Clinical characteristics, in-hospital management, and outcomes of patients with in-hospital vs. community-onset ischaemic stroke: a hospital-based cohort study

Hong-Qiu Gu,[a,b,*] Chun-Juan Wang,[a,b] Xin Yang,[a,b] Xing-Quan Zhao,[c] Yi-Long Wang,[c] Li-Ping Liu,[d] Yong Jiang,[a] Hao Li,[a] Yong-Jun Wang,[a,b,c] and Zi-Xiao Li[a,b,c,e]

[a]China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[b]National Center for Healthcare Quality Management in Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[c]Vascular Neurology, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[d]Neuro-intensive Care Unit, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[e]Chinese Institute for Brain Research, Beijing, China

The Lancet Regional Health - Western Pacific 2023;38: 100890

Published Online 31 August 2023
https://doi.org/10.1016/j.lanwpc.2023.100890

Summary

Background Lack of high-quality national-level data on in-hospital ischaemic stroke hinders the development of tailored strategies for this subgroup's identification, treatment, and management.

Methods We analyzed and compared clinical characteristics, in-hospital management measures, and outcomes, including death or discharge against medical advice (DAMA), major adverse cardiovascular events (MACEs), disability at discharge, and in-hospital complications between in-hospital and community-onset ischaemic stroke enrolled in the Chinese Stroke Center Association registry from August 2015 to December 2022.

Findings The cohort comprised 14,948 in-hospital and 1,366,898 community-onset ischaemic stroke patients. In-hospital ischaemic stroke exhibited greater stroke severity, higher prevalence of comorbidities, more pre-admission medications, and had suboptimal management measures, for example, the onset-to-needle time within 4.5 h (83.3% vs. 93.1%; difference, −9.8% [−11.4% to −8.3%]), and antithrombotics at discharge (78.6% vs. 90.0%; difference, −11.4% [95% CI, −12.1% to −10.7%]). After adjusting for covariates, in-hospital ischaemic stroke remains associated with higher risks of unfavorable outcomes, including in-hospital death/DAMA (13.9% vs. 8.6%; adjusted risk difference [aRD], 2.2% [95% CI, 1.8%–2.7%]; adjusted odds ratio [aOR], 1.35 [95% CI, 1.25–1.45]), MACE (12.6% vs. 6.5%; aRD, 4.1% [95% CI, 3.5%–4.7%]; aOR, 1.68 [95% CI, 1.52–1.85]), and complications (23.7% vs. 12.1%; aRD, 6.5% [95% CI, 5.1%–7.9%]; aOR, 1.72 [95% CI, 1.64–1.80]), except for disability at discharge (41.1% vs. 33.1%; aRD, 0.4% [95% CI, −1.7% to 2.5%]; aOR, 0.99 [95% CI, 0.88–1.11]).

Interpretation In-hospital ischaemic stroke demonstrated more severe strokes, worse vascular risk profiles, suboptimal management measures, and worse outcomes compared to community-onset ischaemic stroke. This emphasizes the urgent need for improved hospital systems of care and targeted quality improvement initiatives for better outcomes in in-hospital ischaemic stroke.

Funding National Key R&D Programme of China and Beijing Hospitals Authority.

Keywords: Acute ischaemic stroke; Health care; Health services; In-hospital; Community-onset

Introduction

In-hospital stroke refers to a stroke occurring during hospitalization for another reason. It was likely under-reported that in-hospital stroke accounts for up to 2.2%–16% of strokes.[1–5] Although the proportion is low, in-hospital stroke was reported to be more severe, poorly managed, and had worse comes than community-onset stroke.[1–5]

*Corresponding author. China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, No. 119 West Road, Southern Fourth Ring Road, Fengtai District, Beijing 100070, China.
E-mail address: guhongqiu@yeah.net (H.-Q. Gu).

Research in context

Evidence before this study

We searched PubMed to identify relevant publications published up to May 20, 2023, on characteristics, in-hospital management, and outcomes of in-hospital ischaemic stroke using the terms "In-hospital stroke" and "China" limited in the title or abstract, but without language restrictions. We identified only one small-sized study from a single center.

Added value of this study

Using a nationwide contemporary registry of patients with ischaemic stroke, we found that patients with in-hospital ischaemic stroke had more severe strokes, worse vascular risk profiles, suboptimal management during hospitalization, and worse outcomes.

Implications of all the available evidence

These findings strengthened the evidence that the development of hospital systems of care and tailored strategy are urgently warranted to improve the identification, treatment, management, and outcomes of in-hospital ischaemic stroke in China.

Reperfusion therapy, including intravenous thrombolysis (IVT)[6–8] with recombinant tissue plasminogen activator (rt-PA) and endovascular thrombectomy[9,10], is the most effective treatment for acute ischaemic stroke, but it's highly time-dependent.[11–15] In-hospital stroke has no delay in time from stroke onset to hospital arrival; however, recent surgery and medications add clinical complexities, and the lack of standardized protocols for hospital staff hampered rapid recognition and early initiation of treatment.[16] Therefore, high-quality national-level data are needed to identify potential differences and opportunities for better informing an evidence-based development of targeted quality improvement for in-hospital stroke, in addition to community-onset stroke.

In this study, we used data from the Chinese Stroke Center Alliance (CSCA) to characterize patients with in-hospital ischaemic stroke and to compare the clinical characteristics, in-hospital management, and outcomes for in-hospital vs. community-onset ischaemic stroke at a national level registry. We hypothesised that in-hospital ischaemic stroke would have more severe strokes, worse vascular risk profiles, suboptimal management measures, and worse outcomes than community-onset ischaemic stroke.

Methods

This report followed the Standards for The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[17] The data that support the findings of this study are available from the corresponding author upon reasonable request.

