ORIGINAL ARTICLE

Correlation of Quality Metrics of Acute Stroke Care with Clinical Outcomes in an Indian Tertiary-care University Hospital: A Prospective Evidence-based Study

Bijoy Kumar Panda[1], Vaibhav R Suryawanshi[2], Gargi Attarde[3], Nilima Borkar[4], Shivakumar Iyer[5], Jignesh Shah[6]

Received on: 09 August 2023; *Accepted on:* 25 September 2023; *Published on:* 30 October 2023

Abstract

Aim: To characterize the impact of adherence to quality metrics of stroke care on the clinical outcomes of ischemic stroke (IS) and intracerebral hemorrhage (ICH) admissions.

Methods: Consecutive patients with acute stroke were prospectively followed up for their demographic and clinical characteristics, acute stroke management, and associated clinical outcomes at discharge. Stroke quality metrics [adopted from the American Heart Association (AHA)/American Stroke Association's Get with The Guidelines (GWTG)] with a specific interest in an association between acute reperfusion therapies and functional recovery in stroke patients are analyzed and presented. A composite measure of care was considered "0 (non-adherence) to 1 (adherence)." An all-or-none measure of care was calculated to check whether eligible patients received all the quality-of-care interventions. Multivariate Cox regression models were used to study an association between optimal adherence and clinical outcomes.

Results: During the study period, of the total 256 stroke admissions, 200 (78.1%) patients had IS, and the remaining 56 (21.9%) patients had ICH. The median [interquartile range (IQR)] age of total stroke admissions was 57 (36–78) years. Male preponderance was observed (IS: 80% and ICH: 67.9%). The conformity of performance metrics in IS patients was from 69.1% [95% confidence interval (CI), 68.5–69.6] for the use of deep vein thrombosis prophylaxis (DVTp) to 97.8% (95% CI, 96.2–98.6) for the use of statins. In ICH patients, it ranged from 61.7% (95% CI, 60.4–62.5) for the use of DVTp to 89.9% (95% CI, 88.6–89.7) for stroke rehabilitation. The unadjusted odds ratio (OR) of mortality (in-hospital plus the 28th-day postdischarge) was higher in ICH patients vs IS patients (4.42, $p = 0.005$). Optimal adherence with intravenous recombinant tissue plasminogen activator (IV-rtPA) therapy [hazards ratio (HR) = 0.23], in-hospital acute measures [IS (HR = 0.41) and ICH (HR = 0.63)], and discharge measures [IS (HR = 0.35) and ICH (HR = 0.45)] were associated with reduced hazards of the 28th-day mortality in both cohorts. Compared to ICH, IS patients had significantly improved neurofunctional recovery [modified Rankin score (mRS) ≤ 2, $p < 0.01$].

Conclusion: Adherence to quality metrics and performance measures was associated with low mortality and favorable clinical outcomes. Also, DVTp as an in-hospital (acute) measure of stroke care needs attention in both cerebrovascular events.

Keywords: Adherence, Clinical outcomes, Intracerebral hemorrhage, Ischemic stroke, Quality metrics, Quality of care.

Indian Journal of Critical Care Medicine (2023): 10.5005/jp-journals-10071-24566

Highlights

- Adherence to intravenous recombinant tissue plasminogen activator (IV-rtPA) therapy, in-hospital (acute) measures, and discharge measures significantly lowered the hazards of the 28th-day mortality in ischemic stroke (IS) and intracerebral hemorrhage (ICH) patients.
- The IS patients compared to the ICH patients showed significant improvement in neurofunctional independence at the 28th-day postdischarge.
- Door-to-imaging time (DIT) and door-to-needle time (DNT) both exhibit scope for improvement, ranging 45–50% and 25–30%, respectively.
- Deep vein thrombosis prophylaxis (DVTp) as an in-hospital (acute) care measure needs attention in both cerebrovascular events.

Introduction

In India, stroke is now the fifth most common cause of disability and the fourth most common cause of death.[1] Despite the development of evidence-based guidelines for stroke care,[2] the incidence of stroke in India ranges between 84 and 262 per 100,000 people in rural areas and between 334 and 424 per 100,000 people in urban areas. This incidence rate is on the rise, despite the fact that the country's overall crude prevalence of stroke, which in the past 10

[1]Department of Pharmacy Practice, Krishna Institute of Pharmacy, Krishna Vishwa Vidyapeeth (Deemed to be University), Karad, Maharashtra, India

[2–4]Department of Pharmacy Practice, Poona College of Pharmacy, Bharati Vidyapeeth (Deemed to be University), Pune, Maharashtra, India

[5,6]Department of Critical Care Medicine, Bharati Vidyapeeth (Deemed to be University), Medical College, Pune, Maharashtra, India

Corresponding Author: Vaibhav R Suryawanshi, Department of Pharmacy Practice, Poona College of Pharmacy, Bharati Vidyapeeth (Deemed to be University), Pune, Maharashtra, India, Phone: +91 95529 56860, e-mail: phdrvaibhav@gmail.com

How to cite this article: Panda BK, Suryawanshi VR, Attarde G, Borkar N, Iyer S, Shah J. Correlation of Quality Metrics of Acute Stroke Care with Clinical Outcomes in an Indian Tertiary-care University Hospital: A Prospective Evidence-based Study. Indian J Crit Care Med 2023;27(11): 806–815.

Source of support: Nil

Conflict of interest: None

years has varied from 44.29 to 559/100,000 people.[3] Registry-based surveillance studies using the WHO stages stroke instrument have been successfully conducted in western and southern parts of India, which have proposed a proportional mortality rate of 6–8%, where, more than 50% of stroke deaths majorly occurred in tertiary-care hospitals, respectively.[4,5]

Considering the intravenous recombinant tissue plasminogen activator (IV-rtPA) therapy which has been used in ischemic stroke (IS) management for >15 years in the United States. The reported administration rate in the United States study was found to be very low (between 1.2 and 9%).[6] Improving the quality of stroke care has become a worldwide priority now. For measuring the performance of an individual hospital in delivering appropriate acute stroke care, certain quality metrics and performance measures have been devised. The American Heart Association (AHA)/American Stroke Association (ASA) "Get With The Guidelines (GWTG) Stroke Program" is such a stroke quality measurement and improvement program that represents the world's largest stroke registry.[7,8] After the adoption and implementation of AHA/ASA's evidence-based guidelines, through continuous quality improvement surveillance and interventions number of patients have benefited from favorable and improved neurofunctional outcomes.[7–10] However, in developing countries this situation is different, where the stroke care services are established but they are not fully developed yet. There is published evidence of the Indian Stroke Association (ISA) recommendations for early management of stroke and transient ischemic attack (TIA) to improve the quality of care.[2] However, the adoption, implementation, and association of adherence to this evidence-based guideline recommendation with clinical outcomes have not been systematically evaluated in clinical practice. Except for one important study by the Indo-US Collaborative Stroke Project (IUCSP) group, there is a big paucity of Indian data on this instance.

