ORIGINAL ARTICLE

An impact of treatment initiation timing on stroke outcome: bridging the time gap

Kuanysh Nikatov[1], Ermek Dyussembekov[1], Rauan Kastey[2], Yevgeniy Zhukov[1], Niyazbek Yerniyazov[3], Mukhtar Korabayev[4], Gani Akhanov[1], Timur Saliev[1], Ildar Fakhradiyev[1]

[1]S.D. Asfendiyarov Kazakh National Medical University, Almaty, [2]City Clinical Hospital No 7, Almaty, [3]Multidisciplinary hospital named after prof. Kh. Zh. Makazhanov, Karagandy, [4]Municipal State Enterprise on the Right of Economic Management "East Kazakhstan Region Specialized Medical Center" of Health Care Administration of East Kazakhstan Region, Ust-Kamenogorsk; Republic of Kazakhstan

ABSTRACT

Aim Stroke treatment is a time-critical condition. Understanding the impact of timing and types of treatment on patient outcomes can help develop and optimize stroke management strategies.

The study aimed to analyse the effect of different time intervals and mechanical thrombectomy methods on outcomes of stroke patients in Kazakhstan.

Methods The patient data, including demographic information, clinical characteristics, and specific time intervals from stroke onset to hospital admission, stroke onset to surgery initiation, and hospital admission to surgery initiation were collected. A total of 100 patients were analysed. Patients' neurological status was evaluated using the National Institutes of Health Stroke Scale (NIHSS), Modified Rankin Scale (mRS), and Glasgow Coma Scale (GCS) before and after the surgical treatment.

Results Most patients had concomitant arterial hypertension, and almost 25 % had diabetes mellitus. The average time from stroke onset to hospital admission was 123.2±7.6 minutes, and from hospital admission to surgery initiation, it was 134.7±13.1 minutes. A shorter duration from the onset of stroke to hospitalization and surgery was associated with better clinical outcomes. Our results demonstrated a statistically significant decrease in NIHSS, mRS after surgical treatment compared to baseline. The association between the extended time from stroke onset to hospitalization and reduced survival rates was observed.

Conclusion Our findings indicate the essential role of timely intervention in managing stroke patients, as well as the need for a comprehensive and patient-centred approach to stroke care.

Key words: cerebrovascular accident, hospitalization, mechanical thrombolysis, treatment delays

Corresponding author:
Ildar Fakhradiyev
S.D. Asfendiyarov Kazakh
National Medical University
Tole-bi str., 94, Almaty, 050020,
Republic of Kazakhstan;
E-mail: fakhradiyev.i@kaznmu.kz
Phone: +7 707 500 1190;
Kuanysh Nikatov ORCID ID: https://orcid.org/ 0000-0002-3606-2874

Original submission:
07 August 2023;
Revised submission:
17 August 2023;
Accepted:
23 September 2023
doi: 10.17392/1658-23

Med Glas (Zenica) 2024; 21(1):98-106

INTRODUCTION

Globally, stroke is recognized as the second leading cause of mortality and the one of the main causes of disability (1). The situation with stroke is similar to a global trend. Based on data for the period from 2014-2019, 177 947 stroke patients were registered in Kazakhstan, which is similar with other countries worldwide. Even though the annual incidence rate remained stable, a two-fold increase in the all-cause mortality rate among stroke patients was observed during this period (2).

This alarming rise in mortality indicates the urgency to refine and optimize stroke patient care, focusing on modifiable factors. An area that demands attention is the correlation between the time of stroke onset and both the short-term and long-term outcomes (3). It is crucial to expedite both the patient examination process and the initiation of appropriate treatment following stroke onset (4). The mantra "Time is Brain" in acute ischemic stroke management encompasses this notion, and includes both "onset-to-door time" and "door-to-needle time" (5). In fact, the reperfusion therapy employing tissue plasminogen activator (tPA) can enhance clinical outcomes in stroke if provided within the first 4.5 hours (6). Reports suggest that less than 30% of patients have been admitted to the hospital within this timeframe due to pre-hospital delays (7). Previous studies have shown that reperfusion within six hours of symptom onset led to better clinical outcome (8). However, intravenous tPA does not always result in recanalization, and its success rate depends on the severity of the occlusion (9), which often necessitates mechanical thrombectomy.

Despite the understanding of the significance of prompt stroke treatment initiation, there remain serious challenges in the stroke care system in Kazakhstan. Factors such as delays in receiving medical care, inefficiencies in prehospital treatment, problems with diagnosis and specialized therapies can severely impede patient's recovery post-stroke (8). This not only compromises patient’s quality of life, but also amplifies the socio-economic burden on the country's healthcare system (10).