The Chinese Stroke Center Alliance

We performed a cohort analysis of CSCA, a national, hospital-based, voluntary, and continuous quality improvement initiative modeled after the American Heart Association's Get With The Guidelines-Stroke (GWTG Stroke) program. Patients aged 18 years or older who had a primary diagnosis of stroke or transient ischemic attack within 7 days of symptom onset were enrolled. The details of the program have been previously described.[17,18] The China National Clinical Research Center for Neurological Diseases serves as the data analysis center and analyses the aggregate de-identified data. Informed consent of individual patients was waived by the ethics committee of Beijing Tiantan Hospital and local hospitals.

Study population

We extracted data on patients enrolled between August 1st, 2015 and December 10th, 2022. For robust estimations, hospitals with a total enrollment of less than 100 patients were excluded first. For the current analyses, we excluded patients transferred from other hospitals, clinic-onset stroke, or unknown location of symptom-onset and limited our study population to patients with in-hospital or community-onset ischaemic stroke, as we focus on the comparison of the two subgroups. Ischaemic stroke was defined as a new onset of focal neurological deficit that cannot be attributed to the presenting lesion and is confirmed with radiographic evidence (CT and/or MRI).[17]

Study variables

Clinical characteristics, including demographics (age, sex, body mass index), smoking and drinking status, the National Institutes of Health Stroke Scale (NIHSS) score, medical history (stroke or transient ischaemic attack [TIA], carotid stenosis, atrial fibrillation, coronary heart disease [CHD], myocardial infarction [MI], heart failure, hypertension, diabetes, dyslipidemia, and peripheral vascular disease [PVD]), and medication usage within 6 months prior to the index stroke and lasting more than 2 weeks (antiplatelet, antihypertensive, hypoglycemic, and statin), were abstracted from chart review by trained researchers.

In-hospital management measures, consisting of nine acute and five discharge management measures, were developed based on the Get with The Guidelines-Stroke (GWTG-Stroke),[19] nationally recommended guidelines,[20] and updated according to quality measures for neurological diseases in 2020.[21] The nine acute

management measures included: (1) intravenous tissue-type plasminogen activator (IV rt-PA) in patients who arrived within 3.5 h after symptom onset and were treated within 4.5 h; (2) onset-to-needle time with 4.5 h for patients received IV rt-PA; (3) endovascular treatment; (4) antithrombotic medication within 48 h of admission; (5) dual antiplatelet for minor stroke; (6) deep vein thrombosis prophylaxis; (7) dysphagia screen; (8) rehabilitation assessment; and (9) vessel assessment. The five discharge management measures included: (1) antithrombotic medication; (2) anticoagulants for atrial fibrillation; (3) antihypertensive medication for hypertension; (4) hypoglycemia medication for diabetes mellitus; (5) Statin for lowering low-density lipoprotein (LDL) for LDL levels ≥100 mg/dl or not documented. Detailed definitions of these management measures are shown in Supplementary Table S1 in the Data Supplement.

In-hospital outcomes, including death or discharge against medical advice (DAMA), major adverse cardiovascular events (MACE), disability at discharge, and complications, were recorded during admission to a neurological ward to discharge in this study. We used the composite outcome of in-hospital death or DAMA because it is common for many patients to withdraw from treatment at unfavorable or terminal status in China.[22] MACE is a composite outcome comprising ischaemic stroke, hemorrhagic stroke, TIA, or MI. It includes any subsequent occurrence of ischemic stroke, hemorrhagic stroke, TIA, or MI that takes place after the initial stroke event and during admission to a neurological ward until discharge. Disability at discharge was measured by the modified Rankin Scale (mRS). The score ranges from 0 (no disability) to 6 (death). An mRS score of 3 or greater was defined as having a disability. Complications included deep vein thrombosis, pneumonia, pulmonary embolism, epileptic seizure, hydrocephalus, urinary infection, respiratory failure or cardiopulmonary arrest, bedsore/decubitus ulcer, depression, and gastrointestinal bleeding at discharge. Complications were identified and recorded by local physicians.

Statistical analysis

Data were summarized by means and standard deviations, or medians (interquartile ranges) for continuous variables, and frequencies along with percentages for categorical variables. Differences between in-hospital stroke and community-onset stroke and the 95% confidence intervals were estimated by risk differences based on binomial proportions for categorical variables and Hodges-Lehmann's estimation of location shift for continuous variables.

We reported the absolute effect measure risk differences (RD) and 95% confidence intervals estimated from binomial regression models with the link function set to identify to assess the differences in in-hospital outcomes between in-hospital and community-onset ischaemic stroke. In addition, we also reported relative effect size in terms of odds ratios (OR) and 95% confidence intervals from logistic regression models, as some of the in-hospital outcome measures were at very low levels. We additionally performed subgroup analyses to assess the influence of sex, smoking status, history of diseases (such as stroke, atrial fibrillation, coronary heart disease/heart attack, heart failure, and diabetes), and hospital level on in-hospital death/DAMA, MACE, disability at discharge, and in-hospital complications. All models for in-hospital outcomes were fitted with general estimation equations and adjusted for the NIHSS score at admission, sex, smoking status, medical history (stroke/TIA, atrial fibrillation, CHD/MI, heart failure, diabetes, and dyslipidemia), medication history (antiplatelet, glucose-lowering, and statin), and hospital level, taking into account the clustering effect of patients within the same hospital. The list of adjusted variables and subgroups was determined by a comprehensive consideration of unbalanced variables in Table 1 and insights from the literature review.

The NIHSS score at admission was missing for 10.5% of participants; therefore, we first reported the adjusted results based on complete data and then on pooled results of five complete datasets generated by multiple imputations according to Rubin's rules.[23] The imputation models included all baseline covariates shown in Table 1. The outcome variable DAMA was missing approximately 12%. We did not impute DAMA and analyzed it based on complete data to avoid introducing a new bias.

