OR: 1.02; 95% CI: 1.01–1.03; $p < 0.001$). Higher GRP per capita was significantly associated with better functional outcome (modified Rankin Scale score ≤2) at discharge after ischemic stroke (adjusted OR: 1.11; 95% CI: 1.02–1.20; $p < 0.001$). A similar association between GRP per capita and prehospital management ($p < 0.001$) and primary outcome ($p < 0.001$) was found for hemorrhagic stroke (subarachnoid hemorrhage/intracranial hemorrhage). Conclusion: Higher GRP per capita was associated with better prehospital, in-hospital quality of stroke care and functional outcome at discharge after acute stroke.

Stroke is one of the leading causes of death and adult disability worldwide [1]. The importance of socioeconomic status (SES) as a predictor of stroke incidence, mortality and impact has been discussed previously [1–4]. However, SES is a multidimensional concept and comprises different indicators [2,5]. Prior studies mainly focused on microindicators of SES, such as education, income, occupation, material ownership and area-based deprivation indices [2,6–13]. Although some studies provided evidence that higher macroindicators of SES, such as gross domestic product (GDP), was associated with reduced stroke incidence and mortality [3,14,15], little is known about the potential impact of macroeconomic status on prehospital management, in-hospital quality of care and functional outcome after stroke.

After implementing The Open Door Policy in the early 1980s, China has experienced high economic growth during the last three decades. The GDP per capita has risen from US$195 in 1980 to US$4428 in 2010 (according to the World Bank). However, due to historical reasons (The Open Door Policy originated in the southeast coastal area and then spread throughout the country), such fast-pace economic growth is unevenly distributed across China. According to the National Bureau of Statistics of China, Shanghai had the highest gross regional product (GRP; 13,698.15 billion Yuan) and the in-land province Guizhou had the lowest (3333.4 billion Yuan) in 2008. Such disparity in economic growth did offer a unique opportunity to study the potential impact of macroeconomic status on stroke care and outcomes.

Using data from the largest stroke registry in China, the China National Stroke Registry (CNSR), we examined the association between macroeconomic status and prehospital management, in-hospital quality of care, and stroke outcomes at discharge.

Methods

Ethics statement

This study was approved by an ethics committee at each site within the CNSR network.

Study population

The methodology of CNSR has been described previously [16]. In brief, hospitals in China are classified into three grades:

- Grade I (community hospitals);
- Grade II (hospitals serving several communities);
- Grade III (central hospitals for a certain district or city).

In total, 242 potential sites, including 114 grade III, 71 grade II and 57 grade I hospitals, from both urban and rural areas, were initially identified by soliciting applications. The CNSR steering committee evaluated the research capability and commitment to the registry of each hospital with a preliminary survey. Finally, a total of 132 hospitals including 100 grade III and 32 grade II were selected, which cover 27 provinces and four municipalities across China. Trained research coordinators at each institute reviewed medical records daily to identify, consent and enroll consecutively eligible patients. To be eligible for this study, subjects had to meet the following criteria:

- Age 18 years or older;
- Hospitalized with a primary diagnosis of subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), acute ischemic stroke (AIS) or transient ischemic attack (TIA) according to WHO criteria [17] and with computed tomography or MRI confirmation;
- Direct admission to hospital from a physician's clinic or emergency department;
- Written informed consent from patients or their legal representatives.

GRP per capita groups

GRP is conceptually equivalent to GDP and measures newly created value through production by regional production unit ('province' in this study). Based on the average GRP per capita in 2008 (25,377.38 Yuan ≈US$3,715.51), provinces in China were classified into: developed areas with GRP per capita above average levels (median interquartile range [IQR]: 38,872.6; 31,558.6.5–62,802.7 Yuan; Shanghai, Beijing, Tianjin, Zhejiang, Jiangsu, Guangdong, Shandong, Inner Mongolia, Fujian, Liaoning and Hong Kong) and underdeveloped areas with GRP per capita below average levels (median IQR: 17,116.2; 14,345.6–19,530.8 Yuan; Jilin, Hebei, Heilongjiang, Shanxi, Xinjiang, Hubei, Henan, Shaanxi, Chongqing, Ningxia, Hunan, Qinghai, Hainan, Sichuan, Guangxi, Jiangxi, Anhui, Tibet, Yunnan, Gansu and Guizhou) **(Figure 1)**.

Measure of prehospital management & in-hospital quality of care

In this study, two variables were adopted to evaluate prehospital stroke management:

- Transportation mode to hospital, which was divided into emergency medical system (EMS) and private transportation (e.g., by taxi or private car);
- Time from symptom onset to hospital arrival, which was separated into ≤2 and >2 h.