To date, no studies have been conducted in Kazakhstan to investigate the impact of stroke onset on hospitalization and surgery timing on patient outcomes. The goal of this study was to bridge this knowledge gap. The findings can serve as a valuable guidepost for the future evolution of stroke services in Kazakhstan.

The primary objective was to examine the role of time in managing patients with stroke in a clinical setting. We aimed to understand the impact of various time intervals on patient outcomes, including the duration from the onset of stroke to hospital admission, from stroke onset to surgery initiation, and from hospital admission to surgery. Furthermore, the study was focused on the assessment of the effectiveness of different types of mechanical thrombectomy (stenting, aspiration, and their combined use) on patient outcomes by analysing changes in National Institutes of Health Stroke Scale (NIHSS) (11), Modified Rankin Scale (mRS) (12), and Glasgow Coma Scale (GCS) (13) scores.

PATIENTS AND METHODS

Patients and study design

The data from 180 patients admitted to the City Clinical Hospital No 7 in Almaty, Kazakhstan, in the period between 2018 and 2022 were analysed. These patients had a primary diagnosis of haemorrhagic or ischemic stroke, aligning with the study's inclusion criteria, based on the International Classification of Diseases, 10th revision (ICD-10) (14). The collected data included gender, age (the age of the patients was classified as up to 35, 36-44, 45-59, 60-74, 75-90, >91), history of arterial hypertension, presence of heart rate (HR) rhythm disturbances, presence of diabetes mellitus, systolic and diastolic blood pressure readings, blood glucose levels.

We conducted follow-up calls with patients or their relatives at 6 and 12 months post-discharge to assess life/death outcomes.

The Ethical Committee of the Higher School of Public School (IRB-A074/A 11/15/2018) approved the performance of this study. All research procedures adhered to the ethical principles of the World Medical Association as per the Declaration of Helsinki.

Methods

Several established scales for assessing stroke patients were used, including the ASPECT (Alberta Stroke program Early CT score) (15), Glasgow Coma Scale (GCS) (13), The Modified Rankin

Scale (mRS) (12), AOL (16), TICI (17), National Institutes of Health Stroke Scale (NIHSS) (11) scales.

ASPECTS scale (Alberta's program for assessing the symptoms of CT changes in stroke) is a 10-point scale for a qualitative topographic assessment of changes detected by computed tomography (15). For ASPECTS of the territory of the middle cerebral artery, 10 points are assigned - 1 point is deducted for the area of early ischemic changes, such as focal oedema or parenchymal hypoattenuation, for each of the identified areas. Conventional computed tomography has an ASPECTS value of 10 points. A score of 0 indicates diffuse ischemia throughout the middle cerebral artery (15).

The Glasgow Coma Scale (GCS) (13) is divided into three behavioural components: eye opening (E), verbal response (V), and motor response (M). Each component is evaluated independently and assigned a score, and the sum of the scores for the three components is the total score. The maximum score is 15 and the minimum is 3, but clinical data should include more than the GCS score because it can be the sum of the various components. A score of 13, for example, may represent a patient who spontaneously opens his eyes (E4), is confused (V4), and is in pain (M5); or it may represent a patient opening her eyes to speak (E3), orienting herself (V5), and localizing to the area of pain (M5) (13).

The Modified Rankin Scale (mRS) is a universal tool for assessing the independence and disability of patients in medical rehabilitation. This scale is a simplified global assessment of function, with the score of 0 indicating no impairment, while the score of 5 indicates severe disability. The mRS score ranges from normal (0) to death (6) (12).

Thrombolysis in Cerebral Infarction (TICI) scale is a widely used scoring system for assessing the degree of reperfusion achieved after mechanical thrombectomy (17). This scale is used to assess the degree of perfusion obtained after recanalization of an arterial occlusion. Recanalization of arterial occlusion increases reperfusion in the distal segments of the artery and restores blood flow to the brain tissue. Scores can range from 0 (no perfusion) to 3 (completely perfused with all distal branches filled).

Arterial Occlusive Lesion (AOL) scale is a scoring system used to determine the degree of arterial occlusion (blockage) in stroke patients. It is designed to predict the possibility of recanalization (restoration of blood flow) after tPA therapy. The AOL scale consists of four levels (0-3) that describe the degree of arterial occlusion (16): AOL - complete occlusion, no contrast agent passing through; AOL 1 - incomplete occlusion, contrast agent passes through the occlusion but does not fill the entire distal (further from the centre of the body) vasculature;

AOL 2 - the contrast agent passes through the site of occlusion and fills more than half of the distal vasculature; AOL 3 - complete passage of the contrast agent with more than 50% filling of the distal vasculature in the usual timeframe.