Given the changing landscape of reperfusion therapy in the endovascular therapy era, we further re-fitted our models with data limited to patients who received reperfusion therapy. The covariates adjusted for were the NIHSS score at admission, sex, smoking status, drinking, medical history (stroke/TIA, atrial fibrillation, CHD/MI, heart failure, diabetes, and dyslipidemia), and medication usage (antiplatelet, antihypertension, glucose-lowering, and statin). The adjusted variable list was determined by carefully considering unbalanced covariates and the insights from literature review.

All statistical analyses were performed using SAS statistical software version 9.4 (SAS Institute Inc.). We used an SAS macro named %ggBaseline to generate the descriptive tables automatically.[24]

Ethics statement

The study was approved by the ethics committee of Beijing Tiantan Hospital (KY2018-061-02). Written informed consent was waived by the ethics committee.

Role of the funding source

The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Variables	In-hospital stroke (n = 14,948 [1.1%])	Community-onset stroke (n = 1,366,898 [98.9%])	Difference (95% CI)
Patient characteristics			
Demographic			
Age, mean (SD), y	67.6 (12.3)	66.3 (12.0)	1.3 (1.1–1.5)
Male	8818 (59.0)	856,964 (62.7)	−3.7 (−4.5 to −2.9)
BMI, mean (SD), y	24.0 (6.2)	24.0 (4.1)	0.0 (−0.1 to 0.1)
Smoker	4914 (32.9)	489,982 (35.8)	−3.0 (−3.7 to −2.2)
Drinking	3052 (20.4)	308,421 (22.6)	−2.1 (−2.8 to −1.5)
NIHSS at admission	4.0 (2.0–9.0)	3.0 (2.0–6.0)	1.0 (0.0–2.0)
Medical history			
Stroke/TIA	6035 (40.4)	444,182 (32.5)	7.9 (7.1–8.7)
Carotid stenosis	404 (2.7)	17,206 (1.3)	1.4 (1.2–1.7)
Atrial fib/flutter	1489 (10.0)	69,182 (5.1)	4.9 (4.4–5.4)
CHD/MI	1431 (9.6)	80,904 (5.9)	3.7 (3.2–4.1)
Heart failure	676 (4.5)	14,658 (1.1)	3.4 (3.1–3.8)
Hypertension	9381 (62.8)	879,104 (64.3)	−1.6 (−2.3 to −0.8)
Diabetes mellitus	3754 (25.1)	298,438 (21.8)	3.3 (2.6–4.0)
Dyslipidemia	1693 (11.3)	92,631 (6.8)	4.5 (4.0–5.1)
PVD	584 (3.9)	19,587 (1.4)	2.5 (2.2–2.8)
Medication history			
Antiplatelet medication	4601 (30.8)	271,382 (19.9)	10.9 (10.2–11.7)
Antihypertension medication	7360 (49.2)	647,850 (47.4)	1.8 (1.0–2.6)
Glucose-lowering medication	3046 (20.4)	236,709 (17.3)	3.1 (2.4–3.7)
Statin	3878 (25.9)	217,022 (15.9)	10.1 (9.4–10.8)
Hospital characteristic			
Hospital level			
Secondary	5476 (36.6)	603,971 (44.2)	−7.6 (−8.3 to −6.8)
Tertiary	9472 (63.4)	762,927 (55.8)	7.6 (6.8–8.3)

BMI, body mass index; SD, standard deviation; NIHSS, the National Institutes of Health Stroke Scale; TIA, transient ischemic attack; CHD/MI, coronary heart disease or myocardial infarction; PVD, peripheral vascular disease.

Table 1: **Clinical characteristics of patients with in-hospital vs. community-onset ischemic stroke.**

Results

A total of 1,946,254 patients with stroke/TIA were enrolled in CSCA between August 1st, 2015 and December 10th, 2022. After exclusion, we obtained 1,381,846 patients included in the current analyses, of whom 14,948 (1.1%) were in-hospital and 1,366,898 (98.9%) were community-onset ischaemic stroke (Fig. 1). Patients included in the current analysis and excluded for the missing value of symptom onset location were largely comparable, except that the former had a higher percentage of patients admitted to secondary hospitals (Supplementary Table S2 in the Data Supplement). Characteristics among patients who received reperfusion therapy were presented in Supplementary Table S3 in the Data Supplement.

Clinical characteristics

Compared with patients with community-onset stroke, patients with in-hospital ischaemic stroke exhibited some notable differences. They had a lower proportion of male patients (59.0% vs. 62.7%; difference, −3.7% [95% CI, −4.5% to −2.9%]), fewer smokers (32.9% vs. 35.8%, difference, −3.0% [95% CI, −3.7% to −2.2%]). Additionally, the severity of stroke was higher in the in-hospital group, as indicated by a higher NIHSS score (4.0 [IQR: 2.0–9.0] vs. 3.0 [IQR: 2.0–6.0]). Furthermore, patients with in-hospital ischemic stroke presented a higher prevalence of prior stroke/TIA (40.4% vs. 32.5%; difference, 7.9% [95% CI, 7.1%–8.7%]), atrial fibrillation (10.0% vs. 5.1%; difference, 4.9% [95% CI, 4.4%–5.4%]), CHD/MI (9.6% vs. 5.9%; difference, 3.7% [95% CI, 3.2%–4.1%]), heart failure (4.5% vs. 1.1%; difference, 3.4% [95% CI, 3.1%–3.8%]), diabetes (25.1% vs. 21.8%; difference, 3.3% [95% CI, 2.6%–4.0%]) and dyslipidemia (11.3% vs. 6.8%, difference, 4.5% [95% CI, 4.0%–5.1%]). Medication before index stroke was also different between the two groups, with higher prescription rates observed among patients with in-hospital ischemic stroke for antiplatelet (30.8% vs. 19.9%; difference, 10.9% [95% CI, 10.2%–11.7%]), glucose-lowering medication (20.4% vs. 17.3%; difference, 3.1% [95% CI, 2.4%–3.7%]), and statin (25.9% vs. 15.9%; difference, 10.1% [95% CI, 9.4%–10.8%]). In addition, a higher percentage of patients with in-hospital