Our tertiary care university hospital follows ISA's recommendations and AHA/ASA's evidence-based guidelines.[2,9,11,12] However, the quality assessment of performance in clinical practice has never been measured systematically. Therefore, the current study's objectives were to describe the hospitalization of stroke patients, investigate the variations in performance metrics stated in evidence-based guidelines, and determine associated clinical outcomes.

Materials and Methods

Study Design, Settings, Patients, and Ethics

A prospective–observational quality metric and performance analysis was performed, including adult patients who were primarily hospitalized with a diagnosis of the cerebrovascular event [either IS or intracerebral hemorrhage (ICH)] during the period of October 2021 to March 2023 (1.5 years) at a tertiary-care university hospital situated in Western Maharashtra, India. Ethical approval was obtained from an institutional review board (IEC/2021/39).

The intent of this quality and performance analysis was to identify any shortcomings in order to ensure that the hospital managers, quality staff, and stroke care teams could work together to formulate and implement a system of quality improvement interventions. A cerebrovascular event was confirmed by brain imaging [either computed tomography (CT or magnetic resonance imaging (MRI)] in patients who were admitted either directly to or through the emergency department. The National Institute of Health Stroke Scale (NIHSS) severity scoring system was applied to both of the cohorts. Patients with other cerebrovascular events, head trauma, polytrauma, recent intracranial and/or intraspinal surgery, pregnancy, pediatric age, and being diagnosed with dementia or psychiatric disorder were excluded. Patients with contraindications to medications used in acute stroke care were also excluded from the study.

Case Identification and Data Abstraction

Various techniques were utilized for prospective identification, but some of them included routine surveillance of emergency department records (i.e., presenting symptoms and primary complaints), ward demographic records, and neurology assessments. Prior to abstraction, a chart review confirmed each admission for IS or ICH. The patients' demographics, medical history, time indicators, initial brain imaging findings, in-hospital treatments and events, discharge treatment and events, counseling, mortality, and discharge destination were all abstracted from the patients' medical case files and registers maintained at the nursing station while admitted. Fully anonymized data were used in these analyses. Verbal and written informed consent were obtained from the patient and patient's family members for the study participation and publication of results.

Quality Metrics and Multifaceted Performance Measures

Two additional quality metrics and a total of 12 guideline-based performance measures (5 acute performance measures and 7 discharge performance measures) for in-hospital stroke management were considered as developed by the GWTG-stroke program and adopted by ASA/AHA.[7,8] These measures have also been endorsed by the National Quality Forum and the ISA.[2] Additional quality metrics included were as follows: (A) Door-to-imaging time (DIT) (within 45 minutes) and (B) door-to-needle time (DNT) (within 60 minutes). Multifaceted performance measures included the following five acute performance measures: (A) The IV-rtPA administration within 3 hours of stroke symptom onset (last known well time); (B) early antithrombotics (EATs) administration within 48 hours of admission; (C) deep vein thrombosis prophylaxis (DVTp) [including unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH)] within 48 hours of admission; (D) dysphagia screening; (E) stroke rehabilitation and included the following seven discharge performance measures: (A) The antithrombotics (ATs); (B) anticoagulants for atrial fibrillation (ACAF); (C) blood pressure (BP)-lowering medications [antihypertension (anti-HTN)]; (D) antidiabetics (ADs); (E) statins in patients with [low-density lipoprotein cholesterol (LDL-C)] levels of >100 mg/dL; (F) smoking cessation interventions (counseling or medications); (G) stroke education and resources given. Only patients who satisfied the criteria for stroke were subjected to quality metrics and performance measures. Two different but crucial measures were also included in this analysis and were compared with the GWTG study[10] and the CNSR study.[13] These standards were used for establishing total performance measure conformance. First, an all-or-none measure of stroke care was used, which was defined as the proportion of eligible patients who received all the performance measure interventions. Second, a composite measure of stroke care [with a range of "0" (non-adherence) to "1" (perfect adherence)] was developed to determine the extent to which eligible patients received evidence-based stroke care. It was calculated by dividing the number of actual performance measures offered by the total

number of performance measures which could have been used for the patient.

Stroke Related Clinical Outcomes and In-hospital Medical Complications

Primary outcomes assessed include the following: (A) mortality (in-hospital, and 28-day postdischarge) and discharge against medical advice (DAMA); (B) major adverse cardiovascular events (MACEs) [TIA, cerebral infarction, cerebral hemorrhage, and myocardial infarction (MI)]. The secondary outcomes assessed include the following: (A) hospital length of stay (LOS) (days) and (B) in-hospital medical complications [deep vein thrombosis, convulsive seizure, pneumonia, urinary tract infection, bedsore (decubitus ulcer), respiratory failure or cardiopulmonary arrest, anxiety, and depression].

Neurofunctional outcome evaluation was performed using a modified Rankin score (mRS).[14,15] Patients (discharged home only) were telephonically contacted for a follow-up at the end of 28th-day postdischarge for assessment of neurofunctional recovery (using the mRS) and postdischarge mortality outcome evaluation. An mRS score of 0 or 1 was considered to be a good clinical outcome, and an mRS score of 0–2 was considered to be a favorable clinical outcome (neurofunctional recovery).

Statistical Analysis

Proportions were used for categorical variables, and mean [standard deviation (SD)] or median [interquartile range (IQR)] were used for nominal variables. The association between the cerebrovascular event group and patient demographics, clinical variables, treatments, performance measures, quality metrics, and in-hospital outcomes were explored using contingency tables (multivariate logistic regression models). Data were examined generally as well as by the two kinds of cerebrovascular events, IS and ICH, for these analyses. All categorical row variables were subjected to Pearson's chi-square tests to assess the statistical connections, and all continuous or ordinal variables were subjected to Kruskal–Wallis tests.

The relationship between cerebrovascular event groups and three binary outcome measures mortality (in-hospital or 28-day postdischarge), discharge home status, and LOS (>4 days vs ≤4 days; this cut-point represented the median LOS) were further examined using multivariate logistic regression models. The variables most predictive of mortality (in-hospital or the 28th-day postdischarge) in logistic regression models for the cerebrovascular event group were also compared. In addition, the association of adherence to performance measures with clinical and functional outcomes was analyzed using a multivariable Cox proportion hazard and multivariate regression model. The models used were not adjusted for patient demographics and clinical characteristics. Comparisons were made between mortality, discharge status, specific performance metrics, and LOS above 4 days. All categorical row variables' probability values were based on Chi-square rank-based group mean score statistics (equivalent to the Wilcoxon test for two levels). All the calculated *p*-values are two sided, and statistical significance is defined as $p < 0.05$. *Post hoc* analysis with the Bonferroni method was used, for which the level of significance was set at $p < 0.05$; for *post hoc* analysis of nonparametric statistics, Bonferroni correction for multiple comparisons was set at $p < 0.0100$ (0.05/5). If an interaction effect of variables in two-way repeated measures was found, the adjusted *p* value for multiple comparisons at each time period was $p < 0.0083$ (0.05/8). Statistical package for the social sciences (SPSS) software, version 21.0, and Microsoft Excel software, version 16.45, were used to conduct all of the statistical analyses. Each author held responsibility for the data's integrity and had full access to it.