The National Institutes of Health Stroke Scale (NIHSS) (before and after treatment) is a 15-item impairment scale designed to assess neurological outcomes and recovery in stroke patients. The scale assesses the level of consciousness, extraocular movements, visual fields, facial muscle function, limb strength, sensory functions, coordination (ataxia), language (aphasia), speech (dysarthria) and semi-attention (neglect) (11). When assessing the severity of stroke at admission, the NIHSS scores were interpreted as follows: a score of up to 4 points was considered a minor stroke, 5 to 15 points a moderate stroke, 16 to 20 points a severe stroke, and 21 points or over a very severe stroke (11).

The time of onset of acute stroke was assessed by paramedics in case of being at home or by a neurologist in case of inpatient conditions based on the clinical diagnostic protocol approved in Kazakhstan’s Republican Centre for Healthcare Development of the Ministry of Health of the Republic of Kazakhstan (18).

Start-to-door time was defined as the time of arrival at the emergency department minus the time of onset of the stroke. The time of arrival at the hospital was the earliest recorded in the medical record. The time of stroke onset was noted by the physicians for each patient as the last time the patient was known to be normal. Thus, the duration of the time intervals from the onset of a stroke to the time of hospitalization, as well as from the onset of a stroke to the start of the operation, was determined, which were divided into 9 categori-

es: 1 - 0 to 1 hour; 2 - from 1 hour to 2 hours; 3 - from 2 hours to 3 hours; 4 - from 3 hours to 4 hours; 5 - from 4 hours to 5 hours; 6 - from 5 hours to 6 hours; 7 - from 6 hours to 7 hours; 8 - from 7 hours to 8 hours; 9 - from 8 hours or more.

Surgical interventions included stent placement, aspiration, and combined treatment. The choice of intervention was based on patient's conditions, such as the location and volume of occlusion, overall health status, and other factors (19).

Statistical Analysis

Data analysis employed measures (M) and standard deviation (SD), with the Student's t-test used to test for statistical significance. Pearson correlation we used to determine the relationship between the treatment initiation time and stroke outcome, and linear regression to assess a correlation between treatment initiation time and hospitalization duration. Confounding factors were controlled for using multivariate analysis, which allowed for the adjustment of odds ratios in analysing long-term outcomes. Kaplan-Meier analysis was utilized for determining patient survival rates.

RESULTS

The study enrolled a total of 180 stroke patients, with a higher number of males, 98 (54.4 %), and the majority falling in the age group of 60-74 years, 88 (48.9%). A significant number of patients had a history of arterial hypertension, 160 (88.9 %), HR rhythm disturbance, 62 (34.4 %), and diabetes mellitus, 44 (24.4 %). The average systolic blood pressure was recorded at 148.6±26.8 mmHg, diastolic blood pressure at 88.1±12.2 mmHg, and the mean blood glucose level was 7.9±3.1mmol/L. The mean ASPECT, AOL, and TICI scores were 6.9±3.7, 1.5±1.3, and 0.5±0.4 respectively (Table 1).

In addition, the study analysed the time characteristics of stroke cases (Table 2). There was no statistically significant difference (p=0.531) between the average time from stroke onset to hospitalization on weekdays and weekends. Similarly, there was no significant difference in the time interval from hospitalization to the start of surgery between weekdays and weekends (p=0.207).

The NISSH, mRS, and GCS scores in relation to the type of surgery (Table 3) showed that patients treated with the combination therapy had a significant postoperative deterioration on the NISSH and mRS scales (p=0.001 and p=0.004, respectively). However, patients who underwent stenting had better scores on the GCS scale both preoperatively and postoperatively (p=0.015).

Table 1. General clinical and demographic characteristics of 180 stroke patients

Variable	Values
	No (%)
Gender	
Male	98 (54.4)
Female	82 (45.6)
Age (years)	
Up to 35	2 (1,1)
36-44	4 (2,2)
45-59	34 (18.9)
60-74	88 (48.9)
75-90	52 (28.9)
A history of hypertension	
Yes	160 (88.9)
No	20 (11.1)
Violation of heart rate rhythm	
Yes	62 (34.4)
No	118 (65.6)
Diabetes mellitus	
Yes	44 (24.4)
No	136 (75.6)
	Mean±SD
Blood pressure	
Systolic BP	148.67±26.833
Diastolic BP	88.11±12.226
Blood glucose	7.9426±3.13333
ASPECT	6.97±3.765
AOL	1.58±1.370
TICI	0.57±0.497