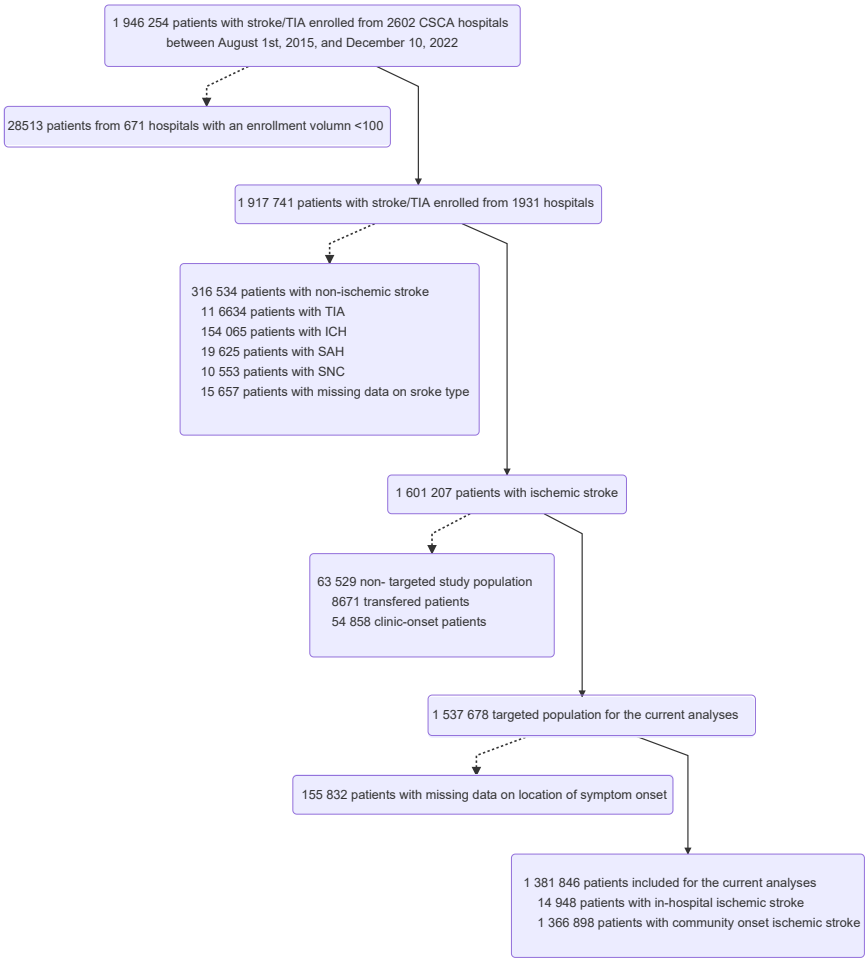

Fig. 1: Patient identification chart. CSCA, the Chinese Stroke Center Alliance; TIA, transient ischemic attack; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; SNC, stroke not classified.

ischaemic stroke were admitted to tertiary hospitals than those with community-onset stroke (63.4% vs. 55.8%; difference, 7.6% [95% CI, 6.8%–8.3%]). However, other characteristics were largely comparable (Table 1).

In-hospital management measures

Compared with community-onset ischaemic stroke, those with in-hospital ischaemic stroke showed worse acute management measures. This included a delay in onset-to-needle time within 4.5 h (83.3% vs. 93.1%; difference, –9.8% [–11.4% to –8.3%]), lower usage of early antithrombotics (73.5% vs. 87.8%; difference, –14.3% [95% CI, –15.0% to –13.5%]) and dual antiplatelets for minor stroke (31.2% vs. 43.9%; difference, –12.8% [95% CI, –13.8% to –11.7%]). Additionally, they were more poorly managed for dysphagia screen (73.3% vs. 82.4%; difference, –9.1% [95% CI, –9.8% to –8.4%]) and vessel assessment (85.8% vs. 90.8%; difference, –4.9% [95% CI, –5.5% to –4.4%]). However, they exhibited slightly better performance in endovascular treatment (4.2% vs. 1.3%; difference 2.9% [95% CI, 2.6%–3.2%]). Furthermore, patients with in-hospital ischaemic stroke also had worse discharge management measures in antithrombotics (78.6% vs. 90.0%; difference, –11.4% [95% CI, –12.1% to –10.7%]), antihypertensive medication for hypertension (62.4% vs. 66.4%; difference, –4.0% [95% CI, –4.9% to –3.0%]), hypoglycemia medication for diabetes (76.0% vs. 79.3%; difference, –3.4% [95% CI, –4.7% to –2.1%]) and statin for lowering low-density lipoprotein (84.9% vs. 91.8%; difference, –6.9% [95% CI, –7.5% to –6.3%]) prescription at discharge. The only exception was the prescription of anticoagulants for atrial fibrillation, which had a slightly higher percentage for in-hospital ischaemic stroke (49.9% vs. 46.3%; difference, 3.6% [95% CI, 1.1%–6.1%]) (Table 2).

In-hospital outcomes

Patients with in-hospital ischaemic stroke showed a higher crude rate of in-hospital death/DAMA (13.9% vs.

