

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



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## 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.

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**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 is likely underreported that in-hospital stroke accounts for

2.2%–16% of strokes.<sup>1–5</sup> Although the proportion is low, in-hospital stroke is reported to be more severe, poorly managed, and had worse outcomes than community-onset stroke.<sup>1–5</sup>

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### 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)<sup>6–8</sup> with recombinant tissue plasminogen activator (rt-PA) and endovascular thrombectomy<sup>9,10</sup>, is the most effective treatment for acute ischaemic stroke, but it's highly time-dependent.<sup>11–15</sup> 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.<sup>16</sup> 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 Reporting of Observational Studies in Epidemiology (STROBE) statement.<sup>17</sup> 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 ischaemic attack within 7 days of symptom onset were

enrolled. The details of the program have been previously described.<sup>17,18</sup> 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 obtained 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 overall 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).<sup>17</sup>

#### 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, hypoglycaemic, 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),<sup>19</sup> nationally recommended guidelines,<sup>20</sup> and updated according to quality measures for neurological diseases in 2020.<sup>21</sup> The nine acute

management measures included: (1) intravenous tissue 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 within 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) delirium assessment. The final 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  $\geq 100$  mg/dl or not documented. Detailed definitions of these management measures are shown in [Supplementar 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 or 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 infeasible or terminal status in China.<sup>22</sup> 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

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| Variables                      | In-hospital stroke<br>(n = 14,948 [1.1%]) | Community-onset stroke<br>(n = 1,366,898 [98.9%]) | Difference (95% CI) |
|--------------------------------|-------------------------------------------|---------------------------------------------------|---------------------|
| <b>Patient characteristics</b> |                                           |                                                   |                     |
| <b>Demographic</b>             |                                           |                                                   |                     |
| 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)       |
| <b>Medical history</b>         |                                           |                                                   |                     |
| 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)       |
| <b>Medication history</b>      |                                           |                                                   |                     |
| 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)     |
| <b>Hospital characteristic</b> |                                           |                                                   |                     |
| <b>Hospital level</b>          |                                           |                                                   |                     |
| 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.**