BP, Blood Pressure; ASPECT, Alberta Stroke Program Early CT Score; AOL, Arterial Occlusive Lesion; TICI, Thrombolysis in Cerebral Infarction;

Table 2. Comparative temporal characteristics of stroke patients included in the study

Time frame (h)	No (%) of patients						Total			p
	Weekdays 134 (74.4)			Weekend 46 (25.6)						
	Mean±SD	95% CI		Mean±SD	95% CI		Mean±SD	95% CI		
		Lower	Upper		Lower	Upper		Lower	Upper	
Time from onset to hospitalization	126.0±99.9	108.9	143.1	115.0±108.3	82. 9	147.2	123.2±7.6	108.2	138.2	0.531
Time from hospitalisation time to operation start time	144.4±196.1	110.9	177.9	106.4±90.6	79.5	133.3	134.7±13.1	108.9	160.6	0.207
Time from onset to operation start time	270.4±238.5	229.7	311.2	221.5±119.3	186.0	256.9	257.9±16.0	226.3	289.6	0.184

CI, confidence interval

Table 3. Comparative characteristics of indicators on the National Institutes of Health Stroke Scale (NISSH), Modified Rankin Scale (mRS) and Glasgow Coma Scale (GCS) scales depending on the type of operation in pa tients with stroke

Characteristics	Type of surgery									p
	Stenting			Aspiration			Combined			
	Mean±SD	95% CI		Mean±SD	95% CI		Mean±SD	95% CI		
		Lower	Upper		Lower	Upper		Lower	Upper	
NISSH before	14.41±4.2	13.72	15.09	14.8± 8.9	8.48	21.12	14.73±3.8	13.01	16.45	0.926
NISSH after	11.23±8.7	9.81	12.65	5.8± 6.7	1.02	10.58	18.82±11.4	13.77	23.87	0.00 1
p		0.025 _								
mRS before	3.91±1.9	3.59	4.22	3.0± 2.6	1.15	4.85	4.82 ± 0.4 _	4.64	4.99	0.026
mRS after	3.30±2.0	2.97	3.63	2.4±2.7	.46	4.34	4.64 ± 0.6	4.34	4.93	0.004
p		0 .00 1								
GCS before	13.36±1.7	13.09	13.64	11.2±5.9	6.92	15.48	12.91±1.5	12.23	13.59	0.007
GCS after	12.51±4.2	11.83	13.20	9.0 ±7.7	3.46	14.54	10.55± 4.8	8.43	12.66	0.015
p		0 .00 1								