Results

For the 200 (78.1%) IS and 56 (21.9%) ICH patients included in the study, the median (IQR) age was 58 (35–75) and 53 (38–79) years, and more than half (77.3%) were male (overall). Table 1 summarizes the patient demographics and clinical characteristics by cerebrovascular event type. Patients with ICH had a relatively high prevalence of hypertension (71.4%) compared to IS (60%). Prior stroke/TIA was comparable in both the cerebrovascular event types, whereas diabetes (35%), dyslipidemia (21%), atrial fibrillation, or flutter (14%) were majorly present in IS patients. Overall median NIHSS on admission was 10 (5–16), where ICH patients had high stroke severity compared to IS.

According to the ISA consensus statement,[2] patients who managed to arrive at the stroke unit within 3 hours of symptom onset had better 3-month neurofunctional outcomes. In our study patients, a major time median (P_{25}–P_{75}) was elapsed from symptom onset to emergency medicine department (EMD) arrival [9.2 (2.5–45.2) hours]. The DIT in patients who arrived in less than 3 hours of stroke symptom onset was 40 (22–68) minutes, whereas the DNT in the eligible patients was 55 (45–65) minutes. Furthermore, IV-rtPA was administered at 2.2 (1.5–2.7) hours from the symptom onset (Table 1).

Quality Metrics and Multifaceted Performance Measures

- Additional quality metrics: The guideline recommends that door-to-imaging should take 25 minutes, and the interpretation should be done within 45 minutes, whereas DNT for the eligible patients should be 60 minutes so as to improve the viability of IV-rtPA administration at 3–4.5 hours. For every 15-minute reduction in DNT (from arrival to emergency room to thrombolysis), there are 5% lower odds ratio (OR) of in-hospital mortality.[2,9] In our study patients, door-to-imaging within 45 minutes was observed in 55–60% of the patients in both cerebrovascular event types. Adherence to additional quality metrics is detailed in Table 2.
- Acute performance measures: The mean (SD) composite score ranged from 0.74 (0.1) in patients with ICH to 0.87 (0.1) in patients with IS, and the all-or-none measure was in the range of 71.5% [95% confidence interval (CI), 70.2–72.1] in patients with IS to 73.2% (95% CI, 72.7–73.9) in patients with ICH. In India, IV-rtPA is approved for use up to 4.5 hours, and endovascular treatment is also available. An additional 4 patients received IV-rtPA between 3 and 4.5 hours for an overall IV-rtPA rate of 92.8% (52/56); in addition, endovascular treatment alone was administered to 6 (3%) patients. Among measures that were applicable to stroke types, the proportions of those who undergone DVTp were 69.1% (95% CI, 68.5–69.6, $p = 0.02$), and stroke rehabilitation were 91% (95% CI, 90.4–92.6). This was higher among patients with IS compared to ICH ($p = 0.04$). The gap in performance measures among cerebrovascular event groups was seen in DVTp in the range of 7.4% ($p = 0.02$) (Table 2).

Table 1: Patient demographics, clinical characteristics, and time windows for IS and ICH admissions

Variables	*IS* *N = 200 (78.1%)*	*ICH* *N = 56 (21.9%)*	*Total* *N = 256 (100%)*
Age			
Mean (SD)	58.1 (±15.7)	53.1 (±15.8)	57.1 (±15.7)
Median (IQR)	58 (35–75)	53 (38–79)	57 (36–78)
Gender			
Male	160 (80)	38 (67.9)	198 (77.3)
Female	40 (20)	18 (32)	58 (22.7)
Current/history of smoking	101 (50.5)	24 (43)	125 (48.8)
Current tobacco use	92 (46)	21 (39.3)	113 (44.1)
Medical history			
Hypertension	120 (60)	40 (71.4)	152 (59.4)
Diabetes mellitus	70 (35)	14 (25)	84 (32.8)
Previous stroke/TIA	38 (19)	10 (18)	48 (18.8)
Dyslipidemia	42 (21)	2 (3.6)	44 (17.2)
Atrial fibrillation or flutter	28 (14)	0	28 (11)
CAD/previous MI	10 (5)	8 (14.3)	18 (7.0)
DVTp/PE	6 (3)	0	6 (2.3)
NIHSS			
Median (IQR)	9 (5–15)	11 (6–16)	10 (5–16)
Undocumented	36 (18)	12 (21.5)	48 (18.7)
1–4	82 (41)	14 (28.6)	96 (37.5)
5–14	70 (35)	20 (32)	90 (35.2)
>15	12 (6)	10 (17.9)	22 (8.6)
Time windows (eligible stroke patients only)			
Time of symptom onset to EMD arrival (within 3 hours) median (P_{25}–P_{75})	8.15 (2.55–45.5)	8.25 (1.4–23)	9.2 (2.5–45.2)
Door-to-imaging time (within 45 mins) median (P_{25}–P_{75})	40 (22–68)	40 (22–65)	41 (23–68)
Door-to-needle time (within 60 minutes) median (P_{25}–P_{75})	55 (45–65)	–	55 (45–65)
Time of symptom onset to IV-rtPA administration (within 3 hours) median (P_{25}–P_{75}), ($n = 52$)	2.2 (1.5–2.7)	NA	2.2 (1.5–2.7)
Administration of EAT (within 48 hours) median (P_{25}–P_{75})	4 (2.1–7.7)	NA	4 (2.1–7.7)
ATs after IV-rtPA (after 24 hours) median (P_{25}–P_{75})	30.2 (26.5–36.8)	NA	30.2 (26.5–36.8)
DVTp (within 24 hours) median (P_{25}–P_{75})	21.4 (8.7–25.5)	NA	21.4 (8.7–25.5)
DVTp after IV-rtPA (after 24 hours) median (P_{25}–P_{75})	32.2 (25.1–37.8)	NA	32.2 (25.1–37.8)
DVTp (after 48 hours) median (P_{25}–P_{75})	NA	63.4 (48.6–132.9)	63.4 (48.6–132.9)

CAD, coronary artery disease; DVTp, deep vein thrombosis prophylaxis; EAT, early antithrombotic; EMD, emergency medicine department; IV-rtPA, intravenous recombinant tissue plasminogen activator; MI, myocardial infarction; NIHSS, National Institutes of Health Stroke Scale; PE, pulmonary embolism; TIA, transient ischemic attack

- Discharge performance measures: Antihypertensives were administered to 86.4% (95% CI, 85.3–87.1) eligible ICH patients compared to 82.8% (95% CI, 81.2–84.1) eligible IS patients ($p = 0.03$). Both cerebrovascular event groups used the smoking cessation strategy at an ideal level (>85%). The all-or-none measures were significant ($p = 0.01$) in the range of 75.8% (95% CI, 74.7–76.5) in patients with IS to 83.3% (95% CI, 82.2–84.8) in patients with ICH (Table 2). The composite score varied from 0.88 (0.06) in patients with ICH to 0.91 (0.07) in patients with IS.
- Overall performance measures: The composite measure of care ranged from a mean (SD) of 0.80 (0.15) in ICH patients to 0.87 (0.11) in IS patients. Similarly, all-or-none care measures ranged from 69.5% (95% CI, 68.2–70.3) in IS patients to 75.1% (95% CI, 74.3–76.2) in ICH patients (IS vs ICH, $p < 0.01$) (Table 2).