Variables	No./Total no. (%)		Difference (95% CI)
	In-hospital stroke	Community-onset stroke	
Acute management measures			
IV rt-PA ≤ 4.5 h	1326/4373 (30.3)	98,530/331,096 (29.8)	0.6 (−0.8 to 1.9)
Onset-to-needle time ≤4.5 h	1907/2290 (83.3)	101,471/108,963 (93.1)	−9.8 (−11.4 to −8.3)
Endovascular treatment	627/14,948 (4.2)	18,000/1,366,898 (1.3)	2.9 (2.6–3.2)
Early antithrombotics	10,409/14,159 (73.5)	1,178,548/1,342,568 (87.8)	−14.3 (−15.0 to −13.5)
Dual antiplatelets for minor stroke	2465/7910 (31.2)	362,900/826,328 (43.9)	−12.8 (−13.8 to −11.7)
DVT prophylaxis	1350/6655 (20.3)	72,431/411,345 (17.6)	2.7 (1.7–3.7)
Dysphagia screen	10,961/14,948 (73.3)	1,126,483/1,366,898 (82.4)	−9.1 (−9.8 to −8.4)
Rehabilitation assessment	10,915/14,948 (73.0)	1,003,586/1,366,898 (73.4)	−0.4 (−1.1 to 0.3)
Vessel assessment	12,830/14,948 (85.8)	1,240,837/1,366,898 (90.8)	−4.9 (−5.5 to −4.4)
Discharge management measures			
Antithrombotics	10,505/13,361 (78.6)	1,173,097/1,303,465 (90.0)	−11.4 (−12.1 to −10.7)
Anticoagulants for atrial fibrillation	808/1619 (49.9)	41,101/88,769 (46.3)	3.6 (1.1–6.1)
Antihypertensive medication for hypertension	6473/10,369 (62.4)	674,372/1,015,589 (66.4)	−4.0 (−4.9 to −3.0)
Hypoglycemia medication for diabetes	3270/4304 (76.0)	296,561/373,769 (79.3)	−3.4 (−4.7 to −2.1)
Statin for lowering low-density lipoprotein	11,783/13,884 (84.9)	1,216,185/1,324,766 (91.8)	−6.9 (−7.5 to −6.3)

IV rt-PA, intravenous recombinant tissue plasminogen activator; DVT, deep vein thrombosis.

Table 2: **Management measures of patients with in-hospital vs. community-onset ischemic stroke.**

8.6%), MACE (12.6% vs. 6.5%), disability at discharge (41.1% vs. 33.1%), and complications (23.7% vs. 12.1%) than those with community-onset ischaemic stroke. After adjusting for covariates, In-hospital ischaemic stroke remains independently associated with a higher risk of all the above-mentioned composite outcomes, including in-hospital death/DAMA (the NIHSS score imputation-based adjusted risk difference [aRD], 2.2% [95% CI, 1.8%–2.7%]; adjusted odds ratio [aOR], 1.35 [95% CI, 1.25–1.45]), MACE (aRD, 4.1% [95% CI, 3.5%–4.7%]; aOR, 1.68 [95% CI, 1.52–1.85]), and complications (aRD, 6.5% [95% CI, 5.1%–7.9%]; aOR, 1.72 [95% CI, 1.64–1.80]), except for disability at discharge (aRD, 0.4% [95% CI, −1.7% to 2.5%]; aOR, 0.99 [95% CI, 0.88–1.11]).

The data also revealed that in-hospital ischaemic stroke was significantly associated with increased odds of all the components of the above-mentioned composite outcomes, including in-hospital death (aOR, 1.51 [95% CI, 1.40–1.62]), DAMA (aOR, 1.24 [95% CI, 1.10–1.38]), cerebral infarction (aOR, 1.46 [95% CI, 1.33–1.58]), cerebral hemorrhage (aOR, 1.91 [95% CI, 1.71–2.11]), TIA (aOR, 3.98 [95% CI, 3.41–4.55]), myocardial infarction (aOR, 2.50 [95% CI, 2.22–2.78]), and all the individual component of in-hospital complications, although the absolute risk differences were small. The most notable complication was pneumonia (16.9% vs. 8.5%; aRD, 4.7% [95% CI, 3.2%–6.2%]; aOR, 1.62 [95% CI, 1.54–1.70]) (Fig. 2). Both crude analysis and adjusted analysis without adjustment of the NIHSS score yield similar results, except for disability at discharge (Supplementary Table S4 in the Data Supplement).

In-hospital outcomes among subgroups

The results from the subgroup analyses did indicate some degree of heterogeneity in relation to smoking status, disease history (stroke, heart failure, and diabetes), and hospital levels (Supplementary Tables S5–S8 in the Data Supplement). Regarding patients who underwent reperfusion therapy, they exhibited higher crude rates of in-hospital outcomes when compared to the overall population. The disparities in in-hospital outcomes between in-hospital and community-onset ischaemic stroke among this group resemble those observed in the overall population (Fig. 3). This included in-hospital death/DAMA (20.5% vs. 14.1%; aRD, 2.8% [95% CI, 1.2%–4.5%]; aOR, 1.31 [95% CI, 1.19–1.43]), MACE (14.6% vs. 8.6%; aRD, 4.2% [95% CI, 2.8%–5.5%]; aOR, 1.51 [95% CI, 1.38–1.64]), disability at discharge (49.0% vs. 42.8%; aRD, 0.8% [95% CI, −1.2% to 2.8%]; aOR, 1.04 [95% CI, 0.94–1.14]), and complications (30.4% vs. 18.9%; aRD, 5.9% [95% CI, 4.9%–7.0%]; aOR, 1.55 [95% CI, 1.44–1.65]). Comparable results were obtained from both crude analyses and adjusted analyses without adjustment of the NIHSS score, except for disability at discharge (Supplementary Table S9 in the Data Supplement).