CI, confidence interval

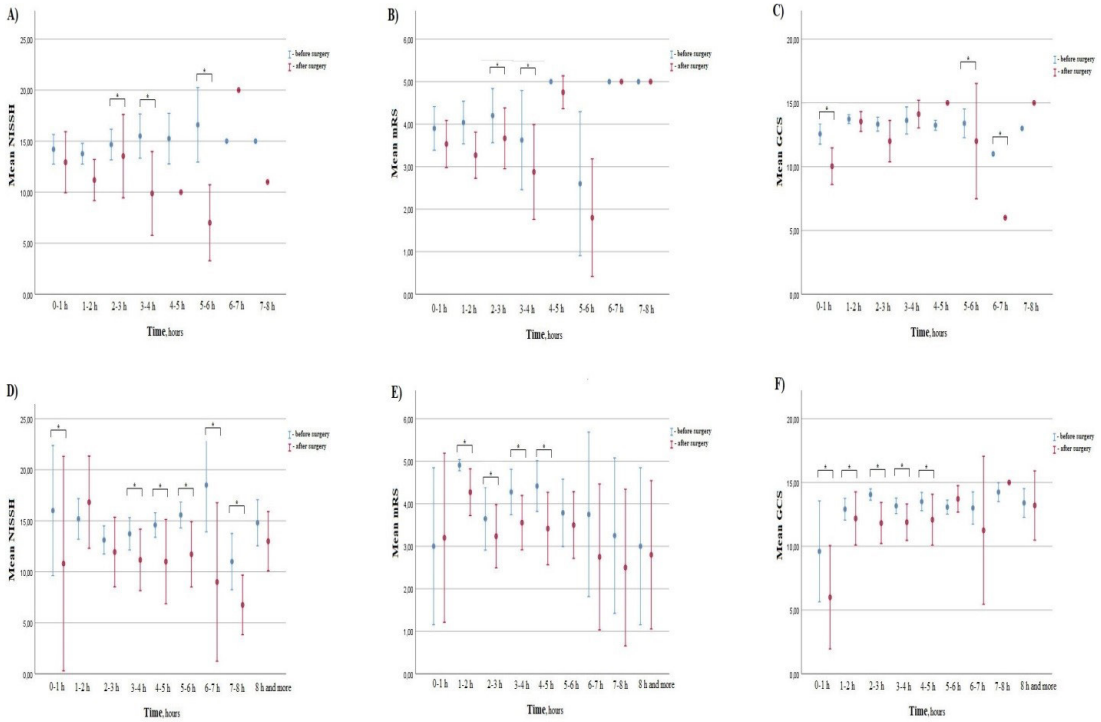

Figure 1. Evaluation of the effect of time from: A) stroke onset to time of hospitalization on National Institutes of Health Stroke Scale (NISSH) scores; B) stroke onset to time of hospitalization on Modified Rankin Scale (mRS) scores; C) stroke onset to time of hospitalization on Glasgow Coma Scale (GCS) scores; D) the onset of stroke to surgery on NISSH scores; E) the onset of stroke to surgery on the mRS scores; F) the onset of stroke to surgery on the GCS scores

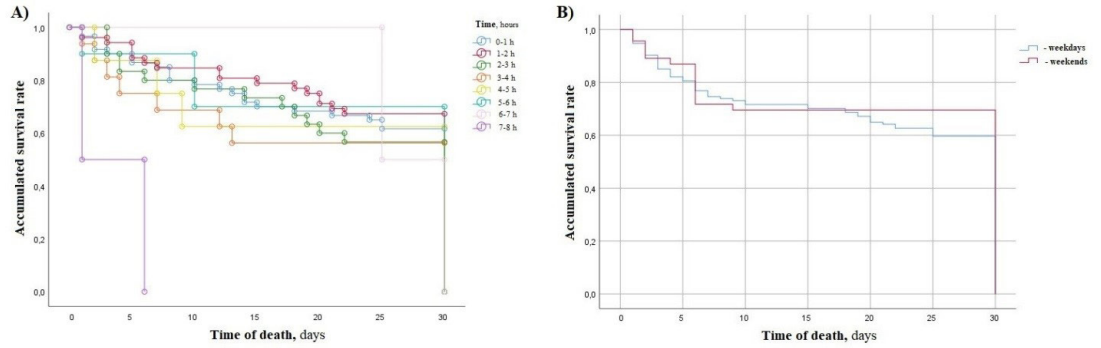

Figure 2. Survival rate of patients with stroke depending on the duration of: A) the time interval from the onset of stroke to the time of hospitalization; B) the registration of stroke on weekdays or on weekends

The majority of the patients, absolute number (52.2%) had an interval of 2-5 hours from the onset of stroke to the start of surgery. Further evaluation showed that the time from the onset of stroke to hospitalization had a significant impact on the NISSH, mRS, and GCS scale indicators before and after surgery, with scores improving after surgery ($p \leq 0.05$) in these scores (Figure 1).

There was a statistically significant relationship ($p=0.015$) between increased duration from the onset of stroke to hospitalization and decreased survival rates (Figure 2A). However, there was no significant difference in survival rates based on whether the stroke was registered on a weekday or a weekend ($p=0.300$) (Figure 2B).

DISCUSSION

The data of the demographic and clinical characteristics of stroke patients in a major city in Kazakhstan showed a mean patient age above 65 years, with arterial hypertension being a common comorbidity, and nearly one-quarter of patients also had diabetes mellitus. These findings align with previous research findings indicating such characteristics in stroke patients (20).

Our investigation is focused on the importance of time in the treatment of stroke patients, specifically the time interval from stroke onset to surgery initiation. Our findings substantiate existing literature indicating better clinical outcomes for patients who receive treatment within the first 6 hours of stroke onset (21). The efficiency of treatment during this window is mainly due to the time-dependent nature of reperfusion treatments, which help restore the ischemic penumbra by reopening occluded arteries (22).

Various clinical trials have similarly stressed the importance of timely intervention in stroke treatment. The MR CLEAN trial revealed that mechanical thrombectomy, combined with standard therapy within 6 hours of stroke onset, led to better functional outcomes (23). The DAWN trial also highlighted the benefits of mechanical thrombectomy performed beyond 6 hours of symptom onset, especially when a mismatch existed between clinical symptoms and the infarct area (24). DEFUSE 3 presented evidence that patients who underwent mechanical thrombectomy within 16-24 hours of symptom onset had significantly better functional outcomes (25), and the ESCAPE trial emphasized the importance of minimizing the time from CT to recanalization (26).

Further, we examined the impact of different types of mechanical thrombectomy, specifically stenting and aspiration, on patient outcomes. Stenting, which restores blood flow in blocked arteries (27), and aspiration, which performs direct removal of blood clots (28), have different mechanisms of action and can result in varied outcomes (29). Our results suggested that patients undergoing the combination therapy could experience a greater deterioration in their condition due to the invasiveness of these procedures (30).