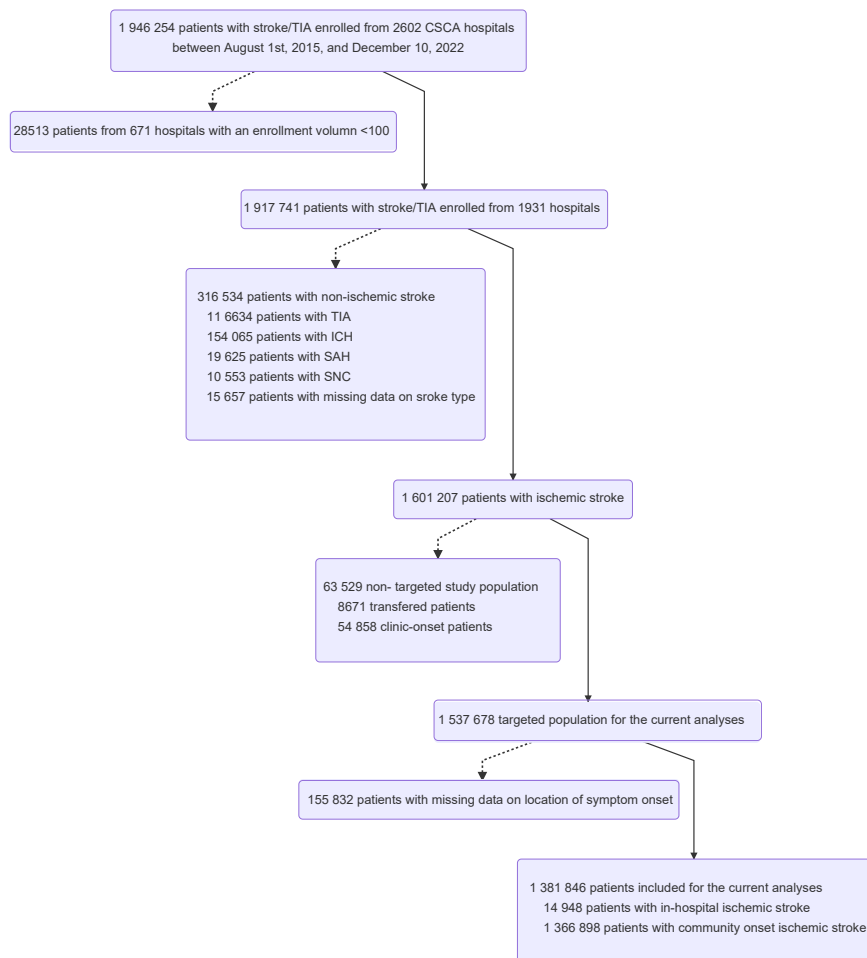
**Results**

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 analyses 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 (Supplemental Table S2 in the Data Supplement). Characteristics among patients who received reperfusion therapy were presented in Supplemental 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% *s.* 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% *s.* 93.1%; difference, –9.8% [–11.4% to –8.3%]), lower usage of early antithrombotics (73.5% *s.* 87.8%; difference, –14.3% [95% CI, –15.0% to –13.5%]) and dual antiplatelets for minor stroke (31.2% *s.* 43.9%; difference, –12.8% [95% CI, –13.8% to –11.7%]). Additionally, they were more poorly managed for dysphagia screen (73.3% *s.* 82.4%; difference, –9.1% [95% CI, –9.8% to –8.4%]) and swallow assessment (85.8% *s.* 90.8%; difference, –4.9% [95% CI, –5.5% to –4.4%]). However, they exhibited slightly better performance in

endo-vascular treatment (4.2% *s.* 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% *s.* 90.0%; difference, –11.4% [95% CI, –12.1% to –10.7%]), anti-hypertensive medication for hypertension (62.4% *s.* 66.4%; difference, –4.0% [95% CI, –4.9% to –3.0%]), hypoglycaemic medication for diabetes (76.0% *s.* 79.3%; difference, –3.4% [95% CI, –4.7% to –2.1%]) and statin for lowering low-density lipoprotein (84.9% *s.* 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% *s.* 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% *s.*

| Variables                                    | No./Total no. (%)    |                            | Difference (95% CI)    |
|----------------------------------------------|----------------------|----------------------------|------------------------|
|                                              | In-hospital stroke   | Community-onset stroke     |                        |
| <b>Acute management measures</b>             |                      |                            |                        |
| 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)    |
| <b>Discharge management measures</b>         |                      |                            |                        |
| 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 confounders, 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 improvement-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]).

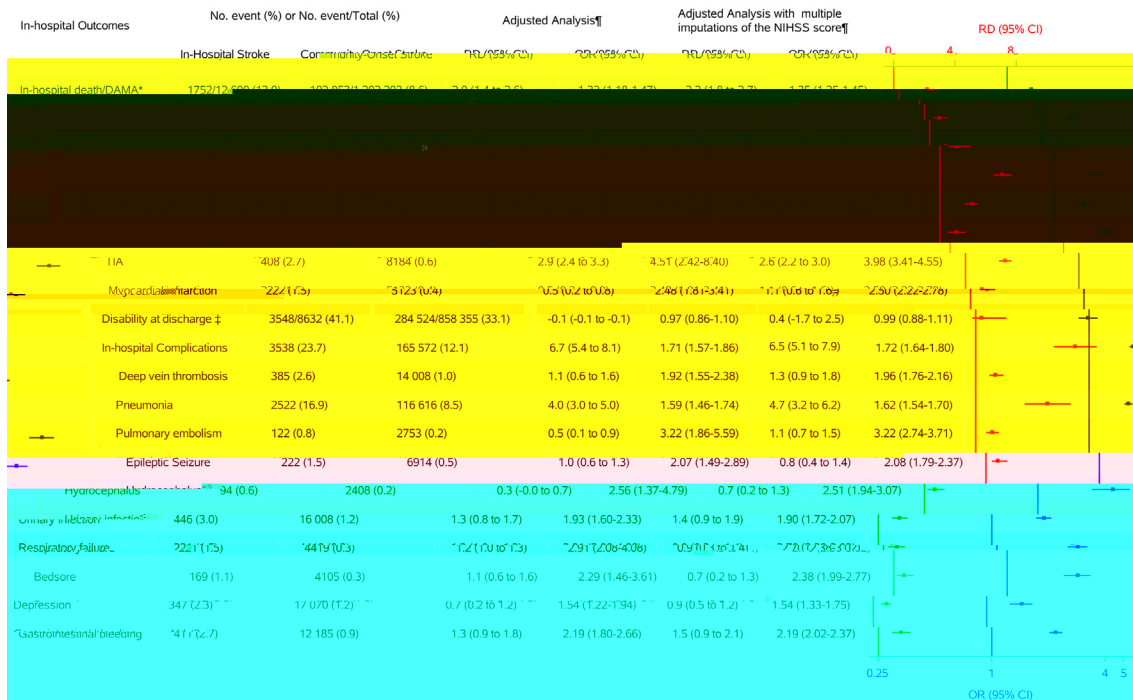
The data also revealed that in-hospital ischaemic stroke was significantly associated with increased odds of all the components of the above-mentioned composite outcomes, including in-hospital death (aOR, 1.51 [95% CI, 1.40–1.62]), DAMA (aOR, 1.24 [95% CI, 1.10–1.38]), cerebral infarction (aOR, 1.46 [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 analyses and adjusted analyses with adjustment of the NIHSS score yielded similar results, except for disability at discharge (Supplementar 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 level (Supplementar Tables S5–S8 in the Data Supplement). Regarding patients who underwent reperfusion therapy, the 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 with adjustment of the NIHSS score, except for disability at discharge (Supplementar Table S9 in the Data Supplement).