According to prior studies [18], ten performance measures were used as quality indicators for in-hospital stroke care including:

- Intravenous tissue plasminogen activator in patients who arrive ≤2 h after symptom onset;
- Dysphagia screening prior to oral intake;
- Deep vein thrombosis (DVT) prophylaxis within 48 h of admission for nonambulatory patients;
- Antithrombotics within 48 h of admission;
- Rehabilitation assessment;
- Stroke education;
- Smoking cessation counseling;
- Discharge on anticoagulation for patients with atrial fibrillation;
- Discharge on antithrombotic medication;
- Discharge on cholesterol-reducing agent according to the National Cholesterol Education Panel Adult Treatment Panel III guidelines [19].

Patient adherence to individual performance measures was recorded and those with documented reasons for ineligibility were excluded

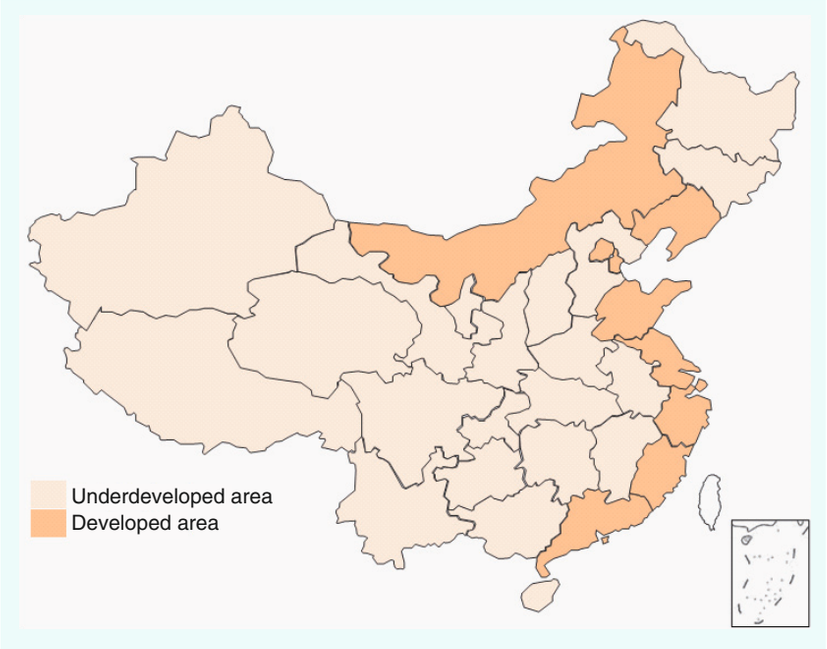

Figure 1. Developed and underdeveloped areas based on average national gross regional product per capita. Based on China's national average gross regional product per capita in 2008, provinces are classified into developed areas (Shanghai, Beijing, Tianjin, Zhejiang, Jiangsu, Guangdong, Shandong, Inner Mongolia, Liaoning, Fujian and Hong Kong) and underdeveloped areas (Jilin, Hebei, Heilongjiang, Shanxi, Xinjiang, Hubei, Henan, Shaanxi, Chongqing, Ningxia, Hunan, Qinghai, Hainan, Sichuan, Guangxi, Jiangxi, Anhui, Tibet, Yunnan, Gansu and Guizhou).

from the analysis for that measure. The results showed that the denominator, which indicated the total number of eligible patients, varied according to the measure. The proportion of eligible patients for each measurement was calculated by dividing the total number of patients receiving the intervention by the total number of patients who were eligible for the intervention. A summary composite measure of prehospital management and in-hospital quality of care was calculated by using an opportunity-based score [20], which was defined as the total number of measures performed in each subject divided by the total number of measures the subject was eligible for.

Stroke outcome assessment

In the study, stroke outcomes at hospital discharge were evaluated. The primary outcome was a modified Rankin Scale (mRS) score of ≤2 at hospital discharge. Secondary outcomes included in-hospital mortality and in-hospital stroke-associated pneumonia (SAP). SAP was defined as newly developed pneumonia (auscultatory respiratory crackles and fever [>38°C] or radiographic evidence or new purulent sputum) that occurred during the index hospitalization after acute stroke [21].