In-hospital outcomes and complications

We observed significant variations in both the cerebrovascular event groups in mortality, DAMA, MACEs, LOS, and in-hospital

Table 2: Additional quality metrics (time), individual performance measures (acute, discharge, and overall), and all-or-none measures by cerebrovascular event type (IS vs ICH)

Variables	*IS (N = 200) Number/ Total Number*[#]	*Frequency (%) (95% CI)*	*ICH (N = 56) Number/ Total Number*[#]	*Frequency (%) (95% CI)*	*p-value*
*(a) Additional quality metrics (time)**					
Door-to-imaging time (within 45 minutes)	31/56	55.3 (54.2–57.6)	13/22	59.1 (57.8–61.2)	0.05
Door-to-needle time (within 60 mins)	39/52	75.1 (74.3–75.6)	–	–	–
(b) Acute performance measures[†]					
The IV-rtPA administration within 3 hours of stroke symptom onset	48/56	85.7 (84.2–86.3)	NA	NA	–
EATs administration within 48 hours	173/188	92.1 (91.4–93.5)	NA	NA	–
DVTp administration within 48 hours	130/188	69.1 (68.5–69.6)	21/34	61.7 (60.4–62.5)	0.02
Dysphagia screening	170/200	85 (84.4–85.5)	48/56	85.7 (85.1–86.2)	0.45
Stroke rehabilitation	182/200	91 (90.4–92.6)	50/56	89.9 (88.6–89.7)	0.04
Composite score, mean (SD)	0.87 (0.1)		0.74 (0.1)		0.01
All-or-none measures	143/200	71.5 (70.2–72.1)	41/56	73.2 (72.7–73.9)	
(c) Discharge performance measures[‡]					
ATs	163/176	92.6 (91.3–93.1)	NA	NA	–
ACAF	32/37	86.5 (85.2–87.6)	NA	NA	–
BP-lowering medications (anti-HTN)	111/134	82.8 (81.2–84.1)	38/44	86.4 (85.3–87.1)	0.03
ADs	80/96	83.3 (82.6–83.9)	21/25	84.1 (83.4–85.5)	0.10
Statins for LDL-C ≥100 mg/dL	182/186	97.8 (96.2–98.6)	NA	NA	–
Smoking cessation intervention (counseling or medications)	56/62	90.3 (89.6–90.9)	14/16	87.5 (87.2–87.7)	0.08
Stroke education and resources given	158/186	84.9 (84.2–85.3)	36/42	85.7 (85.2–86.1)	0.32
Composite score, mean (SD)	0.91 (0.07)		0.88 (0.06)		0.01
All-or-none measures	141/186	75.8 (74.7–76.5)	35/42	83.3 (82.2–84.8)	
(d) Overall performance measures (acute plus discharge)					
Composite score, mean (SD)	0.87 (0.11)		0.80 (0.15)		<0.01
All-or-none measures	139/200	69.5 (68.2–70.3)	42/56	75.1 (74.3–76.2)	

[#]Number of patients who received quality metric or performance measure (numerator) divided by number of total eligible patients (denominator). *Only the patients who arrived in EMD within 3 hours of stroke symptom onset. Patients with missing data were excluded from the denominator. [†]Only eligible patients were included in the denominator. [‡]Only eligible patients were included. Deaths and missing data were excluded from the denominator. ACAF, anticoagulation for atrial fibrillation; ADs, antidiabetics; AF, atrial fibrillation; ATs, antithrombotics; BP, blood pressure; CT, computed tomography; DVTp, deep vein thrombosis prophylaxis; IVrtPA, intravenous recombinant tissue plasminogen activator; LDL-C, low-density lipoprotein cholesterol; MRI, magnetic resonance imaging

medical complications (Table 3). Mortality and DAMA were 51.8% (95% CI, 50.3–52.5) in ICH patients, which was significantly ($p < 0.01$) higher compared to 24% (95% CI, 23.3–25.7) in IS patients. Patients with ICH compared to IS had higher rates of MACEs (21.4% vs 11%, $p = 0.05$) and longer LOS (days) [7 (1–31) vs 9 (2–39), $p < 0.01$]. The median LOS >4 days was higher in ICH patients compared to IS patients (96.4% vs 78%, $p < 0.01$). Additionally, ICH patients experienced considerably higher rates of in-hospital medical complications (60.7% vs 37.0%, $p < 0.01$), particularly convulsive seizure ($p = 0.03$), pneumonia ($p < 0.01$), urinary tract infection ($p = 0.05$), and respiratory failure or cardiopulmonary arrest ($p < 0.01$).

All-or-none care measures and clinical outcomes by cerebrovascular event type are summarized in Table 4A. The unadjusted OR of mortality (in-hospital or the 28th-day postdischarge) were higher in ICH patients compared to IS patients. The OR of being hospitalized for more than 4 days remained significantly elevated for ICH patients compared to IS patients (6.76, $p = 0.0003$). The multivariable-unadjusted estimates between IV-rtPA therapy, optimal adherence with additional quality metrics, acute measures, discharge measures, and 28-day postdischarge neurofunctional outcomes are shown in Table 4B. For patients with IS and ICH, optimal adherence with acute measures was associated with reduced 28-day mortality (HR = 0.41; 95% CI, 0.31–0.57) and (HR = 0.63; 95% CI, 0.49–0.67), respectively, whereas optimal adherence with discharge measures was associated with reduced 28-day deaths after discharge (HR = 0.35; 95% CI, 0.20–0.46) for IS patients and (HR = 0.45; 95% CI, 0.31–0.56) for ICH patients. Also, IV-rtPA therapy was associated with a lower risk of death (HR = 0.23; 95% CI, 0.19–0.37). Interventions such as IV-rtPA therapy, in-hospital (acute) care measures, and discharge care measures were associated with improved neurofunctional outcomes at the 28th-day postdischarge in both cerebrovascular event types (OR > 1).