Discussion

Using a nationwide contemporary registry of patients with ischaemic stroke, we found that patients with in-hospital ischaemic stroke were more severe, had higher prevalences of comorbidities, and were suboptimal in management measures during hospitalization for the in-hospital delay, medication prescription,

In-hospital Outcomes	No. event (%) or No. event/Total (%)		Adjusted Analysis¶		Adjusted Analysis with multiple imputations of the NIHSS score¶	
	In-Hospital Stroke	Community-Onset Stroke	RD (95% CI)	OR (95% CI)	RD (95% CI)	OR (95% CI)
In-hospital death/DAMA*	1752/12 600 (13.9)	102 853/1 202 293 (8.6)	2.0 (1.4 to 2.6)	1.32 (1.18-1.47)	2.2 (1.8 to 2.7)	1.35 (1.25-1.45)
In-hospital death	847 (5.7)	34 796 (2.5)	1.0 (0.3 to 1.8)	1.49 (1.33-1.67)	1.0 (0.6 to 1.5)	1.51 (1.40-1.62)
DAMA †	905/11 753 (7.7)	68 057/1 167 497 (5.8)	1.1 (0.6 to 1.6)	1.21 (1.04-1.41)	1.3 (0.6 to 2.0)	1.24 (1.10-1.38)
In-hospital MACE	1884 (12.6)	88 689 (6.5)	4.2 (2.1 to 6.3)	1.70 (1.42-2.04)	4.1 (3.5 to 4.7)	1.68 (1.52-1.85)
Cerebral infarction	1341 (9.0)	72 046 (5.3)	1.7 (1.2 to 2.2)	1.44 (1.27-1.63)	2.1 (1.6 to 2.5)	1.46 (1.33-1.58)
Cerebral hemorrhage	360 (2.4)	11 902 (0.9)	0.8 (0.4 to 1.2)	1.89 (1.52-2.36)	1.1 (0.5 to 1.7)	1.91 (1.71-2.11)
TIA	408 (2.7)	8184 (0.6)	2.9 (2.4 to 3.3)	4.51 (2.42-8.40)	2.6 (2.2 to 3.0)	3.98 (3.41-4.55)
Myocardial infarction	222 (1.5)	5123 (0.4)	0.5 (0.2 to 0.8)	2.48 (1.81-3.41)	1.1 (0.6 to 1.6))	2.50 (2.22-2.78)
Disability at discharge ‡	3548/8632 (41.1)	284 524/858 355 (33.1)	-0.1 (-0.1 to -0.1)	0.97 (0.86-1.10)	0.4 (-1.7 to 2.5)	0.99 (0.88-1.11)
In-hospital Complications	3538 (23.7)	165 572 (12.1)	6.7 (5.4 to 8.1)	1.71 (1.57-1.86)	6.5 (5.1 to 7.9)	1.72 (1.64-1.80)
Deep vein thrombosis	385 (2.6)	14 008 (1.0)	1.1 (0.6 to 1.6)	1.92 (1.55-2.38)	1.3 (0.9 to 1.8)	1.96 (1.76-2.16)
Pneumonia	2522 (16.9)	116 616 (8.5)	4.0 (3.0 to 5.0)	1.59 (1.46-1.74)	4.7 (3.2 to 6.2)	1.62 (1.54-1.70)
Pulmonary embolism	122 (0.8)	2753 (0.2)	0.5 (0.1 to 0.9)	3.22 (1.86-5.59)	1.1 (0.7 to 1.5)	3.22 (2.74-3.71)
Epileptic Seizure	222 (1.5)	6914 (0.5)	1.0 (0.6 to 1.3)	2.07 (1.49-2.89)	0.8 (0.4 to 1.4)	2.08 (1.79-2.37)
Hydrocephalus	94 (0.6)	2408 (0.2)	0.3 (-0.0 to 0.7)	2.56 (1.37-4.79)	0.7 (0.2 to 1.3)	2.51 (1.94-3.07)
Urinary infection	446 (3.0)	16 008 (1.2)	1.3 (0.8 to 1.7)	1.93 (1.60-2.33)	1.4 (0.9 to 1.9)	1.90 (1.72-2.07)
Respiratory failure	221 (1.5)	4419 (0.3)	1.2 (1.0 to 1.3)	2.91 (2.08-4.08)	0.9 (0.3 to 1.4)	2.70 (2.38-3.02)
Bedsore	169 (1.1)	4105 (0.3)	1.1 (0.6 to 1.6)	2.29 (1.46-3.61)	0.7 (0.2 to 1.3)	2.38 (1.99-2.77)
Depression	347 (2.3)	17 070 (1.2)	0.7 (0.2 to 1.2)	1.54 (1.22-1.94)	0.9 (0.5 to 1.2)	1.54 (1.33-1.75)
Gastrointestinal bleeding	411 (2.7)	12 185 (0.9)	1.3 (0.9 to 1.8)	2.19 (1.80-2.66)	1.5 (0.9 to 2.1)	2.19 (2.02-2.37)

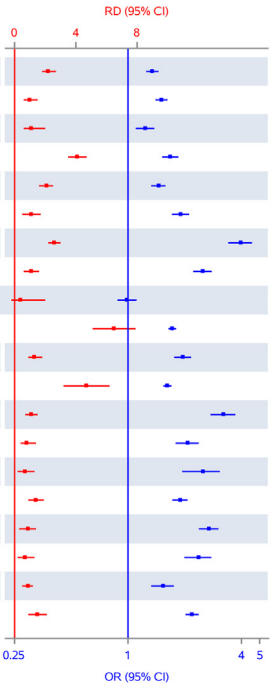

Fig. 2: In-hospital outcomes of patients with in-hospital vs. community-onset ischemic stroke. DAMA, discharge against medical advice; MACE, major adverse cardiovascular events; TIA, transient ischemic attack; NIHSS, the National Institutes of Health Stroke Scale. *Data were missing for 2348 (15.7%) in-hospital and 164,605 (12.0%) community-onset ischemic strokes, respectively. †Data were assessed among survivals, and missing for 2348 (16.7%) in-hospital and 164,605 (12.4%) community-onset ischemic strokes, respectively. ‡Data were available from July 1, 2018. ¶Adjusted for the NIHSS score at admission, sex, smoking status, medical history (stroke or transient ischemic attack, atrial fibrillation, coronary heart disease or myocardial infarction, heart failure, diabetes, and dyslipidemia), medication history (antiplatelet, glucose-lowering, and statin), and hospital level.

screening, and vessel assessments, compared with patients with community-onset ischaemic stroke. After covariates adjustment, in-hospital ischaemic stroke remains associated with a higher risk of unfavorable outcomes, including in-hospital death/DAMA, MACE, and complications, except for disability at discharge. Collectively, these findings strengthened the evidence that the development of hospital systems of care and tailored strategy are urgently warranted to improve the identification, treatment, management, and outcomes of in-hospital ischaemic stroke in China.

