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REVIEW

Impact of Pre-Hospital and in-Hospital Optimization on the Management of Intravenous Thrombolysis in Hyperacute Ischemic Stroke: A Scoping Review

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Introduction: Stroke is the second leading cause of death worldwide and ranks third as a cause of disability. The American Heart Association/American Stroke Association (AHA/ASA) recommends that treatment begin within three hours of onset with intravenous thrombolysis therapy. This scoping review aimed to identify the factors that influence the delay in intravenous thrombolysis (IVT) management in patients with ischemic stroke.

Methods: We searched relevant studies in PubMed, ScienceDirect, and EBSCO and this review includes studies on ischemic stroke patients that analyze the factors contributing to delays in intravenous thrombolysis therapy, and it demonstrates that such delays are present in the management of IVT.

Results: A total of 48 studies were included in this study. Among pre-hospital factors, the most frequently reported contributors to delays in IVT for acute ischemic stroke (AIS) patients were the use of Emergency Medical Services (EMS) (12 studies), mode of hospital presentation (12 studies), comorbidities (6 studies), symptom recognition (5 studies), and timing of event (5 studies), with several studies reporting statistically significant associations ($p<0.05$). Emergency department use shortened hospital admission time by an average of 30 minutes, $p<0.05$Regarding in-hospital delay factors, the main contributors to delays included long scan times (5 studies), low NIHSS scores (5 studies), and limited implementation of stroke programs (5 studies). Other in-hospital delay variables included delayed activation of stroke codes (3 studies), inefficiency of human resources (3 studies), suboptimal triage processes (2 studies), diagnostic process (1 study), and logistics (1 study).

Conclusion: Delayed thrombolysis in ischemic stroke patients is caused by various factors, both pre-hospital and in-hospital. Community education and telemedicine can reduce delays by 30%. Collaboration between the community, stroke units, medical personnel, and the government through comprehensive programs is key in accelerating stroke treatment and improving patient clinical outcomes.

Keywords: hyperacute ischemic stroke, delay factor, intravenous thrombolysis, pre-hospital, in-hospital

Introduction

Stroke is the second leading cause of death worldwide and ranks third as a cause of disability.[1] Globally, approximately 68% of all stroke cases are ischemic.[1] Ischemic stroke occurs due to the blockage of blood vessels that limits blood supply to the brain.[1] In 2020, the number of ischemic stroke patients globally was recorded at 68.16 million, with new cases accounting for 65% of the total 11.71 million stroke cases overall.[2] The number of deaths from ischemic stroke cases in the same year reached 3.48 million.[2]

The lack of blood supply in ischemic stroke patients causes brain function disturbances or even leads to nerve cell death (necrosis).[3] In the first few hours after the onset of neurological dysfunction, this period becomes crucial in preventing death or permanent disability.[3] Rapid and precise intervention is critical during this phase, as it can reduce

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brain damage and increase the chances of recovery in ischemic stroke patients.[4] One of the tools used to assess the severity of a patient's initial stroke is the National Institutes of Health Stroke Scale (NIHSS) score.[5] The NIHSS score is obtained through an initial neurological examination aimed at determining the severity of the stroke, monitoring changes in the patient within the first 24 hours, and predicting the patient's likelihood of future recovery.[6,7]

The American Heart Association/American Stroke Association (AHA/ASA) recommends intravenous thrombolysis therapy as the primary treatment method for ischemic stroke patients who arrive within 3 hours of onset.[1] For patients who meet certain criteria, the therapeutic window can be extended up to 4.5 hours from onset.[1] Thrombolytic agents in the form of recombinant tissue plasminogen activator (r-tPA) have been proven effective in reducing the negative impact of ischemic stroke attacks by increasing blood flow to the brain.[8] This therapy focuses on restoring cerebral circulation through r-tPA intravenous thrombolysis (IVT), as a strategy to reduce the morbidity and mortality rates of stroke.[9] However, it is unfortunate that there is often a delay in the recognition and management of stroke, which impacts the final treatment outcomes.[4]

Although effective treatments such as intravenous thrombolysis therapy are available, only a few ischemic stroke patients qualify for access to the therapy.[9] Globally, only 1–13% of patients who meet the criteria receive the therapy.[9] Research reveals that the low recovery rates of ischemic stroke patients are caused by various factors, ranging from delays in patient arrival at the hospital to factors present within the hospital itself.[10] Ischemic stroke patients with symptom onset more than 4.5 hours, a history of non-traumatic intracranial hemorrhage, suspected thoracic aortic dissection, or showing ischemic changes on Magnetic Resonance Imaging (MRI), are considered ineligible for intravenous thrombolysis therapy. The administration of intravenous thrombolysis therapy in such conditions increases the risk of somatic intracranial hemorrhage, up to death.[11]

Various challenges lead to delays in administering r-tPA IVT therapy, which ultimately affects the treatment outcomes of ischemic stroke patients. Every minute of delay can reduce the chances of achieving a good quality of life.[12] Therefore, the time from the patient's arrival at the hospital to the start of intravenous thrombolysis therapy, known as Door-to-Needle Time (DNT), becomes an important indicator in assessing the quality of ischemic stroke care.[12] Not only does it play a role in reducing mortality rates and the risk of symptomatic intracranial hemorrhage, but a shorter DNT also improves the independent ambulation of ischemic stroke patients upon discharge from the hospital, as well as better functional outcomes within 3 months post-treatment.[13]

The concept of "Time is brain" underscores the importance of the speed of intravenous thrombolysis administration to improve the prognosis of ischemic stroke patients, reducing Door-to-Needle Time (DNT), a priority in enhancing the quality of care.[12] Additionally, the time difference between the onset of stroke symptoms and the patient's arrival at the hospital, Onset-to-Door Time (ODT), is also an important parameter in the management of ischemic stroke.[14] If the patient cannot recall when the symptoms first appeared, the onset time is considered unknown.[12] This time factor is closely related to high rates of mortality, complications, and long-term neurological disabilities. Every 10-minute delay reduces the chance of recovery by 50%. Therefore, early identification and recognition of patient care are crucial in maximizing the benefits of treatment.[15]

Following the increase in stroke incidence, it is crucial to enhance understanding of strategies that focus on the critical time window. This aims to strengthen the ability to recognize, respond to, and manage acute ischemic stroke cases effectively.[16] However, delays in administering treatment remain a challenge. In Indonesia, the majority of ischemic stroke patients experience delays in receiving therapy, with 83.69% of patients diagnosed with ischemic stroke falling into the delay category.[15]

Considering the complexity of the factors influencing thrombolysis delay, this study aims to conduct a scoping review to comprehensively identify and analyze these factors. In 2021, Sharobeam et al published a systematic review regarding the factors that delay intravenous thrombolytic therapy in acute ischemic stroke.[17] In their publication, they highlighted the factors causing delays in pre-hospital and in-hospital therapy, with an emphasis on vulnerable groups, particularly patients with a long onset-to-needle time. Since the last systematic review, many new studies have been published, necessitating an update to examine the latest developments related to the topic.

A deeper understanding of the factors influencing delays in intravenous thrombolysis is not only important for improving the response time for ischemic stroke patients but also for formulating effective strategies to enhance the

healthcare system, ultimately improving clinical outcomes for ischemic stroke patients. Through the writing of this scoping review, it is hoped to provide new perspectives based on articles published from 1996 until December 31, 2024, and contribute to the development of a more responsive and timely stroke healthcare system, particularly in developing countries, including Indonesia.

This scoping review aimed to identify the factors that influence the delay in intravenous thrombolysis management in patients with ischemic stroke.