Statistical analysis

The association between macroeconomic status and prehospital management, in-hospital quality of care and stroke outcomes was analyzed for ischemic stroke (AIS/TIA) and hemorrhagic stroke (SAH/ICH), respectively. χ^2 test was used to compare the categorical variable and Mann–Whitney test or an independent t-test was employed to compare the continuous variable. Multivariate regression analysis using the generalized estimation equation (GEE) was performed to determine whether macroeconomic status (developed vs underdeveloped area) was associated with prehospital management, in-hospital quality of care and stroke outcomes. The GEE models considered clustering effects within hospitals [22] and adjusted for sociodemographics, risk factors (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, coronary heart disease, history of stroke/TIA and current smoking), stroke subtypes (AIS, TIA, SAH and ICH), Oxfordshire Community Stroke Project classification (partial anterior circulation infarct, total anterior circulation infarct; lacunar infarction and posterior circulation infarct) for ischemic stroke, admission NIH Stroke Scale score, length of hospital stay and hospital facilities (hospital grade, total number of beds in the hospital, academic status, equipment with emergency department, Neurointensive care unit and stroke unit). All tests were two-tailed and statistical significance was determined at an α-level of 0.05. Statistical analysis was performed using SAS 9.1 (SAS Institute, NC, USA) and SPSS 16.0 (SPSS Inc., IL, USA).

Results

Baseline characteristics

From September 2007 to August 2008, a total of 22,216 patients with acute cerebrovascular events were enrolled in the CNSR. Among them, 767 were diagnosed with SAH, 5221 with ICH, 14,702 with AIS, 1387 with TIA and 139 with stroke of an undetermined type. For this study, 139 (0.6%) patients with stroke of an undetermined type were excluded. Based on average GRP per capita in 2008, study subjects

(n = 22,077) were subgrouped into patients in developed areas (n = 11,828) and underdeveloped areas (n = 10,249). The baseline characteristics of the study population are listed in Table 1. The median age was 65 years (IQR: 55–74) and 38.8% were female. Compared with stroke patients in the underdeveloped areas, those in the developed areas were older ($p < 0.001$), more frequently had healthcare insurance ($p = 0.001$), had a higher rate of hypertension ($p < 0.001$), diabetes mellitus ($p < 0.001$), hyperlipidemia ($p = 0.005$), atrial fibrillation ($p < 0.001$) and coronary artery disease ($p < 0.001$), a lower rate of smoking ($p < 0.001$), had more SAH ($p < 0.001$) and less TIA ($p < 0.001$), had a higher NIH Stroke Scale score on admission ($p < 0.001$) and were more likely to be treated in hospitals with better facilities ($p < 0.001$).

Table 1. Baseline characteristics by macroeconomic status.

Baseline characteristic	Total (n = 22,077)	Developed areas (n = 11,828)	Underdeveloped areas (n = 10,249)	p-value
Sociodemographics, n (%)				
Age, years, median (IQR)	65 (55–74)	66 (55–75)	63 (54–72)	<0.001
Gender (female)	8550 (38.7)	4633 (39.2)	3917 (38.2)	0.15
Education level (high school or above)	5999 (27.2)	3177 (26.9)	2822 (27.5)	0.26
Marital status (married)	19,798 (89.7)	10,566 (89.3)	9232 (90.1)	0.07
Health insurance	–	–	–	<0.001
Having no insurance (self-payment)	4725 (21.4)	2439 (20.6)	2286 (22.3)	–
Basic or government insurance	12,090 (54.8)	7153 (60.5)	4937 (48.2)	–
New rural cooperative insurance	4416 (20.0)	1722 (14.6)	2694 (26.3)	–
Commercial insurance	846 (3.8)	514 (4.3)	332 (3.2)	–
Vascular risk factors, n (%)				
Hypertension	13,927 (63.1)	7644 (64.6)	6283 (61.3)	<0.001
Diabetes mellitus	3876 (17.6)	2271 (19.2)	1605 (15.7)	<0.001
Hyperlipidemia	2146 (9.7)	1211 (10.2)	935 (9.1)	0.005
Atrial fibrillation	1204 (5.5)	755 (6.4)	449 (4.4)	<0.001
Coronary artery disease	2588 (11.7)	1512 (12.8)	1076 (10.5)	<0.001
Family history of stroke	2753 (13.4)	1453 (13.3)	1300 (13.5)	0.70
History of any stroke/transient ischemic attack	6408 (29.0)	3410 (28.8)	2998 (29.3)	0.49
Current smoking	8551 (38.9)	4405 (37.5)	4146 (40.6)	<0.001
Prestroke disability (mRS ≥3)	1843 (8.3)	975 (8.2)	868 (8.5)	0.56
Stroke subtype, n (%)				
Subarachnoid hemorrhage	767 (3.5)	486 (4.1)	281 (2.7)	<0.001
Intracranial hemorrhage	5221 (23.6)	2826 (23.9)	2395 (23.4)	0.36
Acute ischemic stroke:	14,702 (66.6)	7870 (66.5)	6832 (66.7)	0.85
▪ Partial anterior circulation infarct	8168 (55.6)	4311 (54.8)	3857 (56.5)	0.07
▪ Total anterior circulation infarct	1327 (9.0)	721 (9.2)	606 (8.9)	0.57
▪ Lacunar infarction	2719 (18.5)	1495 (19.0)	1224 (17.9)	0.12
▪ Posterior circulation infarct	2488 (16.9)	1343 (17.1)	1145 (16.8)	0.67
Transient ischemic attack	1387 (6.3)	646 (5.5)	741 (7.2)	<0.001
Admission NIHSS score, median (IQR)				
Stroke severity on admission	5 (2–10)	5 (2–11)	4 (1–10)	<0.001
Hospital facility, n (%)				
Academic center	12,570 (56.9)	7131 (60.3)	5439 (53.1)	<0.001
Hospital with emergency department	14,677 (69.1)	8745 (78.7)	5932 (58.6)	<0.001
Hospital with N-ICU	16,885 (78.3)	9678 (85.6)	7207 (70.3)	<0.001
Hospital with stroke unit	12,189 (57.2)	7199 (64.7)	4990 (49.0)	<0.001
Hospital with stroke outpatient clinic	21,702 (98.3)	11,828 (100)	9874 (96.3)	<0.001