### Discussion

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



**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 survivors, 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 multivariate 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 strategies 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 register in Japan,<sup>1</sup> the National Get With The Guidelines-Stroke register in US,<sup>2</sup> the Ontario Stroke Register in Canada,<sup>3</sup> and the South London Stroke Register<sup>5</sup> 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

as more poorly managed during hospitalization.<sup>2,3,5</sup> 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.<sup>4</sup> Results from patients who received reperfusion therapy in the Get With the Guidelines-Stroke demonstrated similar conclusions to our analyses.<sup>25,26</sup>

In contrast to previous reports,<sup>2-4,25</sup> we found that in-hospital ischaemic strokes were not independently associated with disability at discharge. Results from our descriptive and adjusted analyses, including adjustment of the NIHSS 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 shrink but remained significant after the adjustment of the NIHSS score and other potential





**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 survivors, 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.<sup>27,28</sup> Therefore, differences in baseline characteristics may account for differences in care and outcomes, and the solutions should 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.<sup>16</sup>

To the best of our knowledge, this might be the largest sample-sized, multi-center registered trial 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 should 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. Fourth, 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 hospitalisation, and worse outcomes. In addition, disparities in outcomes between in-hospital ischaemic stroke and community-onset ischaemic stroke persist even if reperfusion therapy were administered. 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.lan.2023.100890>.