Table 5 summarizes the characteristics that were most predictive of mortality for both types of cerebrovascular events. In our datasets of IS patients, atrial fibrillation (OR = 5.5) and diabetes (OR = 5.2) were among the highest predictors of mortality, followed by hypertension (OR = 4.4), coronary artery disease (CAD)/MI

Table 3: Stroke related clinical outcomes and in-hospital medical complications by cerebrovascular event type (IS vs ICH)*

Variables	*IS (n = 200) (%) (95% CI)*	*ICH (n = 56) (%) (95% CI)*	*p-value*
(a) Primary outcomes			
Discharge home[†]	152 (76) (75.3–77.2)	27 (48.2) (47.5–49.6)	<0.01
Mortality & DAMA[‡]	48 (24) (23.3–25.7)	29 (51.8) (50.3–52.5)	<0.01
• In-hospital mortality	14 (7) (6.3–7.7)	12 (21.4) (20.7–22.3)	<0.01
• 28-day mortality (postdischarge)	6 (4) (3.5–4.5)	8 (23) (22.3–23.6)	<0.01
• DAMA	28 (14) (13.3–14.7)	9 (16.1) (15.4–16.9)	<0.01
In-hospital MACEs	22 (11) (10.3–11.7)	12 (21.4) (20.1–22.7)	0.05
• TIA	2 (1) (0.3–1.7)	0 (0)	–
• Cerebral infraction	8 (4) (3.3–4.7)	4 (7.1) (5.8–8.4)	0.35
• Cerebral hemorrhage	2 (1) (0.3–1.7)	6 (10.7) (9.4–12.1)	<0.01
• MI	10 (5) (4.3–5.7)	2 (3.6) (2.3–4.9)	0.31
(b) Secondary outcomes			
Hospital LOS (days) median (IQR)	7 (1–31)	9 (2–39)	<0.01
ICU LOS (days) median (IQR)	4 (1–22)	6 (2–31)	<0.01
Hospital LOS (> 4 days)	156 (78) (77.3–78.7)	54 (96.4) (95.1–97.7)	<0.01
In-hospital medical complications	74 (37) (36.3–37.7)	34 (60.7) (60.1–61.4)	<0.01
• Deep vein thrombosis	6 (3) (2.3–3.7)	2 (3.6) (2.3–4.9)	0.70
• Convulsive seizures	2 (1) (0.3–1.7)	4 (7.1) (5.8–8.4)	0.03
• Pneumonia	14 (7) (6.3–7.7)	22 (39.3) (38.1–40.5)	<0.01
• Urinary tract infection	12 (6) (5.3–6.7)	8 (14.3) (12.1–15.6)	0.05
• Bedsore (decubitus ulcer)	2 (1) (0.3–1.7)	2 (3.6) (2.3–4.9)	0.17
• Respiratory failure or cardiopulmonary arrest	18 (9) (8.3–9.7)	12 (21.4) (20.1–22.7)	<0.01
• Anxiety or depression	24 (12) (11.3–12.7)	12 (21.4) (20.1–22.7)	0.08

*Data are represented as number [percentage (95% CI)] of events unless otherwise indicated. [†]Indicates patient discharged home, remained alive and showed up for 28th-day postdischarge follow-up. [‡]Discharge against medical advice was assessed among discharge surviving patients. DAMA, discharge against medical advice; ICU, intensive care unit; LOS, length of stay; MACEs, major adverse cardiovascular events

Table 4A: All-or-none care measure and clinical outcomes by cerebrovascular event type: Unadjusted OR

		Unadjusted			
Outcome	*Event type (vs IS as reference)*	*OR**	*Lower (95% CI)*	*Upper (95% CI)*	*p-value*
All-or-none measure	ICH	0.65	0.37	1.16	0.07
Mortality (in-hospital or 28-day postdischarge)	ICH	4.42	4.16	4.82	0.005
Discharge home	ICH	0.47	0.25	0.88	0.009
LOS > 4 days	ICH	6.76	6.24	7.07	0.0003

*OR indicates odds ratio. CI, confidence interval; ICH, intracerebral hemorrhage; IS, ischemic stroke; LOS, length of stay

Table 4B: Association of optimal adherence with mortality and with mRS ≤ 2 (favorable functional outcome) at the end of 28th-day postdischarge

	Mortality, HR (95% CI)[†]*		*Favorable functional outcome, OR (95% CI)[†]*	
Variables	*IS*	*ICH*	*IS*	*ICH*
IV-rtPA therapy	0.23 (0.19–0.37)	NA	4.2 (3.3–4.9)	NA
Additional quality metrics	0.37 (0.23–0.48)	0.67 (0.53–0.78)	2.0 (1.1–2.4)	2.2 (1.5–2.5)
Acute performance measures	0.41 (0.31–0.57)	0.63 (0.49–0.67)	4.7 (3.1–4.4)	2.1 (1.2–3.7)
Discharge performance measures	0.35 (0.20–0.46)	0.45 (0.31–0.56)	4.5 (3.7–4.9)	3.4 (2.6–4.2)

*Death after IS onset for intravenous rtPA usage, death 48-hours postadmission of acute measures, and death after discharge for discharge measures. [†]Hazards ratios and odds ratios were unadjusted for patient demographics and clinical characteristics. CI, confidence interval; HR, hazard ratio; mRS, modified Rankin score; NA, not applicable; OR, odds ratio; rtPA, recombinant tissue plasminogen activator

(OR = 3.9), and previous stroke/TIA (OR = 3.7). A history of CAD/MI and previous stroke/TIA was associated with a higher mortality risk for both the cerebrovascular event groups. Whereas, hypertension (OR = 6.6) was relatively associated with higher mortality in patients with ICH but lower risk among IS patients. Delayed EMD arrival was comparatively a low predictor of mortality in ICH but

Table 5: Variables predictive of mortality among IS and ICH admissions

Variables	*IS OR, (95% CI), Chi-square value*	*p-value*	*Variables*	*ICH OR, (95% CI), Chi-square value*	*p-value*
Atrial fibrillation	5.5 (5.1–5.8), 24.1	0.0001	Hypertension	6.6 (6.2–6.9), 32.6	0.0001
Diabetes	5.2 (5.0–5.8), 30.4	0.0001	CAD/MI	3.5 (3.1–3.8), 8.1	0.004
Hypertension	4.4 (4.1–4.9), 19.4	0.0001	Previous stroke/TIA	2.4 (2.1–2.6), 5.9	0.01
CAD/MI	3.9 (3.8–4.0), 6.1	0.01	Delayed EMD arrival	1.2 (0.9–1.3), 27.1	0.0001
Previous stroke/TIA	3.7 (3.5–3.9), 16.1	0.0001	Current smoking	0.6 (0.5–0.7), 4.5	0.18
Delayed EMD arrival	2.8 (2.6–3.0), 12.6	0.0001	Diabetes	0.5 (0.4–0.6), 6.6	0.009
Current smoking	0.9 (0.7–1.0), 3.1	0.07	Dyslipidemia	0.5 (0.4–0.5), 2.8	0.12
Dyslipidemia	0.6 (0.5–0.7), 2.2	0.14			