Another crucial aspect of stroke treatment that our study addresses is the door-to-needle time. We found no statistically significant difference in this time interval on weekdays or weekends. Nevertheless, our analysis revealed a statistically significant correlation between an increase in the duration of the time interval from the onset of stroke to hospitalization and a decrease in survival rates. Previous research corroborates our findings, demonstrating an increase in short-term mortality and disability at discharge for patients with extended door-to-needle times at weekends (31).

The delay in the prehospital phase, which prevents early arrival and administration of rTPA, could be due to the patient's lack of awareness of stroke symptoms, the expectation of symptom resolution, or lack of knowledge about the availability of emergency stroke intervention (32). Therefore, public health initiatives aimed at improving awareness about stroke symptoms and the criticality of seeking immediate medical help are imperative.

To summarize, our research underscores the essential role of time in managing stroke patients, emphasizing the necessity of rapid hospitalization and prompt initiation of treatment. Health promotion activities aiming at reducing prehospital delays could be the key to achieving optimal stroke treatment outcomes. Ultimately, patient's prognosis post-stroke depends on a complex interplay of individual characteristics, treatment choices, and time - emphasizing the need for a comprehensive, patient-centred, and timely approach to stroke care.

While our study provides useful insights, there are several limitations that should be taken into consideration. We could not account for variables such as the distance from the place where

the stroke occurred or from where the patient lived to the hospital (in terms of the distance). We also did not consider factors related to patient's perception of stroke symptoms and symptom recognition, or patient-specific characteristics like education level, pre-disease health status, socioeconomic status, social support, or psychological status, which may affect patient referral delays. Future prospective studies are needed to explore these factors further. Despite its limitations, this study highlights the importance of reducing prehospital waiting times and the need for health promotion activities aimed at increasing public awareness about the warning signs of stroke. Such efforts could significantly contribute to reducing delays in hospital visits and achieving optimal stroke treatment outcomes.

The uniqueness of this study refers to its detailed evaluation of time intervals and their impact on stroke patient outcomes in a specific geographic region of Kazakhstan. The incorporation of various types of mechanical thrombectomy treatments (stenting, aspiration, or combination) in the study design enhances its novelty, providing a comprehensive view of the effectiveness of each treatment modality.

Moreover, the investigation of clinical characteristics and demographics within the context of a largely unexplored patient population contributes to its uniqueness. By presenting this analysis, the study provides valuable insights that may inform local healthcare practices and policies, as well as contributing to the global understanding of stroke treatment and outcomes.

Lastly, the study's retrospective design allows for a realistic and practical view of current practices, offering valuable insights that can be used to guide future prospective studies and interventions to improve patient outcomes.

Overall, our research emphasizes the urgent need for a comprehensive, patient-cantered, and timely approach to stroke care. Health promotion activities aiming at reducing prehospital delays could be the key to achieving optimal stroke treatment outcomes. Our results highlight the importance of further clinical trials and studies to refine and optimize the time-sensitive management of stroke patients.

ACKNOWLEDGMENTS

The authors express their gratitude for the administrative and technical support provided by the S.D. Asfendiyarov Kazakh National Medical University.

FUNDING

No specific funding was received for this study.

TRANSPARENCY DECLARATION

Conflict of interest: None to declare.

REFERENCES

1. Ma Q, Li R, Wang L, Yin P, Wang Y, Yan C, Ren Y, Qian Z, Vaughn MG, McMillin SE, Hay SI, Naghavi M, Cai M, Wang C, Zhang Z, Zhou M, Lin H, Yang Y. Temporal trend and attributable risk factors of stroke burden in China, 1990-2019: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health 2021; 6:e897-e906.
2. Zhakhina G, Zhalmagambetov B, Gusmanov A, Sakko Y, Yerdessov S, Matmusaeva E, Imanova A, Crape B, Sarria-Santamera A, Gaipov A. Incidence and mortality rates of strokes in Kazakhstan in 2014-2019. Sci Rep 2022; 12:16041.
3. Schott AM, Termoz A, Viprey M, Tazarourte K, Vecchia CD, Bravant E, Perreton N, Nighoghossian N, Cakmak S, Meyran S, Ducreux B, Pidoux C, Bony T, Douplat M, Potinet V, Sigal A, Xue Y, Derex L, Haesebaert J. Short and long-term impact of four sets of actions on acute ischemic stroke management in Rhône County, a population based before-and-after prospective study. BMC Health Serv Res 2021; 21:12.
4. Yafasova A, Fosbøl EL, Johnsen SP, Kruuse C, Petersen JK, Alhakak A, Vinding NE, Torp-Pedersen C, Gislason GH, Køber L, Butt JH. Time to thrombolysis and long-term outcomes in patients with acute ischemic stroke: a nationwide study. Stroke 2021; 52:1724-32.
5. Shokri HM, El Nahas NM, Aref HM, Dawood NL, Abushady EM, Abd Eldayem EH, Georgy SS, Zaki AS, Bedros RY, Wahid El Din MM, Roushdy TM. Factors related to time of stroke onset versus time of hospital arrival: a SITS registry-based study in an Egyptian stroke center. PLoS One 2020; 15:e0238305.
6. Gonzalez-Aquines A, Cordero-Perez AC, Ramirez-Martinez LA, Sanchez-Teran H, Escobedo-Zuñiga N, Treviño-Herrera AB, Gongora-Rivera F, Pérez-Vázquez G, Contreras-Salazar K, Gómez-Padilla D. Onset-to-alarm time in patients with acute stroke: Results from a Mexican population. International journal of stroke: official journal of the Int J Stroke 2018; 13:NP19-NP21.