IQR: Interquartile range; mRS: Modified Rankin Scale; N-ICU: Neurointensive care unit; NIHSS: NIH Stroke Scale.

GRP per capita & prehospital management

Prehospital management for ischemic stroke and hemorrhagic stroke are shown in Tables 2 & 3 and Tables 4 & 5, respectively. For ischemic stroke (AIS/TIA), patients in the developed areas were more likely to use EMS (18.0 vs 12.1%; p < 0.001) and present at hospital within 2 h from symptom onset (12.7 vs 9.9%; p < 0.001) (Table 2). After GEE adjustment, higher GRP per capita was significantly associated with better individual measures (p < 0.001) and composite measures of prehospital management for ischemic stroke (adjusted odds ratio [OR]: 1.03; 95% CI: 1.02–1.04; p < 0.001) (Table 3). A similar association between GRP per capita and individual and composite measures of prehospital management were found for hemorrhagic stroke (SAH/ICH) (Tables 4 & 5).

GRP per capita & in-hospital quality of care

In-hospital quality of care for ischemic stroke and hemorrhagic stroke are shown in Tables 2 & 3 and Tables 4 & 5, respectively. For ischemic stroke (AIS/TIA), patients in the developed areas received more evidence-based care of dysphagia screening (p < 0.001), DVT prophylaxis (p < 0.001), rehabilitation assessment (p < 0.001), discharge on antithrombotics (p < 0.001) and cholesterol-reducing medications (p < 0.001); while patients in the underdeveloped areas received more evidence-based care in getting antithrombotic therapy within 48 h after hospitalization (p < 0.001), in-hospital stroke education (p = 0.004) and smoking cessation counseling (p = 0.002) (Table 2). The mean opportunity-based score of in-hospital quality of care was 0.62 (standard deviation: 0.25). After GEE adjustment, higher GRP per capita was significantly associated with higher opportunity-based score of in-hospital quality of care for ischemic stroke (adjusted OR: 1.02; 95% CI: 1.01–1.03; p < 0.001) (Table 3).

For hemorrhagic stroke (SAH/ICH), patients in the developed areas received more evidence-based care of DVT prophylaxis (p < 0.001) and rehabilitation assessment (p = 0.01); while patients in the underdeveloped areas received more evidence-based care in getting in-hospital

Table 2. Prehospital management, in-hospital quality of care and outcomes at discharge of ischemic stroke (acute ischemic stroke/transient ischemic attack) by macroeconomic status.

Measures of quality of care and outcome	Total (n = 16,089)	Developed areas (n = 8516)	Underdeveloped areas (n = 7573)	p-value
Prehospital management, n (%)				
Transportation to hospital via EMS	2453 (15.2)	1533 (18.0)	920 (12.1)	<0.001
Transportation to hospital within 2 h	1832 (11.4)	1082 (12.7)	750 (9.9)	<0.001
Opportunity-based score , mean (SD)	0.13 (0.25)	0.15 (0.27)	0.11 (0.23)	<0.001
In-hospital quality of care†, n (%)				
Intravenous thrombolysis with rt-PA	86 (10.8)	54 (10.8)	32 (10.8)	0.98
Dysphagia screening	5555 (37.4)	3207 (41.2)	2348 (33.2)	<0.001
Deep vein thrombosis prophylaxis	3321 (63.2)	1923 (65.5)	1398 (60.2)	<0.001
Antithrombotics within 48 h after hospitalization	12,808 (82.8)	6620 (80.8)	6188 (85.1)	<0.001
Anticoagulation for atrial fibrillation	224 (25.5)	131 (23.9)	93 (28.1)	0.18
Antithrombotics at discharge	11,060 (69.7)	5893 (70.4)	5167 (69.0)	0.05
Cholesterol-reducing agents at discharge	5860 (61.0)	3181 (64.0)	2679 (57.8)	<0.001
Rehabilitation assessment	7393 (46.0)	4187 (49.2)	3206 (42.3)	<0.001
Stroke education	13,771 (85.6)	7247 (85.1)	6524 (86.1)	0.06
Smoking cessation counseling	2989 (69.7)	1484 (67.3)	1505 (72.3)	<0.001
Opportunity-based score, mean (SD)	0.62 (0.25)	0.64 (0.26)	0.61 (0.24)	<0.001
Outcomes at discharge, n (%)				
mRS ≤2 at discharge	11,320 (70.4)	5914 (69.4)	5406 (71.4)	0.007
In-hospital mortality	507 (3.2)	300 (3.5)	207 (2.7)	0.004
In-hospital SAP	1697 (10.5)	941 (11.0)	756 (10.0)	0.03