Methods

Guidelines for the scoping review (ScR) methodology developed by the Joanna Briggs Institute (JBI)[18] and the PRISMA-ScR checklist for a scoping review were used.[19]

Review Questions

The review addressed the primary question: What are the factors that influence the delay in the management of intravenous thrombolysis in ischemic stroke patients?

A bibliographic search of the literature was conducted from March to May 2025. The relevant studies were identified based on a search of publications. The "PCC" mnemonic (Population, Concept, and Context) was used to identify meaningful criteria for this scoping review.[18]

Inclusion Criteria

a) *Population*: This study included patients with ischemic stroke.
b) *Concept*: Studies showing delayed management of intravenous thrombolysis.
c) *Context*: Studies examining the factors contributing to delays in intravenous thrombolysis therapy.
d) *Type of studie*s: Literature searches were performed using electronic databases with relevant keywords. The included studies were observational in design, specifically cohort, case-control, and cross-sectional studies, published in either English or Indonesian. Only full-access articles were considered for inclusion.

Exclusion Criteria

a) Studies that are not observational research.
b) Studies with research designs of review articles, editorial commentaries, case reports, case series, trial protocols, and opinion pieces.
c) Studies that are not in English or Indonesian.
d) Studies that were not published in peer-reviewed journals.
e) Studies that are not freely accessible through electronic databases.

Search Strategy

The following search terms and their combinations were identified to encompass all long-term consequences, as per previously published reviews (Table 1). We combined MeSH terms and keywords for three concepts, namely ischemic stroke, delay factor, and intravenous thrombolysis. We combined MeSH terms and keywords in the same concept with the Boolean operator "OR" and different concepts with "AND".

Study Selection

Study selection was conducted independently by two reviewers (TE, LD) using the eligibility criteria. If different results were obtained, a discussion was held to reach a consensus or involve a third reviewer (LK). In the study selection stage, Rayyan AI was utilized in the initial screening process based on the article's title and abstract. In the selection process, Rayyan AI serves to flag relevant studies according to the inclusion and exclusion criteria. In the second stage of full-text article selection, Rayyan AI is utilized to identify articles that have passed the title and abstract selection stage.

Table 1 Keywords Criteria in Each Database

Database	Keywords
PubMed	("ischemic stroke"[MeSH Terms] OR "ischemic strokes" OR "stroke ischemic" OR "ischaemic stroke" OR "ischaemic strokes" OR "stroke ischaemic" OR "acute ischaemic stroke" OR "acute ischemic strokes" OR "ischemic stroke acute" OR "stroke acute ischemic") AND ("delay factor" OR "delay" OR "time delay" OR "treatment delay" OR "onset to treatment" OR "delayed treatment") AND ("intravenous thrombolysis" OR "iv thrombolysis" OR "thrombolysis" OR "rtPA" OR "recombinant tissue plasminogen activator" OR "thrombolytic therapy")
ScienceDirect	(ischemic stroke) AND (delay factor) AND (rtPA)
EBSCO	(ischemic stroke OR acute ischaemic strokes) AND (delay factor OR onset to treatment OR delayed treatment) AND (intravenous thrombolysis OR thrombolytic therapy OR recombinant tissue plasminogen activator)

Study Quality Assessment

In this scoping review, no assessment of study quality was performed, as it was considered optional.

Data Extraction and Analysis

All selected studies were collected and thoroughly reviewed by two independent reviewers (TE and LD), with relevant data recorded using a standardized data extraction form. If there was any disagreement between the two reviewers, the third reviewer (LK), provided their opinion to resolve the issue.The extracted data included key information such: the author, year of publication, study period, country, study design, and sample size. Additionally, characteristics of ischemic stroke patients, such as mean age (SD) and sex distribution, were noted. The extraction also captured each study's objectives, main findings, and study results. The extracted data were synthesized and analyzed using both table-based and narrative formats and synthesis. Factors contributing to pre-hospital and in-hospital delays were presented in separate tables to clearly distinguish between the two categories.

Results

A total of 776 articles were identified through the search process. After removing duplicates, 744 records remained. Of these, 640 articles were screened based on their titles and abstracts using the predefined inclusion and exclusion criteria. Following this, 114 full-text articles were assessed for eligibility, and 48 articles were finally included in the scoping review (Figure 1).

Characteristics of Included Studies

Studies included in this scoping review were conducted across multiple countries, and most were carried out in Asian countries. A total of 98,740 patients were involved, most of whom were male. The predominant study design was retrospective, which included retrospective chart reviews and register-based cohort studies (n = 23). Prospective designs, including follow-up studies and prospective registry studies, accounted for (n = 15). There were studies with mixed retrospective and prospective designs (n = 2), case-control studies (n = 2), and cross-sectional studies (n = 3). Other study types included one for each of the following: an unspecified cohort design (retrospective or prospective), a nationwide register-based study, and a study based on the GWTG-S registry (Table 2).

Pre-Hospital Factors

Among the 48 studies included in this scoping review, both pre-hospital and in-hospital factors were identified as key contributors to delays in administering intravenous thrombolysis for patients with acute ischemic stroke (AIS) (Table 3). Twelve studies[8,13,22–26,36,38,45,48,59] consistently reported that use of emergency medical services (EMS) reduced onset-to-door time. Patients transported via EMS are significantly more likely to arrive within the therapeutic window and to receive thrombolysis compared to those using private or delayed transport (Table 3).

The mode of hospital transportation, whether direct or indirect, is also a critical pre-hospital factor influencing treatment delays in AIS. Twelve studies[9,26,29–31,38,39,46,54,55,60,64] demonstrated that patients transported directly to stroke-

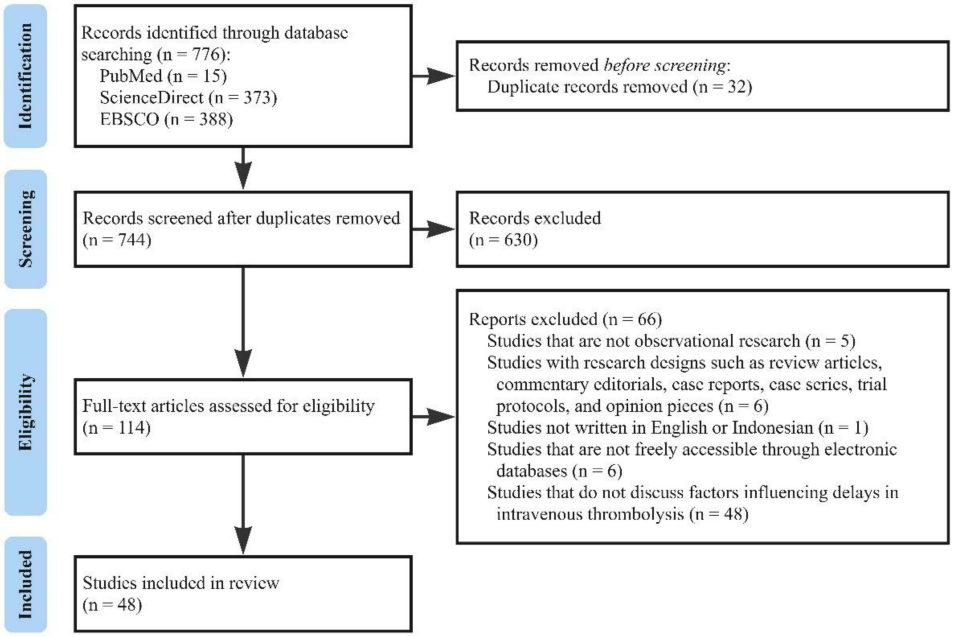

Figure 1 Flow diagram of the study selection process.

ready hospitals experience shorter travel and treatment times compared to those who first present at non-specialized facilities. Direct admission to hospitals equipped with thrombolysis services is closely associated with faster intervention and improved clinical outcomes. In contrast, patients who arrive indirectly, either by self-transport, referral from other facilities, or non-emergency transport, often face significant treatment delays, diminishing their chances of timely thrombolytic therapy.