## References

- Kimura K, Minematsu K, Yamaguchi T. Characteristics of in-hospital onset ischaemic stroke. *Eur Neurol*. 2006;55(3):155–159.
- Cambler E, Wald H, Bhatt DL, et al. Quality of care and outcomes for in-hospital ischemic stroke: findings from the national get with the guidelines-stroke. *Stroke*. 2014;45(1):231–238.
- Saltman AP, Silmer FL, Fang J, Stamplecoski M, Kapral MK. Care and outcomes of patients with in-hospital stroke. *JAMA Neurol*. 2015;72(7):749–755.
- Li Z-Y, Han G-S, Wang J-J, et al. Comparing characteristics and outcomes of in-hospital stroke and community-onset stroke. *J Neurol*. 2022;269(10):5617–5627.
- Emmett ES, Dorigatti A, Marshall JJ, Wolfe CDA, Rudd AG, Bhalla A. A comparison of trends in stroke care and outcomes between in-hospital and community-onset stroke - the South London Stroke Register. *PLoS One*. 2019;14(2):e0212396.
- Emmerson J, Lees KR, Lindley P, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. *Lancet*. 2014;384(9958):1929–1935.
- Wardlaw JM, Murray V, Berge E, et al. Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. *Lancet*. 2012;379(9834):2364–2372.
- Thomalla G, Boertjies F, Ma H, et al. Intravenous alteplase for stroke with unknown time of onset guided by advanced imaging: a systematic review and meta-analysis of individual patient data. *Lancet*. 2020;396(10262):1574–1584.
- Gozal M, Menon BK, Zaim W, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387(10029):1723–1731.
- Rodrigues FB, Neves JB, Caldeira D, Ferro JM, Ferreira JJ, Costa J. Endovascular treatment versus medical care alone for ischaemic stroke: a systematic review and meta-analysis. *BMJ*. 2016;353:i1754.
- Saer JL, Fonaro GC, Smith EE, et al. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. *JAMA*. 2013;309(23):2480–2488.
- Man S, Xian Y, Holmes DN, et al. Association between thrombolysis door-to-needle time and 1-year mortality and readmission in patients with acute ischemic stroke. *JAMA*. 2020;323(21):2170–2184.
- Fonaro GC, Smith EE, Saer JL, et al. Timeliness of tissue plasminogen activator therapy in acute ischemic stroke: patient characteristics, hospital factors, and outcomes associated with door-to-needle times within 60 minutes. *Circulation*. 2011;123(7):750–758.
- Kim JT, Fonaro GC, Smith EE, et al. Treatment with tissue plasminogen activator in the golden hour and the shape of the 4.5-hour time-benefit curve in the national United States get with the guidelines-stroke population. *Circulation*. 2017;135(2):128–139.
- Jahan R, Saer JL, Schumm LH, et al. Association between time to treatment with endovascular reperfusion therapy and outcomes in patients with acute ischemic stroke treated in clinical practice. *JAMA*. 2019;322(3):252–263.
- Noth A, Amin-Hanjani S, Frie KL, et al. Identifying best practices to improve evaluation and management of in-hospital stroke: a scientific statement from the American Heart Association. *Stroke*. 2022;53(4):e165–e175.
- Wang Y, Li Z, Wang Y, et al. Chinese Stroke Center Alliance: a national effort to improve healthcare quality for acute stroke and transient ischaemic attack: rationale, design and preliminary findings. *Stroke Vasc Neurol*. 2018;3(4):256–262.
- HQ, Yang X, Wang CJ, et al. Clinical characteristics, management, and in-hospital outcomes in patients with stroke or transient ischemic attack in China. *JAMA Netw Open*. 2021;4(8):e2120745.
- Fonaro GC, Rees MJ, Smith EE, et al. Characteristics, performance measures, and in-hospital outcomes of the first one million stroke and transient ischemic attack admissions in get with the guidelines-stroke. *Circ Cardiovasc Qual Outcomes*. 2010;3(3):291–302.
- Li L, Chen W, Zhou H, et al. Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders: executive summary and 2019 update of clinical management of ischaemic cerebrovascular diseases. *Stroke Vasc Neurol*. 2020;5(2):159–176.
- National Health Commission of the People's Republic of China. *Healthcare quality management measures for neurological diseases (2020 Version)*; 2020. <http://www.nhc.gov.cn/gj/s7657/202001/61297c8b37914c4798c9b2c39735c769/files/080c17e2bc0e49a69226ad2ba297c1a4.pdf>. Accessed March 8, 2023.
- Wang YJ, Li ZX, G HQ, et al. China Stroke Statistics 2019: a report from the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, the Chinese Stroke Association, National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention and Institute for Global Neuroscience and Stroke Collaborations. *Stroke Vasc Neurol*. 2020;5(3):211–239.
- Rubin DB. *Multiple imputation for nonresponse in surveys*. Hoboken: Wiley; 1987.
- HQ, Li DJ, Li C, Rao ZZ. %ggBaseline: a SAS macro for analyzing and reporting baseline characteristics automatically in medical research. *Ann Transl Med*. 2018;6(16):326.
- Akbik F, Xie H, Xian Y, et al. Trends in reperfusion therapy for in-hospital ischemic stroke in the endovascular therapy era. *JAMA Neurol*. 2020;77(12):1486–1495.
- Moradi A, Levine SR. Comparison of short-term outcomes of thrombolysis for in-hospital stroke and out-of-hospital stroke in United States. *Stroke*. 2013;44(7):1903–1908.
- Vera R, Lago A, Fontes B, et al. In-hospital stroke: a multi-center prospective register. *Eur J Neurol*. 2011;18(1):170–176.
- Gardino M, Benesch C, Bakaeen F, et al. Considerations for reduction of risk of perioperative stroke in adult patients undergoing cardiac and thoracic aortic operations: a scientific statement from the American Heart Association. *Circulation*. 2020;142(14):e193–e209.