CAD, coronary artery disease; EMD, emergency medicine department; MI, myocardial infarction; TIA, transient ischemic attack

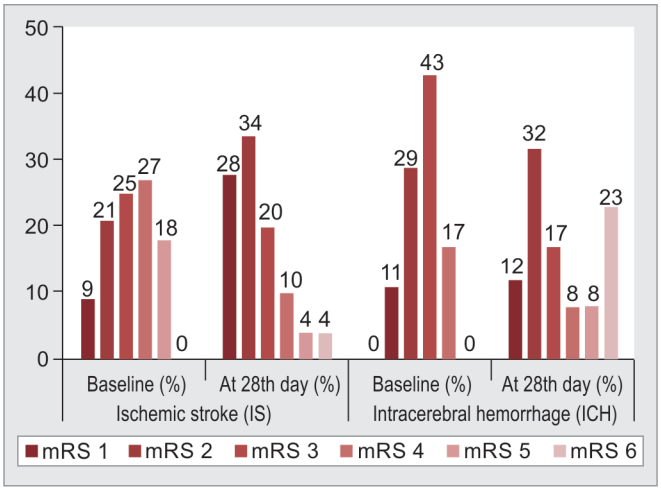

Fig. 1: Temporal changes in mRS at admission (baseline) and at the end of 28th-day postdischarge in IS and ICH admissions. *Note:* In IS patients, the mean (SD) mRS at admission (baseline) and at the end of the 28th-day postdischarge was 3.0 (1.3) and 2.0 (1.1), respectively ($p < 0.01$). In ICH patients, the mean (SD) mRS at admission (baseline) and at the end of the 28th-day postdischarge was 4.0 (1.2) and 3.0 (1.6), respectively ($p < 0.01$). Comparing neurofunctional recovery in IS vs ICH patients, significant differences were observed ($p < 0.01$)

three times the likelihood predictor of mortality in IS (1.2 vs 2.8, $p < 0.01$) patients.

The temporal changes in mRS at admission (baseline) and at 28th-day postdischarge are shown in Figure 1. The favorable outcomes were based on improvements in mRS ≤ 2 from baseline to the end of 28th-day postdischarge. At end of the 28th-day postdischarge, significant neurofunctional recovery was observed in both the cerebrovascular event groups. Compared to ICH, patients with IS had better neurofunctional recovery ($p < 0.01$). As the rates of MACEs, in-hospital medical complications, and hypertension were higher among ICH patients, neurofunctional recovery at the end of the 28th-day postdischarge was less favorable and was delayed at the same time.

Discussion

This prospective study has provided some crucial understanding of the variances in stroke risk factors, in-hospital (acute) care, discharge care, and clinical outcomes in cohorts of hospitalized patients with IS and ICH. Stroke is on the rise in developing countries. An Indian population registry study reported that IS was present to the tune of range 67.3–80.5%, whereas ICH was responsible for 6.5–19.6% of the cerebrovascular event cases. The present study showed a comparable prevalence and characteristics of IS and ICH patients with those of previously published Indian,[3,16] Chinese,[13,16,17] and the United States studies.[7,10] Both the cerebrovascular event groups developed stroke at relatively younger ages compared to the reports from the Western population. The patients in the present study were younger by an average of 10–12 years than the median age reported by the GWTG-stroke study (United States),[10] the China Stroke Center Alliance (CSCA)-stroke study (China),[17] Close the GAP-stroke study (Japan),[18] and the Arbeitsgemeinschaft Deutschsprachiger Schlaganfall Register (ADSR): stroke study (Germany)[19] patients. Comparable age demographics were observed in the IUCSP-stroke study (India).[16] The gender distribution in the present study showed a male preponderance (>75%), similar to other studies.[13,16–18] However, this was not the case in the GWTG-stroke study patients where 52.4% of females had IS and 49.3% had ICH.[10] There was a relatively high burden of modifiable risk factors in both the cerebrovascular event groups. Hypertension and diabetes prevention require more efforts in India as predicted by other studies as well.[16] The rates of smoking and tobacco use in the present study were much higher compared to other similar studies.[10,16–18] The rates of hypertension and atrial fibrillation were much lower in the present study, the IUCSP-stroke study (India)[16] and China[17] compared to the rates from other studies.[10,18–20]

In our study, we compared the critical time targets set by the AHA/ASA and National Institute of the Neurological Disorders and Stroke (NINDS) on stroke management to those accomplished in our study group. Stroke thrombolysis in Indian settings has struggled to match the worldwide criteria set for door-to-imaging time (DIT) and DTN time.[21] In a recently published Indian study, the majority (73%) of patients had a DIT of 30–60 minutes, whereas only 19% of the patients had less than 30 minutes.[22] In our analysis, nearly 45–50% of the patients admitted with ischemic stroke (IS) had DIT below 30 minutes. This means, that a 50% scope of improvement exists at our center. On the contrary, shorter DTN time is associated with minimal complications to thrombolytics and improved patient outcomes (mRS < 2 at 90 days poststroke).[9,23] The DTN time in our study (55 minutes) was comparable with the recently published Indian study (54 minutes),[24] whereas it was significantly delayed in another study (100 minutes).[25] We still have scope for more improvement, and efforts are on to further reduce DTN time at our center.

There were comparable differences between the present study and other similar studies in regard to stroke severity (measured with the NIHSS). Among IS patients, both the stroke severity and the rates of adherence to IV-rtPA therapy differed significantly ($p < 0.05$)

from the published studies from other parts of the world.[10,13,16–20] Fifty-two of 56 (92.8%) eligible patients received IV-rtPA therapy within 4.5 hours. Reasons for non-adherence to the guideline in four patients, though eligible, were stroke severity (NIHSS range, 5–10) and unaffordability issues as not covered under insurance schemes. The reason for ineligibility in the rest of the 144 (72%) IS patients was a delay in reporting to EMD (triage). Delay in presentation is the most common reason for exclusion from IV-rtPA therapy. Studies have found that only approximately 20–25% of patients with acute stroke could arrive in the hospital within 3 hours of symptom onset.[6,26,27] Similar findings (28%) were also observed in our study. Although in the present study there was high adherence to IV-rtPA therapy among eligible patients, insurance coverage among overall patients was very low (< 40%). Possible lack of stroke awareness as a neurological life-threatening emergency ("time is brain"), compounded with no or low insurance coverage, and unaffordability of medical expenses for some of the patients in the present study were the primary reasons attributed to the delay in getting admitted to EMD (triage). Also, many of the patients were from the outskirts of the city and rural areas around the city. The unavailability of emergency medical services or nearby health clinic facilities in the rural or outskirts of the city and inaccessibility to governmental health schemes at local hospitals were some additional but unavoidable reasons for not getting IV-rtPA therapy.