Comorbidities such as prior stroke, atrial fibrillation, and uncontrolled hypertension have been consistently linked to prolonged door-to-needle times (DNT) and lower eligibility for intravenous thrombolysis, as reported in six studies.[32,41,44,46,55,64] This delay often arises from diagnostic challenges, such as changes in neurological symptoms, a nonspecific clinical presentation, and uncertainty regarding anticoagulant status. Symptom recognition also plays a crucial role in influencing the onset-to-arrival (OAT) time, as reported in five studies.[28,29,44,59,64] Whereas, earlier hospital arrival is more likely when symptoms are considered severe or correctly identified as stroke, while misinterpreting or waiting for spontaneous recovery often leads to significant delays. Delayed presentation and slower imaging processes are also associated with the appearance of atypical symptoms, especially in posterior circulation strokes.

Time of onset further affects access to treatment, as reported in five studies.[13,49,52,54,64] Patients presenting outside working hours, especially at night, experience longer DNT due to staffing limitations and CT interpretation delays. A stroke occurring while the patient is awake is a major contributor to delayed arrival at the emergency department (ED), with a significantly reduced likelihood of timely thrombolysis. Demographic factors were contributors to delayed hospital arrival and reduced access to intravenous thrombolysis in AIS. Three other studies[46,50,60] reported that rural residence, longer distance to tertiary care centers, dependence on public transportation, and living in a nuclear family were associated with delayed attendance. Whereas, this delay often exceeds 24 hours after the onset of symptoms. This delay is supported by research showing that treatment at a stroke center is associated with significantly shorter treatment times.

Living situation is another factor influencing pre-hospital delays, with individuals living alone or in nuclear families more likely to present late and have reduced access to reperfusion therapy, as reported in three studies.[46,57,60] This delay is mainly seen among immigrant populations and patients with milder symptoms. Age is also associated with delayed thrombolysis, as shown in three studies.[54,55,65] Younger (<65 years) and older (>65 years) patients both presented late due to different factors, namely, around misinterpretation of symptoms, lack of stroke awareness, or challenges in mobilization.

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Table 2 Scoping Review Articles (Key Details)

No	Author (Year)	Study Period	Country	Study Design	Sample Size	Age, Year Mean (SD)	Sex (Male%)	Main Findings and Conclusion
1.	Katz J M et al (2021)[20]	2017 - 2020	United State	Cohort - retrospective	588	71.7 (15.0)	n/a	Imaging-related delays significantly impact timely thrombolysis in acute ischemic stroke care. Rescanning was more frequent and time-consuming at primary stroke centers (59.6% of cases; >65 min delay) than at comprehensive centers (11.8%; 24 min delay, $p < 0.001$). Using a combined NCCT, CTA, and CTP protocol reduced delay risk (OR = 0.34; 95% CI: 0.21–0.55), while rescanning was linked to lower odds of home discharge (OR = 0.53; 95% CI: 0.30–0.95), indicating both time and outcome impacts.
2.	Laurencin C et al (2015)[21]	2010 - 2014	France	Cohort - prospective	1,043	71.91 (13.88)	575 (55.1)	Acute ischemic stroke patients with higher severity (NIHSS > 4) were more likely to receive timely thrombolysis. rtPA was administered within 3 hours in 56% of cases managed by stroke teams and 65% of those without, showing a significant association with early treatment ($p < 0.001$).
3.	Ye S et al (2019)[22]	2016 - 2017	China	Cohort - retrospective	1,370	-	-	The implementation of an EMS-based organizational system proved effective in reducing avoidable delays and enhancing the rate of thrombolysis, as evidenced by an increase in rt-PA administration among stroke patients from 8.3% to 9.7% ($p = 0.003$).
4.	Eleonora I et al (2013)[23]	2004 - 2012	Italy	Cohort - prospective	3,856	74.18 (13.77)	1,991 (51.6)	Only about one-third of acute ischemic stroke patients arrive at the hospital within the time window for intravenous thrombolysis. Earlier arrivals (within 2 hours) were generally younger (mean age 72.1 vs 75.0 years, $p < 0.001$) and had more severe strokes (NIHSS 8.1 vs 6.5, $p = 0.001$). Older adults, particularly those over 80, were more likely to arrive late (38.4% vs 31.7%, $p < 0.001$), highlighting how age and stroke severity influence the urgency of seeking care.
5.	Chen H et al (2023)[24]	2017 - 2020	China	Cohort - retrospective	2,303	68 (13)	1,397 (60.7)	The use of EMS was associated with a shorter onset-to-door time (ODT) and onset-to-needle time (ONT), with statistically significant correlations ($\rho = –0.051$, $p = 0.014$ for ODT; $\rho = –0.041$, $p = 0.048$ for ONT). However, EMS utilization did not lead to a reduction in door-to-needle time (DNT) ($\rho = 0.019$, $p = 0.362$).
6.	Gude M F et al (2023)[25]	2017 - 2018	Denmark	Cohort - retrospective	3,546	72.93 (12.81)	2,042 (57.59)	Timely contact with healthcare and stroke recognition by EMS dispatchers in AIS patients was linked to shorter prehospital delays (–44.8 minutes, 95% CI: –66.9 to –22.6) and reduced EMDC delay (–10.3 minutes, 95% CI: –11.9 to –8.6). Recognized strokes were more likely to receive intravenous thrombolysis (46.7% vs 37.7%; adjusted risk difference: 9.5%, 95% CI: 5.7–13.2) and to be admitted to hospitals offering acute stroke care.

7.	Kulkarni G B et al (2022)[8]	2016 - 2017	India	Cohort - prospective	103	-	-	A large number of eligible AIS patients in public hospitals do not receive thrombolysis, mainly due to limited awareness, financial barriers, and in-hospital delays. Most who were treated (77.7%) received care in high-volume stroke units. Direct hospital arrivals had significantly shorter onset-to-door times (103.6 vs 154.9 minutes; $p < 0.001$), with private transport being faster than ambulance among referred patients (130 vs 176.1 minutes; $p < 0.001$). Indirect referrals, especially inter-hospital transfers, led to substantial treatment delays and lower thrombolysis rates.
8.	Raty S et al (2017)[26]	2010 - 2015	Finland	Cohort - retrospective	245	67.51 (13.67)	154 (62.86)	Occipital stroke patients with isolated visual symptoms often experience delayed recognition and complex prehospital routes, reducing their chances for thrombolysis. Faster arrival was linked to EMS use (51.0% vs 11.9%, $p < 0.001$) and direct hospital access (88.7% vs 37.3%, $p < 0.001$), the strongest predictor of timely treatment (OR 13.31; 95% CI: 6.47–27.38; $p < 0.0001$).
9.	Fong W-C et al (2015)[27]	2009 - 2012	Hong Kong	Cohort - prospective	152	66 (11)	88 (57.9)	Telemedicine offers a safe and effective way to deliver intravenous thrombolysis for acute ischemic stroke patients in hospitals without on-site neurologists. Patients in the telemedicine group arrived at the ED faster (46 vs 54 minutes, $p = 0.015$) but experienced longer treatment delays due to remote coordination. This included longer CT-to-needle (67 vs 41 minutes), door-to-needle (97 vs 73 minutes), and onset-to-needle times (150 vs 134 minutes).
10.	Gonzalez-Aquines A et al (2019)[28]	2018	Mexico	Cohort - prospective	163	61 (13)	101 (62)	Delayed hospital arrival in acute ischemic stroke is strongly influenced by patients' perception of symptoms. Those who recognized signs of stroke (OR = 3.35; 95% CI: 1.25–8.94) or considered their symptoms serious (OR = 2.43; 95% CI: 1.08–5.45) were more likely to seek prompt care. In contrast, delays were common among patients who waited for symptoms to resolve on their own (OR = 14.77; 95% CI: 2.52–86.46) or misattributed them to non-stroke causes (OR = 2.79; 95% CI: 1.03–7.53).