7. Nepal G, Yadav JK, Basnet B, Shrestha TM, Kharel G, Ojha R. Status of prehospital delay and intravenous thrombolysis in the management of acute ischemic stroke in Nepal. BMC Neurol 2019; 19:155.
8. Ni W, Kunz WG, Goyal M, Chen L, Jiang Y. Quality of life and cost consequence of delays in endovascular treatment for acute ischemic stroke in China. Health Econ Rev 2022; 12:4.
9. Hasan TF, Hasan H, Kelley RE. Overview of acute ischemic stroke evaluation and management. Biomedicines 2021; 9:1486.
10. Kunz WG, Hunink MG, Almekhlafi M A, Menon BK, Saver JL, Dippel DWJ, Majoie C, Jovin TG, Davalos A, Bracard S, Guillemin F, Campbell BCV, Mitchell PJ, White P, Muir KW, Brown S, Demchuk AM, Hill MD, Goyal M. Public health and cost consequences of time delays to thrombectomy for acute ischemic stroke. Neurology 2020; 95:e2465-e75.
11. Budinčević H, Meštrović A, Demarin V. Stroke Scales as Assessment Tools in Emergency Settings: A Narrative Review. Medicina (Kaunas) 2022; 58:1541.
12. Rebchuk AD, O'Neill ZR, Szefer EK, Hill MD, Field TS. Health utility weighting of the modified rankin scale: a systematic review and meta-analysis. JAMA Netw Open 2020; 3:e203767.
13. Bodien YG, Barra A, Temkin NR, Barber J, Foreman B, Vassar M, Robertson C, Taylor SR, Markowitz AJ, Manley GT, Giacino JT, Edlow BL. Diagnosing level of consciousness: the limits of the Glasgow Coma Scale total score. J Neurotrauma 2021; 38:3295-305.
14. Centers for Disease Control and Prevention. International Classification of Diseases,Tenth Revision (ICD-10). https://www.cdc.gov/nchs/icd/icd10.htm#. (13 June 2023).
15. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. Lancet 2000; 355:1670-4.
16. Marks MP, Lansberg MG, Mlynash M, Kemp S, McTaggart R, Zaharchuk G, Bammer R, Albers GW. Correlation of AOL recanalization, TIMI reperfusion and TICI reperfusion with infarct growth and clinical outcome. J Neurointerv Surg 2014; 6:724-8.
17. Behme D, Tsogkas I, Colla R, Gera RG, Schregel K, Hesse AC, Maier IL, Liman J, Liebeskind DS, Psychogios MN. Validation of the extended thrombolysis in cerebral infarction score in a real world cohort. PLoS One 2019; 14:e0210334.
18. Clinical Protocol of Stroke in Kazakhstan; 2016. http://www.rcrz.kz/index.php/ru (7 June 2023).
19. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2019; 50:e344-e418.
20. Ari BC. Retrospective analysis of the data of patients who were admitted to the secondary care hospital with the diagnosis of acute ischemic stroke and received intravenous thrombolytic therapy. North Clin Istanb 2023; 10:139-45.
21. Li X, Wu L, Xie H, Bao Y, He D, Luo X. Endovascular treatment for ischemic stroke beyond the time window: a meta-analysis. Acta Neurol Scand 2020; 141:3-13.
22. de Havenon A, Alexander MD, Nogueira RG, Haussen DC, Castonguay AC, Linfante I, Johnson M. A, Nguyen TN, Mokin M, Zaidat OO. Duration of symptomatic stroke and successful reperfusion with endovascular thrombectomy for anterior circulation large vessel occlusive stroke. J Neurointerv Surg 2021; 13:1128-31.
23. Fransen PS, Beumer D, Berkhemer OA, van den Berg LA, Lingsma H, van der Lugt A, van Zwam WH, van Oostenbrugge RJ, Roos YB, Majoie CB, Dippel DW. MR CLEAN, a multicenter randomized clinical trial of endovascular treatment for acute ischemic stroke in the Netherlands: study protocol for a randomized controlled trial. Trials 2014; 15:343.
24. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, Sila CA, Hassan AE, Millan M, Levy EI, Mitchell P, Chen M, English JD, Shah QA, Silver FL, Pereira VM, Mehta BP, Baxter BW, Abraham MG, Cardona P, Veznedaroglu E, Hellinger FR, Feng L, Kirmani JF, Lopes DK, Jankowitz BT, Frankel MR, Costalat V, Vora NA, Yoo AJ, Malik AM, Furlan AJ, Rubiera M, Aghaebrahim A, Olivot J.-M, Tekle WG, Shields R, Graves T, Lewis RJ, Smith WS, Liebeskind DS, Saver JL, Jovin TG.Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. N Engl J Med 2017; 378:11-21.
25. Albers GW, Lansberg MG, Kemp S, Tsai JP, Lavori P, Christensen S, Mlynash M, Kim S, Hamilton S, Yeatts SD, Palesch Y, Bammer R, Broderick J, Marks MP. A multicenter randomized controlled trial of endovascular therapy following imaging evaluation for ischemic stroke (DEFUSE 3). Int J Stroke 2017; 12:896-905.
26. Demchuk AM, Goyal M, Menon BK, Eesa M, Ryckborst KJ, Kamal N, Patil S, Mishra S, Almekhlafi M, Randhawa PA, Roy D, Willinsky R, Montanera W, Silver FL, Shuaib A, Rempel J, Jovin T, Frei D, Sapkota B, Thornton JM, Poppe A, Tampieri D, Lum C, Weill A, Sajobi TT, Hill MD. Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times (ESCAPE) trial: methodology. Int J Stroke 2015; 10:429-38.
27. Veunac L, Saliou G, Knebel JF, Bartolini B, Puccinelli F, Michel P, Hajdu SD. Revascularization of carotid artery occlusion using stenting versus non stenting in endovascular management of tandem occlusion stroke. J Clin Neurosci 2022; 98:15-20.
28. Sheng K, Tong M. Aspiration thrombectomy for posterior circulation stroke: a systematic review and meta-analysis. Asian J Neurosurg 2020; 15:251-61.