Many of the ICH patients (25% with all-or-none measures) did not get the eligible treatments, even those explicitly indicated by the consensus guidelines.[2,9,11,12] These guidelines advocate a quick radio imaging for stroke, DVTp following 48 hours of ICH admission, and smoking cessation. The provision of evidence-based DVTp therapy (UFH or LMWH) was much less frequent in ICH patients compared to IS patients, with the exception that ICH patients were more likely to get rapid radio imaging. The adherence to dysphagia screening as an acute measure was equivalent in both cerebrovascular event types. The relatively better but still suboptimal performance on rapid CT/MRI imaging and dysphagia screening in ICH patients could be related to the known increased ICH severity compared to IS patients. We were able to directly test this hypothesis because the NIHSS is routinely documented in our clinical practice and is a mandatory data element at our tertiary care center. A relatively struggling DVTp adherence rate may be a result of clinicians' concerns about high NIHSS, the degree of hematoma, and worries about expanding hematoma.

In IS patients, the use of ATs on arrival and at discharge is crucial and is advised to cut down the risk of stroke recurrence, or TIA.[2,9,11] In the present study, the use of ATs was optimal (92.6% in eligible patients) during hospitalization or at discharge, and more than three-quarters of patients with atrial fibrillation received anticoagulants at discharge as international normalized ratio (INR) monitoring was routinely advised in our university hospital. The utilization of lipid-lowering therapies was considerably higher (97.8%) in the present study, which was in line with the findings regarding the utilization of secondary prevention methods for IS in the United States[7,10] and China[17] after a continuous quality improvement program.

Hypertension is the most important risk factor for stroke in India.[28] Therefore, it was evident in the present study that the optimal (>80%) use of antihypertensive therapy was present in eligible patients at hospital discharge as a performance measure. Recent data[29] proves that diabetes is an important modifiable risk factor for stroke, especially IS. Case–control and cohort studies give insights into the association of diabetes with ICH.[30] Hyperglycemia during the acute stroke phase is associated with poor neurofunctional outcomes in both IS and ICH patients. Hence, more than 80% of eligible patients were administered ADs in the present study. There is some evidence that ICH incidence is linked to diabetes and obesity, implying that treating these illnesses might lessen the likelihood of recurrent ICH.[30] Whether or not addressing these risk factors minimizes the likelihood of recurrent ICH, primary prevention guidelines for coronary heart disease and IS support their management.

To understand the clinical and statistical relationship between adherence to clinical performance measures and clinical outcomes (especially neurofunctional outcomes), the American Hospital Association/American College of Cardiology task force on performance measures has recommended that stroke outcomes be measured at least 28 days after hospital discharge.[11,12] We observed that adherence to all 5 in-hospital (acute) performance measures was associated with reduced hazards of mortality after admission in both the IS and ICH patients. Also, it was evidently found that optimal adherence to the secondary prevention measures at discharge was associated with a reduced rate of mortality and an increased rate of favorable functional outcome (at the 28th-day postdischarge). This supports the need for such timely guideline-based interventions and continuous monitoring of the processes to enhance stroke quality of care.

Strengths and Limitations

The prospective, consecutive data collection on patient cohorts with IS and ICH, as well as the extensive data collection on a variety of particular care processes and outcomes up until the 1-month follow-up, are significant strengths of this study. Only patients who met the requirements for each quality metric and no documented patient objections or contraindications to the particular processes of care were included.

Due to the limitations, when we looked at the relationship between the cerebrovascular event and the clinical outcomes, we did not adjust for a wide range of patient characteristics to reduce confounding. This was due to the lack of previous data at the hospital, the lack of nationwide and registry-based standardized data. As the present study hospital was an urban tertiary-care academic center with stroke and other multidisciplinary experts who are constantly engaged in quality improvement to deliver optimum stroke care, the present data likely do not reflect the nationwide risk factor, prevalence, and quality of care in India. Therefore, the results of our study may have limited generalizability to academic hospital practice.

Conclusion

The present study showed that both, but especially IS patients, compared to ICH patients who have received an optimal acute and discharge-eligible process of care showed significantly improved functional independence at the end of the 28th-day postdischarge. The provided optimal stroke quality metrics showed a positive relationship between acute reperfusion treatments and neurofunctional recovery in IS patients. DVTp as an in-hospital (acute) care quality metric needs attention in both cerebrovascular event types. Nationwide registry development and such quality assessment and improvement studies are required for the generalization of these results.

Authors' Contributions

Authors BKP and VRS conceived the idea; GA, NB, and VRS were involved in data acquisition, interpretation, and statistical analysis; VRS, GA, NB, and BKP performed the review of the literature and drafted the manuscript; BKP, VRS, SI, and JS supervised the study, reviewed the manuscript, improved for intellectual content, and approved the final version.

Acknowledgments

The authors acknowledge the staff and the experts of the Departments of Medicine, Neurology, Emergency Medicine, and Critical Care Medicine for their immense support in the smooth conduction of the study and providing their valuable insights.

Orcid

Bijoy Kumar Panda https://orcid.org/0000-0001-8807-196X
Vaibhav R Suryawanshi https://orcid.org/0000-0001-8334-4025
Gargi Attarde https://orcid.org/0009-0003-4795-1145
Nilima Borkar https://orcid.org/0009-0008-9402-9504
Shivakumar Iyer https://orcid.org/0000-0001-5814-2691
Jignesh Shah https://orcid.org/0000-0002-8812-8791