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Table 2 (Continued).

No	Author (Year)	Study Period	Country	Study Design	Sample Size	Age, Year Mean (SD)	Sex (Male%)	Main Findings and Conclusion
11.	Sobral S et al (2019)[29]	2010 - 2015	Portugal	Case control	222	-	125 (56.3)	Delays in hospital arrival for intravenous thrombolysis in AIS patients are strongly influenced by socioeconomic and logistical barriers. Poverty, low stroke awareness, and limited emergency access reduce timely treatment. Patients with social income support (OR: 0.286; 95% CI: 0.124–0.662), posterior strokes (OR: 0.266; 95% CI: 0.087–0.811), individuals without a phone (OR: 0.145; 95% CI: 0.039–0.536) or using only a landline (OR: 0.055; 95% CI: 0.014–0.210) were far less likely to seek prompt care. In contrast, direct ambulance use greatly improved timely arrival (OR: 6.478; 95% CI: 2.751–15.254).
12.	Kim D -H et al (2015)[30]	2011 - 2012	Korea	Cohort - prospective	820	67.3 (12.3)	490 (55.7)	Direct access to thrombolysis-capable hospitals significantly improved treatment timelines in acute ischemic stroke. Patients who arrived directly had shorter onset-to-door (63 vs 121 minutes) and onset-to-needle times (110 vs 161 minutes; both $p < 0.001$) compared to those transferred from other facilities. Although door-to-needle time was slightly longer by 5 minutes, overall care was faster. Lower educational attainment was associated with indirect hospital access ($P = 0.004$), contributing to delayed treatment and worse outcomes.
13.	Sangari A et al (2021)[31]	2016 - 2020	Iran	Cohort - retrospective	185	-	100 (54.05)	Stroke patients transported via the Structured Ambulance Medical Assistance (SAMA) system experienced significantly shorter treatment times compared to those who arrived by private means. Specifically, SAMA transport was associated with reduced onset-to-needle time (150 vs 180 min)., door-to-needle time (80 vs 100 min)., and door-to-CT time (27 vs 36 min.; all $p < 0.001$).
14.	Gosser R A et al (2015)[32]	2008 - 2012	United State	Cohort - retrospective	105	-	-	The involvement of pharmacists in stroke response teams is linked to faster administration of intravenous thrombolysis. In emergency settings, the presence of a pharmacist during acute stroke care significantly reduced door-to-rtPA time, with a median of 69.5 vs 89.5 min. When no pharmacist was involved ($p = 0.0027$).

15.	Hsieh C-Y et al (2013)[33]	2009 - 2012	Taiwan	Cohort - retrospective	32	67.75 (11.44)	-	Structured stroke response programs, especially those using video-assisted protocols, significantly improved acute ischemic stroke care. After implementation, door-to-needle time dropped from 94 to 57 minutes ($p < 0.001$) and increased the proportion of patients treated within 60 minutes from 11% to 57% ($p = 0.005$; OR: 10.7). Door-to-CT time also decreased by 12 minutes, and AIS case identification increased from 2% to 5% ($p = 0.010$; OR: 2.5), highlighting better workflow and earlier treatment.
16.	Reziya H et al (2023)[34]	2020 - 2022	China	Cohort - retrospective	312	64.44 (12.75)	194 (62.18)	Real-time feedback via a mobile app in stroke care significantly reduced treatment delays. Median door-to-imaging time dropped from 44 to 28 min ($P < 0.01$), and door-to-needle time decreased from 44 to 39 min ($P = 0.02$), improving overall response.
17.	Arkuszewski M et al (2011)[35]	2003 - 2009	Polandia	Cohort - retrospective	90	65.33 (9.79)	55 (61)	Changes in health policy significantly improved access to intravenous thrombolysis in Poland. After the end of the POLKARD program and the introduction of full reimbursement by the National Health Fund (NFZ) in 2009, IVT rates increased from 4.3% to 7.6% ($p = 0.013$), underscoring the critical role of national funding in expanding access to stroke treatment.
18.	Hsieh M -J et al (2013)[36]	2010 - 2011	Taiwan	Cohort - prospective	1,081	69.6 (13)	673 (62.3)	EMS use significantly improves timely thrombolysis in acute ischemic stroke. Patients arriving by EMS had higher odds of receiving treatment (OR = 3.89; 95% CI: 1.86–8.17) and shorter onset-to-needle times (101.3 vs 127.3 minutes, $p = 0.011$), especially in cases with severe strokes or symptoms starting outside the home.
19.	Khurana D et al (2017)[37]	2011 - 2015	India	Cohort	867	60.17 (15.22)	574 (66.2)	Over the years, increasing trends in the administration of IVT may reflect growing public awareness of stroke symptoms and improvements in stroke care quality in developing countries such as India. Median door-to-CT time fell from 27 to 11 minutes ($p = 0.0001$), door-to-needle time from 83 to 67 minutes ($p = 0.011$), and CT within 25 minutes increased from 50% to 78.4% ($p = 0.014$), reflecting enhanced efficiency in acute stroke care.

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Table 2 (Continued).

No	Author (Year)	Study Period	Country	Study Design	Sample Size	Age, Year Mean (SD)	Sex (Male%)	Main Findings and Conclusion
20.	Vidale S et al (2016)[38]	2014	Italy	Cohort - retrospective	1,084	77.00 (11.13)	399 (36.8)	Integrating EMS with high-priority triage codes significantly improved stroke care efficiency. Although only 21–27% of patients were assigned high-priority codes, this group experienced shorter prehospital times ($p < 0.001$), reduced in-hospital delays ($p = 0.026$), and shorter hospital stays ($p < 0.001$). EMS was used in 56.3% of cases, more often among women and those with severe strokes ($p < 0.001$), underscoring the impact of early, prioritized EMS intervention on timely thrombolysis delivery.
21.	Kim D-H et al (2014)[39]	2008 - 2012	South Korea	Cohort - prospective	232	66.6 (11.8)	128 (55.2)	AIS patients directly admitted to thrombolysis-capable hospitals received treatment significantly faster than those transferred from other facilities. Median onset-to-door time was 61 minutes vs 120 minutes, and onset-to-rtPA time was 103 vs 155 minutes (both $p < 0.001$). Direct admission was also independently associated with better 90-day outcomes (OR 2.03; 95% CI: 1.051–3.917; $p = 0.035$), along with younger age, no history of stroke, and lower NIHSS scores.
22.	Mohedano A M I et al (2018)[40]	2009 - 2017	Spain	Cohort - retrospective	461	69.85 (13.85)	259 (56.18)	A new stroke protocol halved door-to-needle time from 52 to 27 minutes, especially when stroke codes were activated before hospital arrival. This change removed delays linked to earlier onset-to-door times and improved door-to-CT rates (78.8% vs 62.8%, $p < 0.001$). Pre-hospital stroke code activation cut treatment time by over 11 minutes ($B = -11.54$; 95% CI: −16.75 to −6.32; $p < 0.001$). However, performing CT angiography before thrombolysis still caused delays ($B = 17.46$; $p < 0.001$).
23.	Liu Y et al (2013)[41]	2011 - 2013	China	Cohort - retrospective	104	-	64 (61.54)	Acute ischemic stroke patients with a history of prior cerebrovascular events are significantly less likely to receive intravenous thrombolysis. A previous ischemic stroke was strongly associated with reduced odds of rtPA administration (OR: 0.11; 95% CI: 0.04–0.34), indicating clinical caution in offering thrombolytic therapy to patients with prior stroke history.