†The denominator was the total number of patients who were eligible for the specific measure and varied according to the measures.
EMS: Emergency medical system; mRS: Modified Rankin Scale; rt-PA: Recombinant tissue plasminogen activator; SAP: Stroke-associated pneumonia; SD: Standard deviation.

Table 3. Unadjusted and adjusted odds ratios for prehospital management, in-hospital quality of care and outcomes at discharge of ischemic stroke (acute ischemic stroke/transient ischemic attack) by macroeconomic status[†].

Measures of quality of care and outcome	Unadjusted OR (95% CI)	p-value	Adjusted OR[‡] (95% CI)	p-value
Prehospital management				
Transportation to hospital by EMS (n = 16,089)	1.59 (1.45–1.73)	<0.001	1.46 (1.33–1.60)	<0.001
Transportation to hospital within 2 h (n = 16,089)	1.32 (1.20–1.46)	<0.001	1.29 (1.17–1.43)	<0.001
Opportunity-based score (n = 16,089)	1.04 (1.03–1.05)	<0.001	1.03 (1.02–1.04)	<0.001
In-hospital quality of care				
Intravenous thrombolysis with rt-PA (n = 797)	1.00 (0.63–1.58)	0.99	1.09 (0.68–1.75)	0.73
Dysphagia screening (n = 14,861)	1.41 (1.32–1.51)	<0.001	1.37 (1.28–1.46)	<0.001
Deep vein thrombosis prophylaxis (n = 5258)	1.26 (1.12–1.41)	<0.001	1.28 (1.14–1.44)	<0.001
Antithrombotics within 48 h after admission (n = 15,470)	0.73 (0.68–0.80)	<0.001	0.76 (0.70–0.83)	<0.001
Anticoagulation for atrial fibrillation (n = 879)	0.80 (0.59–1.10)	0.17	0.86 (0.63–1.19)	0.37
Antithrombotics at discharge (n = 15,860)	1.07 (1.01–1.15)	0.03	1.15 (1.08–1.24)	<0.001
Cholesterol-reducing agents at discharge (n = 9603)	1.30 (1.20–1.41)	<0.001	1.34 (1.23–1.45)	<0.001
Rehabilitation assessment (n = 16,089)	1.32 (1.24–1.40)	<0.001	1.28 (1.20–1.36)	<0.001
Stroke education (n = 16,089)	0.92 (0.84–1.00)	0.06	0.94 (0.86–1.03)	0.94
Smoking cessation counseling (n = 4289)	0.79 (0.69–0.90)	<0.001	0.81 (0.71–0.93)	0.002
Opportunity-based score (n = 16,089)	1.02 (1.01–1.03)	<0.001	1.02 (1.01–1.03)	<0.001
Outcomes at discharge				
mRS ≤2 at discharge (n = 16,089)	0.91 (0.85–0.98)	0.007	1.11 (1.02–1.20)	<0.001
In-hospital mortality (n = 16,089)	1.30 (1.09–1.56)	0.004	1.07 (0.87–1.31)	0.53
In-hospital SAP (n = 16,089)	1.12 (1.01–1.24)	0.03	0.88 (0.79–0.98)	0.03

[†]Patients in the underdeveloped areas were used as a reference.
[‡]The generalized estimation equation models adjusted for age, gender, education level, marital status, health insurance, stroke risk factors (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, coronary heart disease, history of stroke/transient ischemic attack and current smoking), stroke subtypes (acute ischemic stroke and transient ischemic attack), Oxfordshire Community Stroke Project classification, admission NIH Stroke Scale score, hospital facilities (hospital grade, total number beds in the hospital, academic status and equipment within emergency department, neurointensive care unit, and stroke unit) and length of hospital stay.
EMS: Emergency medical system; mRS: Modified Rankin Scale; OR: Odds ratio; rt-PA: Recombinant tissue plasminogen activator; SAP: Stroke-associated pneumonia.

stroke education (p < 0.001) and smoking cessation counseling (p = 0.001) (Table 4). After GEE adjustment, there was no significant association between macroeconomic status and opportunity-based score of in-hospital quality of care for hemorrhagic stroke (adjusted OR: 0.99; 95% CI: 0.98–1.01; p = 0.61) (Table 5).