Consistent with our study, previous reports from the Multicenter Stroke Investigators' Collaboration registry in Japan,[1] the National Get With The Guidelines-Stroke registry in US,[2] the Ontario Stroke Registry in Canada,[3] and the South London Stroke Register[5] also reported that patients with in-hospital ischaemic stroke had a higher prevalence of comorbid illnesses, including atrial fibrillation, carotid stenosis, CHD/MI, diabetes mellitus, or heart failure, experienced more severe strokes, and had worse outcomes in terms of in-hospital death or discharge home. Data from three of these registries also revealed that, compared with community-onset stroke, in-hospital stroke also had longer in-hospital delays or was more poorly managed during hospitalization.[2,3,5] In addition, a single-center study in China showed that in-hospital stroke was associated with higher NIHSS scores, more endovascular therapy, and a higher rate of in-hospital death.[4] Results from patients who received reperfusion therapy in the Get With the Guidelines–Stroke draw similar conclusions to our analyses.[25,26]

In contrast to previous reports,[2–4,25] we found that in-hospital ischaemic strokes were not independently associated with disability at discharge. Results from crude analyses and adjusted analyses without adjustment of the NISHS score at admission showed that in-hospital ischaemic strokes were associated with increased odds of disability at discharge; however, the association was disappeared after adding the NIHSS score at admission in the adjusted models, which indicated that functional disability at discharge might be mainly explained by stroke severity at admission measured by the NIHSS score. The risk differences and odds ratios of in-hospital outcomes vs. community-onset strokes for other in-hospital outcomes, including in-hospital death/DAMA, MACE, and complications, were shrunk but remained significant after the adjustment of the NIHSS score and other potential

In-hospital outcomes	No. event (%) or No. event/Total (%)		Adjusted Analysis¶		Adjusted Analysis with multiple imputations of the NIHSS score¶	
	In-Hospital Stroke	Community-Onset Stroke	RD (95% CI)	OR (95% CI)	RD (95% CI)	OR (95% CI)
In-hospital death/DAMA*	522/2550 (20.5)	16 052/113 571 (14.1)	2.8 (1.4 to 4.3)	1.27 (1.12-1.45)	2.8 (1.2 to 4.5)	1.31 (1.19-1.43)
In-hospital death	335 (12.2)	8549 (7.1)	2.2 (0.5 to 4.0)	1.42 (1.23-1.64)	2.3 (0.6 to 4.0)	1.44 (1.30-1.58)
DAMA †	187/2215 (8.4)	7503/105 022 (7.1)	0.7 (-0.7 to 2.0)	1.08 (0.89-1.32)	1.0 (-0.3 to 2.2)	1.13 (0.95-1.31)
In-hospital MACE	401 (14.6)	10 432 (8.6)	4.0 (2.4 to 5.5)	1.48 (1.30-1.69)	4.2 (2.8 to 5.5)	1.51 (1.38-1.64)
Cerebral infarction	208 (7.6)	5756 (4.8)	1.6 (0.7 to 2.4)	1.32 (1.12-1.56)	1.7 (0.9 to 2.6)	1.37 (1.21-1.54)
Cerebral hemorrhage	155 (5.6)	4297 (3.5)	0.9 (0.1 to 1.7)	1.28 (1.06-1.55)	1.1 (-0.3 to 2.4)	1.29 (1.10-1.48)
TIA	73 (2.7)	840 (0.7)	0.9 (0.2 to 1.6)	3.88 (2.86-5.28)	2.0 (0.9 to 3.2).	3.82 (3.52-4.12)
Myocardial infarction	47 (1.7)	655 (0.5)	2.1 (1.0 to 3.2)	2.05 (1.45-2.91)	1.1 (0.0 to 2.2)	2.05 (1.70-2.40)
Disability at discharge ‡	1023/2088 (49.0)	38 941/91 064 (42.8)	0.9 (0.9 to 0.9)	1.04 (0.94-1.15)	0.8 (-1.2 to 2.8)	1.04 (0.94-1.14)
In-hospital Complications	836 (30.4)	22 878 (18.9)	7.0 (5.2 to 8.8)	1.52 (1.36-1.69)	5.9 (4.9 to 7.0)	1.55 (1.44-1.65)
Deep vein thrombosis	70 (2.5)	2113 (1.7)	0.1 (-0.4 to 0.6)	1.14 (0.87-1.50)	0.4 (-0.6 to 1.3)	1.22 (0.95-1.49)
Pneumonia	657 (23.9)	17 351 (14.3)	5.8 (4.2 to 7.5)	1.51 (1.34-1.71)	4.8 (3.1 to 6.2)	1.54 (1.42-1.66)
Pulmonary embolism	24 (0.9)	300 (0.2)	0.8 (-0.2 to 1.8)	2.58 (1.64-4.06)	0.8 (-0.2 to 2.0)	2.60 (2.17-3.02)
Epileptic Seizure	44 (1.6)	794 (0.7)	0.9 (-0.1 to 1.9)	1.85 (1.31-2.62)	0.9 (-0.2 to 2.0)	1.92 (1.59-2.26)
Hydrocephalus	21 (0.8)	416 (0.3)	0.7 (-0.4 to 1.7)	1.68 (1.09-2.59)	0.7 (0.2 to 1.3)	2.51 (1.94-3.07)
Urinary infection	76 (2.8)	1830 (1.5)	0.7 (0.0 to 1.3)	1.42 (1.10-1.83)	1.4 (0.9 to 1.9)	1.90 (1.72-2.07)
Respiratory failure	72 (2.6)	1210 (1.0)	1.3 (0.2 to 2.4)	1.81 (1.37-2.39)	0.9 (0.3 to 1.4)	2.70 (2.38-3.02)
Bedsore	22 (0.8)	435 (0.4)	0.5 (-0.7 to 1.7)	1.57 (1.01-2.46)	0.8 (0.2 to 1.3)	2.38 (1.99-2.77)
Depression	61 (2.2)	1820 (1.5)	0.5 (-0.1 to 1.0)	1.33 (0.94-1.87)	0.9(0.5 to 1.2)	1.54 (1.33-1.75)
Gastrointestinal bleeding	69 (2.5)	2159 (1.8)	0.4 (-0.6 to 1.3)	1.11 (0.85-1.45)	1.5 (0.9 to 2.1)	2.19 (2.02-2.37)