24.	Kanou S et al (2022)[42]	2015 - 2021	Japan	Cohort - retrospective	121	78.03 (21.77)	75 (61.98)	The stroke protocol led to significantly faster treatment. Median door-to-needle time dropped to 56.5 minutes vs 97 minutes in standard care, and door-to-puncture time dropped to 55 vs 129 minutes (both $p < 0.001$). Timely treatment was far more common with the protocol: 69.9% achieved DNT ≤60 minutes (vs 5.6%), and 87.5% achieved DPT ≤90 minutes (vs 25%).
25.	Shi T et al (2021)[43]	2015 - 2021	China	Cohort - retrospective	89	-	56 (62.92)	In mild stroke patients with vestibular symptoms, the likelihood of receiving IVT was mainly influenced by shorter onset-to-door time and higher initial NIHSS scores. Shorter arrival times increased IVT use (OR = 0.99; 95% CI: 0.983–0.999; $p = 0.027$), and higher NIHSS scores were strongly linked to treatment (OR = 1.02; 95% CI: 1.301–4.190; $p = 0.004$). In contrast, severe vestibular symptoms, oculomotor signs, or imaging results had minimal impact on the decision to administer IVT.
26.	Schaik S M V et al (2015)[44]	n/a	Netherland	Cohort - prospective	334	72 (13)	176 (53)	In secondary hospitals, 19% of ischemic stroke patients received IVT with a median door-to-needle time (DNT) of 25 minutes, and 71% were treated within 30 minutes, showing that rapid thrombolysis is achievable. However, 63% experienced delays, driven by factors such as uncertain symptom onset (OR 6.92), uncontrolled blood pressure (OR 9.06), fluctuating deficits (OR 11.33), prior treatment administration (OR 25.57), unclear anticoagulation status (OR 19.27), patient-related issues (OR 5.21), and inappropriate triage (OR 3.77).
27.	Hill M D et al (2000)[45]	1996 - 1998	Canada	Cohort - prospective	1,196	-	-	Emergency medical services (EMS) are vital for ensuring timely stroke care, with only EMS-transported patients consistently meeting recommended treatment windows. On average, the time from hospital arrival to CT scan was 46.1 minutes (range: 5–130), followed by 55.6 minutes (range: 20–315) to start IV tPA.

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Table 2 (Continued).

No	Author (Year)	Study Period	Country	Study Design	Sample Size	Age, Year Mean (SD)	Sex (Male%)	Main Findings and Conclusion
28.	Terecoasă E O et al (2022)[46]	2018	Romania	Cross sectional	770	72.51 (11.74)	428 (55.58)	Nearly one-third of ischemic stroke patients arrived at the hospital more than 24 hours after symptom onset, making them ineligible for intravenous thrombolysis. Several patient-related factors were associated with late arrival, including living alone (OR 1.7), residing in rural areas (OR 1.4), and using self-transport rather than emergency medical services (OR 2.2). Additionally, clinical factors such as atrial fibrillation (OR 0.5), severe stroke presentation (NIHSS > 15; OR 0.6), and neurological deficits like hemianopsia, facial palsy, and sensory loss were linked to delayed arrival.
29.	Yoo J et al (2018)[47]	2015 - 2016	Korea	Performed retrospectively using the registry data of the prospective	356	68.30 (13.24)	203 (57.02)	Patients with minor ischemic strokes face longer DTN times than those with more severe strokes, mainly due to delays in early-stage care such as team notification and imaging. Median DTN was 43 min for minor strokes vs 37 min for more severe cases. Door-to-notification (7 vs 5 min) and door-to-imaging times (20 vs 16 min) were also significantly delayed (all $p < 0.001$), though imaging-to-needle time showed no difference. Minor stroke was an independent predictor of delay (OR 2.54; $p = 0.001$), suggesting diagnostic uncertainty or lower urgency in these cases.
30.	Fukuda H et al (2023)[48]	2012 - 2018	Japan	Cohort - retrospective	9,651	76.8 (11.3)	5,342 (55.4)	Living in socioeconomically disadvantaged urban areas has been linked to greater prehospital delays in the management of acute ischemic stroke. These delays are likely associated with poorer clinical outcomes due to postponed administration of intravenous rt-PA and endovascular reperfusion therapy. Interestingly, EMS usage was higher among patients with prehospital delays (52%) compared to those without delays (43%) ($p = 0.0011$). Delayed patients were also slightly older, with a mean age of 77.4 years versus 76.0 years ($p < 0.001$).

31.	Chen C-H et al (2014)[49]	2006 - 2013	Taiwan	Cohort - prospective	307	67.90 (12.49)	181 (58.96)	The introduction of stroke code (SC) protocols has significantly improved acute ischemic stroke care by increasing the use of IV-tPA and reducing door-to-needle (DTN) times. IV-tPA administration increased from 2.6% before SC to 8.6% after implementation ($p < 0.001$), and a greater proportion of patients arrived within 3 hours of symptom onset (33.3% during SC vs 13.9% before SC; $p < 0.001$). Patients arriving during regular hours had slightly longer door-to-CT times than those presenting off-hours (12 vs 10 minutes, $p < 0.001$), possibly due to daytime workflow congestion or higher patient volume.
32.	Uchino K et al (2009)[50]	2002 - 2005	United State	Retrospective case-control	254	68.9 (15.0)	-	Patients managed initially at community hospitals after phone consultation with a stroke center had a significantly higher rate of protocol deviations (38.3%) compared to those treated directly at the stroke center (5.8%; $p < 0.001$), indicating potential gaps in triage accuracy and protocol adherence. These deviations may contribute to treatment delays and compromised care quality. Moreover, DTN times were 12 minutes faster at stroke centers than in the treat-and-transfer group ($p = 0.02$).
33.	Hassankhani H et al (2018)[51]	2017	Iran	Cohort - retrospective	394	68.85 (13.39)	210 (53.3)	Emergency department and acute stroke teams demonstrated strong clinical performance in achieving critical in-hospital time targets for patients deemed potentially eligible for intravenous thrombolysis. Brain imaging was completed and interpreted within a median of 33.5 minutes, and even faster, 29 minutes, for those who received r-tPA. Ineligible patients experienced significantly longer delays, with a median door-to-CT time of 75 min., marking an average delay of 39.7 min.
34.	Oluwole S A et al (2017)[52]	2010 - 2015	United State	Registry → retrospective and prospective hospital-collected GWTG-S	6,181	70.70 (14.46)	3,203 (51.82)	Timely administration of IVT remains suboptimal, with few patients meeting door-to-needle time (DTNT) targets of 60 or 45 minutes. Disparities were observed across demographics: women were consistently less likely than men to receive tPA within either timeframe (eg, DTNT ≤ 60 min: OR 0.81). During off-hours, Black patients had lower odds of receiving tPA within 45 minutes compared to White patients (OR 0.68).

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Table 2 (Continued).