■ GRP per capita & stroke outcomes

The median length of hospital stay of the overall study population was 15 days (IQR: 10–21; ischemic stroke [AIS/TIA]: 14 [IQR: 10–20]; hemorrhagic stroke [SAH/ICH]: 18 [IQR: 11–26]). A total of 14,759 patients (66.9%) had good functional outcome (mRS ≤2) at discharge (11,320 for ischemic stroke and 3439 for hemorrhagic stroke); 1124 (5.1%) died during hospitalization (507 of ischemic stroke and 617 of hemorrhagic stroke); and 2655 (12.0%) had SAP during hospitalization (1697 for ischemic stroke and 958 for hemorrhagic stroke). After GEE adjustment, higher GRP per capita was significantly associated with better functional outcome (mRS ≤2) at discharge (adjusted OR: 1.11; 95% CI: 1.02–1.20; p < 0.001) and lower in-hospital SAP (adjusted OR: 0.88; 95% CI: 0.79–0.98; p = 0.03) after ischemic stroke (AIS/TIA) (Table 3). No significant association was found between GRP per capita and in-hospital mortality (adjusted OR: 1.07; 95% CI: 0.87–1.31; p = 0.53). A similar association between macroeconomic status and primary and secondary outcomes was found for hemorrhagic stroke (SAH/ICH) (Table 5).

Discussion

To the best of our knowledge, we are the first to systematically investigate the association between GRP per capita and prehospital management, in-hospital quality of care and functional outcome after acute stroke. It was found that higher GRP per capita was associated with better prehospital management, higher quality of in-hospital care and improved functional outcome at discharge after ischemic stroke (AIS/TIA). A similar association between macroeconomic status and prehospital management, and functional outcome at

Table 4. Prehospital management, in-hospital quality of care and outcomes at discharge of hemorrhagic stroke (subarachnoid hemorrhage/intracranial hemorrhage) by macroeconomic status.

Measures of quality of care and outcome	Total (n = 5988)	Developed areas (n = 3312)	Underdeveloped areas (n = 2676)	p-value
Prehospital management, n (%)				
Transportation to hospital via EMS	1849 (30.9)	1105 (33.4)	744 (27.8)	<0.001
Transportation to hospital within 2 h	1257 (21.0)	718 (21.7)	539 (20.1)	0.15
Opportunity-based score, mean (SD)	0.30 (0.30)	0.32 (0.29)	0.29 (0.31)	<0.001
In-hospital quality of care†, n (%)				
Dysphagia screening	1451 (31.5)	822 (31.9)	629 (31.1)	0.59
Deep vein thrombosis prophylaxis	759 (62.4)	420 (67.3)	339 (57.2)	<0.001
Cholesterol-reducing agents at discharge	352 (100)	200 (100)	152 (100)	–
Rehabilitation assessment	2112 (35.3)	1214 (36.7)	898 (33.6)	0.01
Stroke education	4391 (73.3)	2364 (71.4)	2027 (75.7)	<0.001
Smoking cessation counseling	819 (54.6)	405 (50.5)	414 (59.2)	0.001
Opportunity-based score, mean (SD)	0.49 (0.33)	0.49 (0.33)	0.49 (0.32)	0.66
Outcomes at discharge, n (%)				
mRS ≤2 at discharge	3439 (57.4)	1967 (59.4)	1472 (55.0)	<0.001
In-hospital mortality	617 (10.3)	378 (11.4)	239 (8.9)	0.002
In-hospital SAP	958 (16.0)	543 (16.4)	415 (15.5)	0.36

†The denominator was the total number of patients who were eligible for the specific measure and varied according to the measures.
EMS: Emergency medical system; mRS: Modified Rankin Scale; SAP: Stroke-associated pneumonia; SD: Standard deviation.

discharge, were found for hemorrhagic stroke (SAH/ICH). However, macroeconomic status showed less impact on in-hospital quality of care for hemorrhagic stroke.