References

1. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. Lancet Neurol 2009;8(4):345–354. DOI: 10.1016/S1474-4422(09)70023-7.
2. Khurana D, Padma MV, Bhatia R, Kaul S, Pandian J, Sylaja PN, et al. Guideline Core Committee. Recommendations for the early management of acute ischemic stroke: A consensus statement for healthcare professionals from the Indian Stroke Association. J Stroke Med 2018;1(2):79–113. DOI: 10.1177/2516608518777935.
3. Kamalakannan S, Gudlavalleti ASV, Gudlavalleti VSM, Goenka S, Kuper H. Incidence & prevalence of stroke in India: A systematic review. Indian J Med Res 2017;146(2):175–185. 10.4103/ijmr.IJMR_516_15.
4. Dalal PM, Bhattacharjee M, Vairale J, Bhat P. Mumbai stroke registry (2005–2006): Surveillance using WHO steps stroke instrument—challenges and opportunities. J Assoc Physicians India 2008;56: 675–680. PMID: 19086353.
5. Nagaraja D, Gururaj G, Girish N, Panda S, Roy AK, Sharma GRK, et al. Feasibility study of stroke surveillance: Data from Bangalore, India. Indian J Med Res 2009;130(4):396–403. PMID: 19942742.
6. Reeves MJ, Arora S, Broderick JP, Frankel M, Heinrich JP, Hickenbottom S, et al. Acute stroke care in the US: Results from 4 pilot prototypes of the Paul Coverdell National Acute Stroke Registry. Stroke 2005;36(6):1232–1240. 10.1161/01.STR.0000165902.18021.5b.
7. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, et al. Get with the guidelines—stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. Circulation 2009;119(1):107–115. DOI: 10.1161/CIRCULATIONAHA.108.783688.
8. Reeves MJ, Parker C, Fonarow GC, Smith EE, Schwamm LH. Development of stroke performance measures: Definitions, methods, and current measures. Stroke 2010;41(7):1573–1578. DOI: 10.1161/STROKEAHA.109.577171.
9. Jauch EC, Saver JL, Adams Jr HP, Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013;44(3):870–947. DOI: 10.1161/STR.0b013e318284056a.
10. Fonarow GC, Reeves MJ, Smith EE, Saver JL, Zhao X, Olson DW, et al. Characteristics, quality indicators, 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. DOI: 10.1161/CIRCOUTCOMES.109.921858.
11. Smith EE, Saver JL, Alexander DN, Furie KL, Hopkins LN, Katzan IL, et al. Clinical performance measures for adults hospitalized with acute ischemic stroke: Performance measures for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014;45(11):3472–3498. DOI: 10.1161/STR.0000000000000045.
12. Hemphill III JC, Adeoye OM, Alexander DN, Alexandrov AW, Amin–Hanjani S, Cushman M, et al. Clinical performance measures for adults hospitalized with intracerebral hemorrhage: Performance measures for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2018;49(7):e243–e261. DOI: 10.1161/STR.0000000000000171.
13. Wang Y, Li Z, Zhao X, Liu L, Wang C, Wang C, et al. Evidence-based quality indicators and outcomes in patients with acute ischemic stroke: Findings from the China National Stroke Registry. Circ Cardiovasc Quality Outcomes 2018;11(12):e001968. DOI: 10.1161/CIRCOUTCOMES.115.001968.
14. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: A literature review and synthesis. Stroke 2007;38(3):1091–1096. DOI: 10.1161/01.STR.0000258355.23810.c6.
15. Saver JL, Chaisinanunkul N, Campbell BC, Grotta JC, Hill MD, Khatri P, et al. Stroke Treatment Academic Industry Roundtable. Standardized nomenclature for modified Rankin scale global disability outcomes: Consensus recommendations from stroke therapy academic industry roundtable XI. Stroke 2021;52(9):3054–3062. DOI: 10.1161/STROKEAHA.121.034480.
16. Li Z, Pandian J, Sylaja PN, Wang Y, Zhao X, Liu L, et al. Quality of care for ischemic stroke in China vs India: Findings from national clinical registries. Neurology 2018;91(14):e1348– e1354. DOI: 10.1212/WNL.0000000000006291.
17. Gu HQ, Yang X, Wang CJ, Zhao XQ, Wang YL, Liu LP, et al. Clinical characteristics, management, and in-hospital outcomes in patients with stroke or transient ischemic attack in China. JAMA Network Open 2021;4(8):e2120745. DOI: 10.1001/jamanetworkopen.2021.20745.
18. Ren N, Ogata S, Kiyoshige E, Nishimura K, Nishimura A, Matsuo R, et al. Associations between adherence to evidence-based, stroke quality indicators and outcomes of acute reperfusion therapy. Stroke 2022;53(11):3359–3368. DOI: 10.1161/STROKEAHA.121.038483.
19. Haas K, Rücker V, Hermanek P, Misselwitz B, Berger K, Seidel G, et al. Association between adherence to quality indicators and 7-day in-hospital mortality after acute ischemic stroke. Stroke 2020;51(12):3664–3672. DOI: 10.1161/STROKEAHA.120.029968.
20. Machline–Carrion MJ, Santucci EV, Damiani LP, Bahit MC, Málaga G, Pontes–Neto OM, et al. Effect of a quality improvement intervention on adherence to therapies for patients with acute ischemic stroke and transient ischemic attack: A cluster randomized clinical trial. JAMA neurology 2019;76(8):932–941. DOI: 10.1001/jamaneurol.2019.1012.
21. Samavedam S. If time is neuron, what are we waiting for? Indian J Crit Care Med 2023;27(2):87–88. DOI: 10.5005/jp-journals-10071-24412.
22. Shah A, Diwan A. Stroke thrombolysis: Beating the clock. Indian J Crit Care Med 2023;27(2):107–110. DOI: 10.5005/jp-journals-10071-24405.
23. Fonarow GC, Zhao X, Smith EE, Saver JL, Reeves MJ, Bhatt DL, et al. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. JAMA 2014;311:1632–1640. DOI: https://doi.org/10.1001/jama.2014.3203.
24. Nagendra CV, Kumar TSS, Bohra V, Wilben V, Karan V, Huded V. Factors affecting the effective management of acute stroke: A prospective

observational study. Indian J Crit Care Med 2018;22(3):138–143. DOI: 10.4103/ijccm.IJCCM_232_17.
25. Gurav SK, Zirpe KG, Wadia RS, Pathak MK, Deshmukh AM, Sonawane RV, et al. Problems and limitations in thrombolysis of acute stroke patients at a tertiary care center. Indian J Crit Care Med 2015;19(5): 265–269. DOI: 10.4103/0972-5229.156468.
26. Barber PA, Zhang J, Demchuk AM, Hill MD, Buchan AM. Why are stroke patients excluded from TPA therapy? An analysis of patient eligibility. Neurology 2001;56(8):1015–1020. DOI: 10.1212/wnl.56.8.1015.
27. Kleindorfer D, Kissela B, Schneider A, Woo D, Khoury J, Miller R, et al. Eligibility for recombinant tissue plasminogen activator in acute ischemic stroke: A population-based study. Stroke 2004;35(2): e27–e29. DOI: 10.1161/01.STR.0000109767.11426.17.
28. Turana Y, Tengkawan J, Chia YC, Nathaniel M, Wang JG, Sukonthasarn A, et al. Hypertension and stroke in Asia: A comprehensive review from HOPE Asia. J Clin Hypertens (Greenwich) 2021;23(3):513–521. DOI: 10.1111/jch.14099.
29. Chen R, Ovbiagele B, Feng W. Diabetes and stroke: Epidemiology, pathophysiology, pharmaceuticals and outcomes. Am J Med Sci 2016;351(4):380–386. DOI: 10.1016/j.amjms.2016.01.011.
30. Boulanger M, Poon MT, Wild SH, Al-Shahi Salman R. Association between diabetes mellitus and the occurrence and outcome of intracerebral hemorrhage. Neurology 2016;87(9):870–878. DOI: 10.1212/WNL.0000000000003031.