No	Author (Year)	Study Period	Country	Study Design	Sample Size	Age, Year Mean (SD)	Sex (Male%)	Main Findings and Conclusion
35.	Ganti L et al (2023)[13]	n/a	United State	Prospective observational quality registry study	107	65.84 (19.12)	58 (54.21)	Prolonged DTN time for intravenous thrombolysis in acute ischemic stroke was significantly associated with night-shift arrival, absence of EMS transport, and lack of a dedicated stroke team. Patients arriving at night experienced longer DTN (median 59 minutes) compared to daytime arrivals (median 37 minutes; $p < 0.0001$). Delays were also linked to slower CT interpretation and walk-in presentations. The presence of a specialized stroke team significantly reduced DTN (median 36 vs 51 min; $p < 0.0001$), highlighting the importance of organized stroke protocols and rapid imaging in ensuring timely treatment.
36.	Hsia A W et al (2011)[53]	2008 - 2009	United State	Cohort - prospective	973	-	435 (44.7)	In a predominantly Black urban population with acute ischemic stroke, Black patients were significantly less likely to receive intravenous thrombolysis (3% vs 10% for White patients, $p < 0.001$), mainly due to delayed arrival, higher rates of contraindications, and milder stroke severity. Only 13% of Black patients arrived within 3 hours of symptom onset, compared to 21% of White patients ($p = 0.004$). Even when arriving on time, Black patients were still less likely to receive tPA (27% vs 46%, $p = 0.023$). Public insurance and lower NIHSS scores further reduced the likelihood of thrombolysis, highlighting disparities linked to socioeconomic and clinical factors.
37.	Chen C-H et al (2007)[54]	2004 - 2005	Taiwan	Cohort - prospective	129	-	76 (58.9)	Age has a significant impact on the timeliness of hospital arrival for acute ischemic stroke patients, influencing their eligibility for intravenous thrombolysis. Patients under 65 were significantly more likely to arrive late, with over twice the odds of delayed presentation compared to older individuals (OR 2.27). Delays were also linked to referrals from other facilities ($p = 0.0328$) and wake-up strokes ($p < 0.0001$), as both scenarios often led to longer times from symptom onset to hospital arrival.

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38.	Wang R et al (2021)[55]	2018 - 2019	China	Cross sectional	1,728	66.3 (9.65)	1,033 (57.97)	Pre-hospital delays among stroke patients in China remain longer than in many Western nations, limiting timely access to intravenous thrombolysis. Several factors were independently linked to late hospital arrival, including age over 65 (OR 2.009), prior stroke history (OR 3.478), and blurred vision as the main symptom (OR 3.95). Patients who made their own decision to seek care, rather than relying on family, were also more likely to arrive late (OR 3.097). In contrast, ambulance use significantly reduced delays (OR 0.10).
39.	Siegler J E et al (2013)[56]	2008 - 2010	United State	Cohort - retrospective	368	-	222 (60.2)	Multivariate analysis identified Black race as a significant predictor of delayed emergency department (ED) arrival, beyond 3 hours after last seen normal (LSN). Black patients had a median delay of 339 minutes compared to 151 minutes for White patients (p = 0.0028). Crude logistic regression showed that Black individuals were more than twice as likely to arrive after the 3-hour window (OR = 2.16; 95% CI: 1.39–3.37).
40.	Mkoma G F et al (2022)[57]	2009 - 2018	Denmark	Register-based cohort study	49,817	72.18 (13.39)	21,836 (43.83)	Immigrants are significantly less likely to receive IVT for acute ischemic stroke, even when arriving within 4.5 hours of symptom onset. After adjusting for relevant factors, immigrants had lower odds of receiving treatment than Danish-born patients (AOR 0.67). The disparity was especially pronounced among Polish (AOR 0.30) and non-Western immigrants (AOR 0.61). Immigrants also had longer onset-to-door times, by 15 minutes overall and 18 minutes for non-Western groups. Living alone (AOR 0.86) and having milder strokes (AOR 0.92) further reduced the likelihood of receiving therapy.
41.	Barbour J et al (2021)[58]	2016 - 2020	United State	Cohort - retrospective	164	63.38 (15.16)	90 (54.88)	The involvement of emergency medicine pharmacists (EMPs) in stroke teams significantly improved treatment speed and outcomes. Their presence reduced door-to-needle times (median 35 vs 42 min; p = 0.003) and increased the proportion of patients receiving tPA within 30 and 45 min. Additionally, patients treated with EMP support had better neurological recovery, shown by lower NIHSS scores at discharge (median 2 vs 4; p = 0.049).

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Table 2 (Continued).

No	Author (Year)	Study Period	Country	Study Design	Sample Size	Age, Year Mean (SD)	Sex (Male%)	Main Findings and Conclusion
42.	Anees A et al (2024)[59]	2022	India	Cross sectional	153	62.88 (13.59)	90 (58.8)	Prehospital delays remain a critical obstacle to timely intravenous thrombolysis in stroke care. Contributing factors include misperception of symptom severity, traffic congestion, and limited public awareness of designated stroke centers. Among these, traffic-related delays were strongly associated with late hospital arrival (OR: 0.085). In contrast, patients who accurately recognized the seriousness of their symptoms were significantly more likely to arrive within the treatment window (OR: 18.801).
43.	Gupta A K et al (2023)[60]	2018 - 2019	India	Cohort - prospective	100	-	64 (64)	Pre-hospital delays in acute ischemic stroke are often caused by low awareness of stroke symptoms and practical barriers like transportation and living situation. Patients who recognized stroke symptoms arrived at the hospital much sooner (average 4.95 hours) than those who did not (average 9.17 hours). Those living in nuclear families had longer delays (9.78 hours) compared to those in joint families (7.35 hours). How patients got to the hospital also mattered: private or staff vehicles led to the fastest arrival (2.96 hours), followed by ambulances (6.42 hours), while public transport caused the longest delays (10.35 hours).
44.	Chai E et al (2019)[61]	2014 - 2018	China	Cohort - retrospective	248	64.29 (5.21)	132 (53.23)	Initial stroke severity, time to hospital arrival, and how long it takes to make treatment decisions all significantly affect delays in managing acute ischemic stroke. Patients with milder symptoms (lower NIHSS scores) were more likely to experience treatment delays, while those with more severe strokes received faster care (OR = 0.775). Longer decision-making time was also linked to delayed treatment (OR = 1.224). Faster arrival at the hospital (shorter onset-to-door time) helped reduce delays (OR = 0.963).

45.	Candelaresi P et al (2017)[62]	2013 - 2015	Italy	Cohort - prospective	99	-	-	Continuous education and training of medical personnel involved in stroke care have a significant impact on reducing treatment delays. Measures like giving rt-PA directly at the CT scanner, regular staff training, and improved protocols led to faster treatment, 38% of patients received thrombolysis within 30 minutes, and 80% within one hour of arrival. Workflow improvements, including bedside INR and glucose testing and quicker lab communication, cut door-to-needle time by 17 minutes. The introduction of a structured Stroke Code protocol also significantly shortened median treatment times ($p < 0.001$).
46.	Zhao J et al (2018)[63]	2012 - 2014	China	Cohort - retrospective	188	-	108 (57.45)	The launch of a 24-hour stroke thrombolysis emergency care program in 2013 led to major improvements in both treatment speed and patient outcomes. Median door-to-needle time dropped from 81 minutes in 2012 to 52 minutes in 2013 and further to 42 minutes in 2014 ($p < 0.01$). Other critical time points, such as admission-to-imaging and imaging-to-needle, also decreased, indicating a more efficient workflow. Additionally, patients showed greater improvement in NIHSS scores within 24 hours of rt-PA treatment over the three years ($p < 0.05$).
47.	Zhu Y et al (2020)[64]	2017	China	Cohort - prospective	630	-	392 (62.2)	Pre-hospital delays remain a major challenge for acute ischemic stroke patients in China, limiting timely access to intravenous thrombolysis. Factors like daytime symptom onset (OR: 1.417), dizziness (OR: 1.718), and atrial fibrillation (OR: 0.555) were linked to delayed arrival. In contrast, immediate response to symptoms (OR: 0.002) and ambulance use (OR: 0.15) greatly improved the chances of early hospital presentation.
48.	Mainz J et al (2022)[65]	2016 - 2017	Denmark	Nationwide register-study	5,356	73.33 (13.35)	3,048 (57)	Patient-related delays are the most critical barrier to the administration of reperfusion therapy in acute ischemic stroke cases, even among those who contact emergency services (1-1-2). In contrast, delays within the healthcare system are mostly unrelated to patient behavior. Adjusting for variables like age, sex, living situation, and stroke severity had little effect on the outcomes, with the adjusted relative risk of receiving IV thrombolysis remaining low at 0.20 (95% CI: 0.18–0.23).