Similar to prior studies [14], we found patients in the developed areas had older age of stroke onset. The evidence for the link between SES and stroke risk factors was not consistent for developed and developing countries. Studies in developed counties showed a higher prevalence of classic risk factors in the lower SES groups [4,23–25]; however, in developing countries, a direct relation has been observed between SES and risk factors such as high blood pressure and obesity [26]. An Indian study showed a remarkably similar distribution of classic risk factors between the urban and rural communities [27]. Interestingly, in our study, a higher proportion of vascular risk factors was found among stroke patients in the developed areas (excepting smoking). Caution should be used when interpreting the results. Although the information was collected by trained neurologists, we cannot rule out the potential reporting bias with under-reporting in the underdeveloped areas. Further studies on investigating the relationship between prevalence of classic stroke risk factors and macroeconomic status in China are needed. Additionally, we found more stroke patients in the developed areas had healthcare insurance, especially for basic or government insurance, which is an indicator of healthcare investment by local government.

A Canadian study found a minimal effect of SES on travel patterns after stroke [28]. In our study, it was found that patients in the developed areas were more likely to use EMS and present at hospital within a shorter time in both the ischemic stroke (AIS/TIA) and hemorrhagic stroke (SAH/ICH) cohort. The prehospital delay of acute stroke in urban China had previously been investigated [29]. Generally, there is a longer prehospital delay and less use of EMS in China than that in the western countries [30], and in our study, the situation was shown to be even worse in the underdeveloped areas. Due to the detrimental impact on stroke management and outcomes associated with prehospital delay, continuous efforts are needed to improve prehospital stroke management in China, especially for the underdeveloped areas.

The association between microindicators of SES and delivery of stroke care has been investigated and no consistent pattern has been found. Some studies suggested that socioeconomic differences may exist in stroke care with patients with low SES receiving fewer relevant diagnostic examinations and less stroke care [6,9–11,31]. By contrast, other studies failed to verify such association [7,13,32]. In our study,

higher GRP per capita was shown to be associated with higher quality of in-hospital care for ischemic stroke (AIS/TIA), but not for hemorrhagic stroke (SAH/ICH) by using a composite measure score. This might be attributable to the fact that relatively less attention and effort has been paid to improve quality of care for hemorrhagic stroke as compared with ischemic stroke. A prior study also indicated that performance-of-care measures were generally lower for ICH/SAH compared with AIS/TIA [33]. Although different indicators were used to measure in-hospital quality of care, compared with prior studies [33–35], our study suggested continuous efforts are needed to ensure optimal stroke care to both patient groups in China, especially for intravenous tissue plasminogen activator, anticoagulation for atrial fibrillation and dysphagia screening.

In China, the media, government and authorities have called the attention of the public and of clinicians to stroke. Unfortunately, based on data from the CNSR, only 2.4% of AIS patients were treated with either intravenous or intra-arterial thrombolysis [36]. In our opinion, potential reasons for this dismal record vary and can be classified into the following four categories:

- Prehospital delay;
- In-hospital delay;
- Lack of basic infrastructure;
- Lack of readiness of treating clinicians or patients/families for stroke thrombolysis treatment.

In the future, health and medical care promotion strategies to improve community awareness of stroke, expanded availability and utilization of ambulance services, implementation of stroke center certification project, creation of effective clinical pathways for stroke thrombolysis, strengthening professional training on stroke thrombolysis, and establishment of telemedicine service are necessary and promising methods to expedite stroke thrombolysis in China.

Prior studies demonstrated that a higher GDP level was associated with reduced stroke mortality [2,3,14,25]. In this study, we did not find a significant association between GRP per capita and in-hospital mortality. However, our study provided evidence that higher GRP per capita was associated with improved functional outcome at discharge and reduced in-hospital SAP after stroke. Meanwhile, the finding was verified in both an ischemic (AIS/TIA) and hemorrhagic

Table 5. Unadjusted and adjusted odds ratios for prehospital management, in-hospital quality of care and outcomes at discharge of hemorrhagic stroke (subarachnoid hemorrhage/intracranial hemorrhage) by macroeconomic status†.

Measures of quality of care and outcome	Unadjusted OR (95% CI)	p-value	Adjusted OR‡ (95% CI)	p-value
Prehospital management				
Transportation to hospital by EMS (n = 5988)	1.30 (1.16–1.45)	<0.001	1.27 (1.13–1.43)	<0.001
Transportation to hospital within 2 h (n = 5988)	1.10 (0.97–1.24)	0.15	1.06 (1.01–1.26)	0.03
Opportunity-based score (n = 5988)	1.03 (1.01–1.05)	<0.001	1.02 (1.01–1.04)	0.02
In-hospital quality of care				
Dysphagia screening (n = 4804)	1.04 (0.92–1.18)	0.57	1.01 (0.88–1.14)	0.93
Deep vein thrombosis prophylaxis (n = 1217)	1.54 (1.22–1.95)	<0.001	1.56 (1.23–1.97)	<0.001
Cholesterol-reducing agents at discharge (n = 352)	–	–	–	–
Rehabilitation assessment (n = 5988)	1.15 (1.03–1.28)	<0.001	1.15 (1.03–1.28)	0.01
Stroke education (n = 5988)	0.80 (0.71–0.90)	<0.001	0.80 (0.71–0.90)	<0.001
Smoking cessation counseling (n = 1501)	0.70 (0.57–0.86)	0.001	0.70 (0.57–0.87)	0.001
Opportunity-based score (n = 5988)	1.00 (0.98–1.02)	0.66	0.99 (0.98–1.01)	0.61
Outcomes at discharge				
mRS ≤2 at discharge (n = 5988)	1.20 (1.08–1.33)	0.001	1.41 (1.23–1.61)	<0.001
In-hospital mortality (n = 5988)	1.31 (1.11–1.56)	0.002	1.20 (0.98–1.46)	0.10
In-hospital SAP (n = 5988)	1.06 (0.93–1.22)	0.35	0.93 (0.82–0.97)	0.01