29. Meyer L, Stracke P, Wallocha M, Broocks G, Sporns P, Piechowiak EI, Kaesmacher J, Maegerlein C, Hernandez Petzsche MR, Dorn F, Zimmermann H, Naziri W, Abdullayev N, Kabbasch C, Behme D, Jamous A, Maus V, Fischer S, Möhlenbruch M, Weyland CS, Langner S, Meila D, Miszczuk M, Siebert E, Lowens S, Krause LU, Yeo L, Tan B, Gopinathan A, Gory B, Galván-Fernández J, Schüller M, Navia P, Raz E, Shapiro M, Arnberg F, Zeleňák K, Martínez-Galdámez M, Kastrup A, Papanagiotou P, Kemmling A, Psychogios M, Andersson T, Chapot R, Fiehler J, Hanning U. Aspiration versus stent retriever thrombectomy for distal, medium vessel occlusion stroke in the posterior circulation: a subanalysis of the TOPMOST study. Stroke 2022; 53:2449-57.
30. Texakalidis P, Giannopoulos S, Karasavvidis T, Rangel-Castilla L, Rivet DJ, Reavey-Cantwell J. Mechanical Thrombectomy in Acute Ischemic Stroke: A meta-analysis of stent retrievers vs direct aspiration vs a combined approach. Neurosurgery 2020; 86:464-77.
31. Sorita A, Ahmed A, Starr SR, Thompson KM, Reed DA, Dabrh AM, Prokop L, Kent DM, Shah ND, Murad MH, Ting HH. Off-hour presentation and outcomes in patients with acute ischemic stroke: a systematic review and meta-analysis. Eur J Intern Med 2014; 25:394-400.
32. Zakaria MF, Aref H, Abd ElNasser A, Fahmy N, Tork MA, Fouad MM, ElBokl A, Roushdy T, ElFaramawy S, El-Shiekh MA, Moustafa RR. Egyptian experience in increasing utilization of reperfusion therapies in acute ischemic stroke. Int J Stroke 2018; 13:525-9.