Table 3 Pre-Hospital Factors

Factors	Number of Studies
	Studies showing statistically significant [p<0.05] association n [refs]
Emergency Medical Service	12[8,13,22–26,36,38,45,48,59]
Telemedicine	2[27,29]
Decision-Making	2[43,61]
Race	3[52,53,56]
Immigrant Status	1[59]
Economic Status	3[29,35,53]
Time of Event	5[13,49,52,54,64]
Symptoms	5[28,29,44,59,64]
Educational Background	3[30,60,62]
Comorbidities	6[32,41,44,46,55,64]
Age	3[54,55,65]
Gender	1[52]
Living Situation (Alone or With Family)	3[46,57,60]
Demographics	3[46,50,60]
Mode of Hospital Presentation (Direct or Indirect)	12[9,26,29–31,38,39,46,54,55,60,64]

The racial difference was highlighted in three studies,[52,53,56] which showed that Black patients were significantly less likely to receive timely intravenous thrombolysis than White patients. Worse, Black patients were also more likely to experience delays despite presenting within the treatment window. This is attributed to various other factors, such as delays in hospital arrival, higher rates of contraindications, and continued inequities in access to treatment despite the same clinical presentation. Immigrants are significantly less likely to receive intravenous thrombolysis than native-born patients, even when present within the therapy window. This difference was primarily seen in Polish and non-Western immigrants, who also experienced longer pre-hospital delays.[59] Similarly, a study[52] found that female stroke patients were consistently less likely than males to receive thrombolysis based on the recommended time window, regardless of time of hospital admission.

Economic status is a critical barrier to timely intravenous thrombolysis in acute ischemic stroke (AIS). Three studies[29,35,53] reported that patients living in poverty, relying on public insurance, or with low income were significantly less likely to receive IVT. Similarly, limited educational background and poor stroke awareness, as highlighted in three studies,[30,60,62] were closely associated with indirect hospital admissions and treatment delays. In contrast, patient education and ongoing training for healthcare providers were associated with higher thrombolysis rates and more efficient treatment delivery.

Socioeconomic barriers, such as poverty, also affect aspects of telemedicine. Limited telephone access and low stroke awareness contribute to pre-hospital delays.[27,29] Telemedicine is a safe and effective alternative for delivering intravenous thrombolysis in facilities lacking on-site neurologists. In addition, prolonged decision-making is also associated with delayed thrombolysis. Two studies were found that emphasized the importance of rapid clinical assessment and simpler protocols to ensure timely treatment.[43,61]

In-Hospital Factors

Imaging delays remain a major barrier to timely intravenous thrombolysis (IVT) in acute ischemic stroke (AIS) (Table 4). Patients treated at primary stroke centers frequently undergo repeated or prolonged scans compared to those at comprehensive centers, resulting in longer treatment times and poorer outcomes.[13,20,37,40,51] IVT delays were more common during night shifts, in facilities without specialized stroke teams, and when CT angiography was performed before IVT. In other conditions, patients with higher NIHSS scores tended to be prioritized for imaging and treatment sooner. These patients will usually receive IVT within 3 hours of symptom onset.[21,47,53,58,61] In contrast, those with mild symptoms or lower scores frequently face delays, especially in stroke team activation and imaging initiation.

Table 4 In-Hospital Factors

Factors	Number of Studies
	Studies showing statistically significant [p<0.05] association n[refs]
Scan Time	5[13,20,37,40,51]
NIHSS Score	5[21,47,53,58,61]
Diagnostic Process	1[28]
Human Resources	3[13,32,58]
Stroke Program Implementation	5[33,34,40,42,63]
Logistics	1[39]
Triage Process	2[38,50]
Code Stroke Activation	3[40,49,62]

Five studies[33,34,40,42,63] indicate that structured stroke protocols, particularly those that combine technologies such as video assistance systems, mobile app feedback, early stroke code activation, and 24-hour thrombolysis services, significantly reduce door-to-needle (DTN) and needle-to-imaging (DIT) times. This stroke protocol improved the timeliness of treatment and the proportion of patients receiving thrombolysis within the optimal therapeutic window. In addition, improved workflow efficiency, early imaging, and clinical outcomes (eg, NIHSS score) also reflect a well-coordinated stroke system.

Early stroke code activation also significantly reduced door-to-needle (DTN) time, reducing treatment delays by more than 11 minutes. Three other studies new[40,49,62] showed that a coordinated team response, rapid imaging, and rt-PA administration sometimes performed at the CT bedside also improved treatment efficiency. These results highlight the critical role of proactive in-hospital protocols and team readiness in optimizing acute stroke care. Furthermore, it was reported in two studies[38,50] that EMS triage with high priority codes was closely associated with shorter hospitalization rates and faster thrombolysis.

Three other studies[13,32,58] underlined the role of specialized personnel in improving thrombolysis delivery. The involvement of emergency department pharmacists showed shorter DTN times and a higher number of AIS patients treated. This certainly contributed to better neurological outcomes. Likewise, the presence of a dedicated stroke team was associated with faster treatment initiation and a more efficient diagnostic process, especially in highly critical situations. Logistics[39] demonstrated that direct admission to hospitals with thrombolysis capabilities significantly shortened both onset-to-door and onset-to-treatment times compared to interfacility transfers, leading to improved functional outcomes at 90 days. Diagnostic delays[28] were common among patients with occipital strokes presenting with visual symptoms, often due to misdiagnosis or complex referral routes. Faster treatment was associated with accurate initial diagnosis, no ophthalmology referral, and a history of atrial fibrillation.

Discussion

This scoping review aimed to explore factors contributing to delayed IVT in acute ischemic stroke patients. These delays include both pre-hospital and in-hospital phases. The theoretical benefit of this review is that it contributes to the field of neurology and acute stroke care by synthesizing current evidence on the timely administration of intravenous thrombolysis. In addition, the findings provide a basis for comprehensive and systematic improvements in stroke care pathways, ultimately aiming to reduce post-stroke disability and enhance patient outcomes.

Pre-Hospital

Timely intravenous thrombolysis (IV tPA) intervention is critical in the management of acute ischemic stroke.[12] Delays in stroke treatment can result from a variety of interrelated factors, including individual behavior, community awareness, health facility readiness, and broader national-level factors. These findings emphasize the need for integrated multi-level strategies to effectively address barriers to IVT delivery.

Patients who use emergency medical services (EMS) or go directly to a hospital equipped to administer thrombolysis are far more likely to receive treatment in a timely manner.[8,13,22–26,36,38,45,48,59] In contrast, those who rely on private transport or are referred through other facilities often face longer waits, which can seriously impact their chances of recovery. Patients with limited health knowledge and restricted access to emergency services exacerbate this situation. People from low-income backgrounds are often less familiar with the warning signs of stroke. This leads to patients not being aware that they need to seek help immediately.

To overcome the limitations of EMS, especially in underserved or remote areas, the use of Mobile Stroke Units (MSUs) is one alternative that has been proven effective. Sharobeam et al (2020)[17] reported that ambulances equipped with onboard CT scanners and telemedicine capabilities can improve the evaluation and delivery of immediate thrombolysis on-site. Using emergency services like EMS can help patients receive treatment more quickly by reducing the time between arrival at the hospital and actual thrombolysis.