†Patients in the underdeveloped areas were used as a reference.
‡The generalized estimation equation models adjusted for age, gender, education level, marital status, health insurance, stroke risk factors (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, coronary heart disease, history of stroke/transient ischemic attack and current smoking), stroke subtypes (subarachnoid hemorrhage and intracranial hemorrhage), admission NIH Stroke Scale score, hospital facilities (hospital grade, total beds in the hospital, academic status and equipment within emergency department, neurointensive care unit and stroke unit) and length of hospital stay.
EMS: Emergency medical system; mRS: Modified Rankin Scale; SAP: Stroke-associated pneumonia.

stroke (SAH/ICH) cohort. These benefits might be attributable to better prehospital management, in-hospital quality of care and hospital facilities in the developed areas. A positive relationship between hospital facilities, performance of care and stroke outcomes have been reported [12,37,38].

In the study, we found that the proportion of patients receiving antithrombotics within 48 h is higher than at discharge. For example, 85.1% of patients in underdeveloped areas received antithrombotics within 48 h but only 69% received them at discharge. There might be some potentials reasons:

- Antithrombotics within 48 h after onset includes the use of anticoagulation, such as low-molecular-weight heparins. After the acute phase, these medications would be stopped;
- Nonpersistence of secondary prevention medications, especially in underdeveloped areas. We have carried out an analysis for 3-month persistence of five classic secondary stroke prevention medications, namely, antiplatelet agents, warfarin (for atrial fibrillation anticoagulation), antihypertensives, statins and diabetic agents. Finally, we found that 3-month persistence was highest for diabetic medications (82.7%), followed by antiplatelet agents (80.4%) and antihypertensives (79.2%). Three-month persistence was lowest for warfarin (31.7%) and statins (62.3%) [39];
- Side effects or hemorrhagic complications that prevent the persistent use of antiplatelet agents.

The strengths of the study include a relatively large sample size, complete patient-level information (prehospital management, in-hospital quality of care and functional outcome at discharge) and verification of findings in both the ischemic (AIS/TIA) and hemorrhagic stroke (SAH/ICH) cohort. Our study has some limitations. First, like most registries, our registry required informed consent and selection bias was inevitable [40]. Patients who died before administration might not be included. Second, we used only one indicator of macroeconomic status (GRP per capita). Further studies on investigating the potential relationship between other indicators, such as gross national product per capita, total health expenditure per capita and unemployment rate, and quality of stroke care and outcomes are needed. Third, the effect of macroeconomic status on stroke care and outcomes may lag behind the economic growth itself. It is unclear whether the time-span is long enough for the effect of economic status on stroke to fully take place. Finally, the baseline characteristics of our study were different from those of western countries, such as a younger age of onset, predominance of male gender, lower severity of neurological deficit. It is difficult to explain the reasons due to many differences in study design and population. In the future, if we can do a face-to-face comparison, maybe we can find more clues to interpret this phenomenon.

Conclusion

We systematically investigated the association between macroeconomic status (GRP per capita) and prehospital management, in-hospital quality of care and stroke outcomes at discharge. Higher GRP per capita was found to be associated with better prehospital management, higher quality of in-hospital care and improved functional outcome at discharge after ischemic stroke (AIS/TIA). A similar association between macroeconomic status and prehospital management and functional outcome at discharge were found for hemorrhagic stroke (SAH/ICH). However, macroeconomic status showed less impact on in-hospital quality of care for hemorrhagic stroke.

Future perspective

Our study should encourage studies to pay more attention to the potential impact of macroeconomic status on quality of stroke care and stroke outcome. The findings might be helpful for the Chinese government to develop strategies and reallocate resources to improve stroke prevention and management throughout the country. Future studies may consider determining the financial impact of having worse outcomes in less developed areas.

Financial & competing interests disclosure

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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