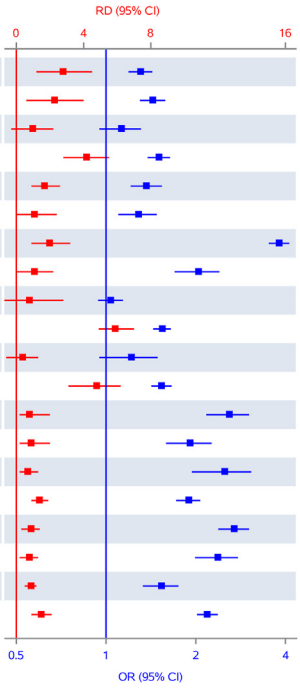

Fig. 3: In-hospital outcomes of patients with in-hospital vs. community-onset ischemic stroke who received endovascular thrombectomy. DAMA, discharge against medical advice; MACE, major adverse cardiovascular events; TIA, transient ischemic attack. *Data were missing for 201 (7.3%) in-hospital and 7537 (6.2%) community-onset ischemic strokes, respectively. †Data were assessed among survivals, and missing for 201 (8.3%) in-hospital and 7537 (6.7%) community-onset ischemic strokes, respectively. ‡Data were available from July 1, 2018. ¶Adjusted for the NIHSS score at admission, sex, smoking status, drinking, medical history (stroke or transient ischemic attack, atrial fibrillation, coronary heart disease or myocardial infarction, heart failure, diabetes, and dyslipidemia), and medication usage (antiplatelet, antihypertension, glucose-lowering, and statin).

cardiovascular risk factors, which indicated that other confounders were not controlled, or in-hospital strokes might have different etiologies or mechanisms, such as perioperative or cardioembolic stroke.[27,28] Therefore, differences in baseline characteristics may account for differences in care and outcomes, and the solutions would depend on the underlying causes of differences, and the development of hospital systems of care and targeted quality improvement for in-hospital stroke are urgently needed and advocated.[16]

To the best of our knowledge, this might be the largest sample-sized, multi-center registry study to characterize the clinical characteristics, in-hospital management, and outcomes of in-hospital ischaemic stroke during hospitalization in China and to compare them with community-onset ischaemic stroke. However, this study has several limitations. First, the clinical department before index stroke for in-hospital stroke and the etiology based on a Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification were not collected, which hampered the mechanism exploration and comparison for subtypes of in-hospital strokes. Second, data on the NIHSS score at admission were missing for 10.5% of the patients, which may introduce bias for the estimation of effect sizes. However, results from adjusted analyses based on complete data and multiple imputed data showed consistent results, indicating our estimations are robust. Nevertheless, the results would be interpreted with caution, since no methods can confirm that the NIHSS scores were missing at random. Third, insufficient data were collected for the determination of indications for endovascular treatments; therefore, we assessed endovascular treatments among all the included participants. Forth, approximately 12% of patients were missing on DAMA, and mRs at discharge were not collected until July 1, 2018, which reduced our sample size and may introduce bias. Fifth, outcomes after discharge and long-term follow-up outcomes were not collected in CSCA; therefore, we only assessed in-hospital outcomes in the current analyses. Sixth, complications were diagnosed and recorded by local physicians, resulting in inevitable variations in definitions and identifications. However, this approach remains practical and acceptable for a large registry.

Conclusions

Compared with community-onset ischaemic stroke, in-hospital ischaemic stroke had more severe strokes, worse vascular risk profiles, suboptimal management measures during hospitalization, and worse outcomes. In addition, disparities in outcomes between in-hospital ischaemic stroke and community-onset ischaemic stroke persist even if reperfusion therapy were administrated. These data highlight the urgent need to develop hospital systems of care and targeted quality improvement to improve outcomes of in-hospital ischaemic stroke further.

Contributors

HQG, ZXL, and YJW conceptualised and designed the study. CJW, XY, and YJ collected the data. HQG drafted the manuscript, analysed, and interpreted the data. HQG analysed the data. HQG and ZXL verified the underlying data. XQZ, YLW, LPL, ZXL, HL, and YJW interpreted the data and revised the manuscript. All authors commented upon and approved the final manuscript.

Data sharing statement

The data used for this analysis can be made available upon reasonable request to the corresponding authors.

Declaration of interests

All authors declare no competing interests.

Acknowledgements

We thank all the participating hospitals for their valuable contributions.

Funding: This work was supported by grant 2022YFC2504902 (ZXL) from the Ministry of Science and Technology of the People's Republic of China (National Key R&D Programme of China), grant 72004146 (HQG) from the National Natural Science Foundation of China, grant PX2021024 (HQG), and QML20210501 (HQG) from Beijing Hospitals Authority.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100890.

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