A patient's health condition also plays a significant role in determining how quickly treatment can begin. If a person with comorbidities, such as uncontrolled high blood pressure or chronic illness, can make it difficult to start treatment immediately. A study by Mowla et al (2017)[66] found that nearly a quarter of patients experienced delays due to their blood pressure being too high upon arrival at the hospital. To help avoid these setbacks, some experts suggest giving blood pressure-lowering medication right after a CT scan confirms the patient is a good candidate for thrombolysis, even while the patient is still on the scan table On the other hand, patients who exhibit more obvious or severe stroke symptoms will tend to be recognized and treated sooner.

Additionally, the timing of symptom onset plays a crucial role in the delay of thrombolysis. Symptoms experienced by patients outside of working hours, such as evenings or weekends, are associated with a longer time to treatment. Implementation of 24-hour stroke services can help address this problem.[67] Demographic and geographical factors also contribute to the timeliness of treatment. Patients living in rural or remote areas often face long distances to stroke centers and limited transportation options. This, of course, is associated with prolonged DNT. Faced with these challenges, the utilization of the Helsinki model can accelerate the delivery of thrombolysis in developing countries at minimal cost.[67]

Where a patient lives also matters. People in rural or remote areas often have to travel farther to reach a stroke center and may face transportation challenges, both of which can lead to longer delays in treatment. That's why it's important to create strategies tailored to local conditions. Yuan et al (2022),[67] for example, successfully adapted the Helsinki model in a developing country using limited resources, showing that with the right approach, faster stroke treatment is possible even in low-resource settings.

The patient's living situation also plays a critical role. Individuals who live alone may experience longer delays[46,57,60] due to the absence of witnesses at symptom onset or difficulties in making urgent decisions. Age is another determinant of delay, both younger (<65 years) and older (>65 years) patients face unique barriers. Younger individuals may underestimate the seriousness of symptoms or lack stroke awareness,[54] while older patients may encounter physical limitations, delayed recognition, or challenges in accessing emergency services.[55] Ferrone et al (2025)[68] noted that patients arriving after the 4.5-hour window were more likely to be aged ≥80 years, male, of Black or Asian ethnicity, and from low-income backgrounds or Medicaid recipients.

Thus, delays in thrombolysis are multifactorial, influenced not only by systemic healthcare inefficiencies but also by individual patient characteristics, socioeconomic disparities, geographic access, and clinical complexity. Therefore, interventions to reduce delays must be holistic and context-sensitive, encompassing public education campaigns, EMS system optimization, implementation of prehospital technologies like MSUs, and localized policy adaptations to ensure equitable and timely stroke care.

Medical and service system factors, social, economic, and racial disparities are significant determinants in the delay of thrombolysis in ischemic stroke patients. This scoping review shows that non-white patients, especially Black and Asian patients, have a lower likelihood of receiving IVT than white patients.[52,53,56] Ferrone, N, G et al 2025[72] emphasized the importance of targeted education, including increased understanding of the warning signs of stroke, the urgency of seeking medical attention, and information on available therapies. Distribution of culturally sensitive educational materials translated into local languages is also considered effective to bridge the knowledge gap, especially among

minority communities. Such interventions can be an important strategy to reduce disparities and accelerate access to IVT, especially in patient groups most vulnerable to delays.

Economic challenges also contribute to factors that result in delays in patients receiving IVT. Individuals living in poverty, patients dependent on public insurance, and patients with low income are much less likely to receive IVT.[29,35,53] This highlights how race, economic status, and access to emergency stroke care often intersect, putting minority and underserved populations at the greatest risk for delayed care. These disparities are exacerbated by low levels of education and health literacy, particularly regarding stroke symptom recognition and understanding the importance of prompt treatment.

Yuan, G et al, 2022[67] and Huang, Q et al, 2018,[69] emphasized that low public awareness is the main cause of delay in the pre-hospital phase, which is the phase with the longest duration of delay, ranging from 3 to 6 hours. Innovative educational approaches such as screening educational videos in the CT waiting room, mentoring by specialized stroke nurses and doctors, and effective communication directly with the patient's family have been shown to help speed up the decision-making process for thrombolysis.

The role of technology in accelerating stroke diagnosis and treatment is becoming increasingly crucial, particularly in regions with limited access to specialized facilities. The use of telemedicine and telestroke systems has been shown to speed up door-to-needle (DTN) times and reduce decision-making delays in IVT delivery. Several studies in this scoping review have shown that strategies such as remote stroke consultation between central and satellite hospitals, computerized inputting of physician orders, and optimization of digital communication can significantly cut in-hospital time, with DCT time reduced from 34 to 18 minutes and CNT time cut to 68.7 minutes.[17,67,69] Programs such as the Victorian Stroke Telemedicine (VST) in Australia are clear examples of the success of this model in improving the efficiency of stroke services, especially in remote areas.[17]

In-Hospital

This scoping review identified various systemic and operational barriers that have a significant impact on the time window for IVT. One of the main causes of in-hospital delays is the brain imaging acquisition process, particularly CT scans and advanced imaging (CTA/CTP). Mowla et al (2017) showed that patients who experience prolonged scans tend to experience treatment delays and worse clinical outcomes. Strategic solutions that have proven effective include pre-registration of patients by EMS before arrival and direct transfer to the CT table without a stopover in the ED. Simultaneous actions while the patient is on the CT table, such as neurological examination, blood glucose and INR measurement using a POC device, intravenous line insertion, and blood draw. Administer IVT bolus immediately after non-contrast CT is completed, before proceeding with CTA/CTP if necessary. Patients with low NIHSS scores or mild symptoms are more likely to experience delays in receiving IVT. This is due to the perceived urgency of the patient, although studies have shown that this group still benefits from therapy.

In addition, advanced age and comorbidities also complicate the initial assessment and prolong the decision-making process. To reduce DTN, Yuan et al (2022) and Huang et al (2018) showed that improvements in workflow, staff education, and standardized stroke management approaches resulted in significant improvements. These improvements can be achieved through the implementation of a dedicated stroke team on standby, with integrated roles among doctors, nurses, and pharmacists. Innovative administrative approaches, such as signing therapy forms before payment to avoid non-medical delays and early preparation of rt-PA before patient arrival, also shortened DTN.[67,69]

The presence of a stroke nurse in the emergency department has been shown to speed up the coordination of imaging and therapy delivery. In addition, early activation of the stroke code, based on early notification from the ambulance, can help the hospital team to prepare equipment and personnel before the patient arrives. Sharobeam et al 2020 showed that this strategy significantly reduced DTN consistently. However, access inequalities remain, with non-academic hospitals and elderly or lone patients less likely to receive stroke alert activation despite arriving by ambulance.[17]

Delays may also occur due to unrecognized stroke diagnosis, complex referral pathways, or interfacility transfers. Yuan et al (2022)[67] and Sharobeam et al (2020)[17] emphasized the importance of having fast and efficient diagnostic protocols performed by trained medical staff. They also highlighted the benefit of keeping thrombolysis kits readily available in the emergency department and skipping unnecessary lab tests before starting IVT unless the patient has a specific medical history, such as being on blood thinners.

Study Limitations

This study employed a scoping review approach, which tends to be qualitative in nature, and therefore does not provide detailed quantitative data. This limits the ability to conduct more in-depth statistical analysis and generalize the results quantitatively, including only studies published in English and Indonesian limits representativeness and may introduce language bias. It may reduce the comprehensiveness of the review and lead to an underestimation of relevant data.

Conclusion

As a result of this scoping review, the timely administration of IVT in patients with acute ischemic stroke is influenced by a wide range of factors occurring both pre-hospital arrival and in-hospital care. By mapping and synthesizing these contributing elements, this review offers deeper insights into the barriers and opportunities for improving access to IVT. The findings can serve as a foundation for developing more effective, context-sensitive strategies to ensure that stroke patients receive timely and equitable treatment.

Disclosure

The authors report no conflicts of interest in this work.

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