

Time is Brain: A Scoping Review of Barriers to Timely Thrombolysis in Ischemic Stroke

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Theme: Care processes and practices

Contributions to the field: This study contributes significantly to the understanding of the multiple barriers that compromise the opportunity for thrombolysis in the care of stroke patients. By reviewing the existing literature on the subject, the study offers a comprehensive and systematic overview of the clinical, structural, organizational, and social aspects that impact the optimal therapeutic window for the administration of thrombolytics. This approach not only identifies bottlenecks in care but also guides managers, healthcare professionals, and policymakers regarding strategic interventions. It is worth emphasizing the importance of nurses being aware of these issues, as they perform a central role from patient intake through the administration of therapy and are directly linked to clinical outcomes and the reduction of sequelae.

Abstract

Introduction: Ischemic stroke is a medical emergency that requires treatment to be initiated within the first 4.5 hours, which is the therapeutic window for alteplase to minimize the onset of severe and irreversible sequelae. Although studies on its management exist, gaps remain in the systematic analysis of the factors that explain delays in treatment. Thus, this review stands out by comprehensively mapping the barriers that compromise timely thrombolysis. **Objective:** To verify, based on the literature, the factors associated with delays in thrombolytic therapy for ischemic stroke. **Materials and Methods:** This is a qualitative, exploratory study, of the scoping review type, conducted in the Web of Science, Scopus, MEDLINE, Embase, and PubMed databases in 2025. The search and screening were conducted by two reviewers in a double-blind process using Rayyan.ai software. The process followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: Extension for Scoping Reviews, resulting in the inclusion of 30 articles. **Results:** Obstacles were identified and categorized as socio-economic conditions, geographic factors, lack of knowledge, cultural habits, health care logistics, variations in the disease's presentation, and medical history; collectively, these factors constitute barriers that hinder timely treatment and contribute to the morbidity and mortality associated with the disease. **Conclusion:** The findings highlight the importance of integrated strategies for public health education, professional training, and strengthening the logistics and infrastructure of health services. Identifying and addressing these gaps helps promote public policies that reduce morbidity and mortality and improve the population's quality of life.

Keywords (Source: MeSH)

Ischemic stroke; thrombolytic therapy; delayed diagnosis; barriers to access of health services; public health; population health.

4 El tiempo es cerebro: una revisión de alcance sobre las barreras para la trombólisis oportuna en el ictus isquémico

Resumen

Introducción: El ictus isquémico es una emergencia clínica que requiere que la persona afectada inicie el tratamiento dentro de las primeras 4,5 horas, ventana terapéutica de la alteplasa, para minimizar la aparición de secuelas graves e irreversibles. Aunque existen estudios sobre su manejo, todavía persisten brechas en la sistematización de los factores que explican los retrasos en el tratamiento. Por ello, esta revisión se diferencia por mapear de forma exhaustiva los obstáculos que comprometen la trombólisis oportuna. **Objetivo:** verificar en la literatura los factores asociados con el retraso en la terapia trombolítica en el ictus isquémico. **Materiales y método:** Este es un estudio cualitativo y exploratorio, del tipo de revisión de alcance, realizado en las bases de datos Web of Science, Scopus, MEDLINE, Embase y PubMed en 2025. La búsqueda y el cribado fueron realizados por dos revisores, en un proceso doble ciego, utilizando el software Rayyan.ai. El proceso siguió las recomendaciones del *Preferred Reporting Items for Systematic Review and Meta-Analyses extension for Scoping Reviews*, con la inclusión de 30 artículos. **Resultados:** Se identificaron obstáculos categorizados en condiciones socioeconómicas, aspectos geográficos, falta de conocimiento, hábitos culturales, logística de los servicios de salud, variación en los patrones de manifestación de la enfermedad y antecedentes de patológicos, configurándose como barreras que dificultan el tratamiento en el momento adecuado y como factores asociados con una mayor morbilidad y mortalidad por la enfermedad. **Conclusión:** Los hallazgos refuerzan la importancia de estrategias integradas de educación sanitaria para la población, la formación profesional, el fortalecimiento de la logística y la infraestructura de los servicios de salud. La identificación y el debate acerca de estas carencias contribuyen a la promoción de políticas públicas que reducen la morbilidad y mortalidad y mejoran la calidad de vida de la población.

Palabras clave (Fuente DeCS)

Accidente cerebrovascular isquémico; terapia trombolítica; diagnóstico tardío; barreras al acceso a la atención sanitaria; salud pública; salud poblacional.

Tempo é cérebro: revisão de escopo das barreiras à trombólise oportuna no acidente vascular encefálico

Resumo

Introdução: O acidente vascular encefálico isquêmico é uma emergência clínica que requer o início do tratamento nas primeiras 4,5 horas, janela terapêutica da alteplase, a fim de minimizar o surgimento de sequelas graves e irreversíveis. Apesar de existirem estudos sobre o manejo, ainda persistem lacunas na sistematização dos fatores que explicam os atrasos no tratamento. Assim, esta revisão se diferencia ao mapear, de forma ampla, as barreiras que comprometem a trombólise em tempo oportuno. **Objetivo:** verificar, na literatura, os fatores associados ao atraso da terapia trombolítica no acidente vascular encefálico isquêmico. **Materiais e método:** Trata-se de um estudo qualitativo e exploratório, do tipo revisão de escopo, realizado nas bases de dados Web of Science, Scopus, MEDLINE, Embase e PubMed em 2025. A busca e a triagem foram conduzidas por dois revisores, em processo duplo-cego, utilizando o software Rayyan.ai. O processo seguiu as recomendações do *Preferred Reporting Items for Systematic Review and Meta-Analyses extension for Scoping Reviews*, resultando na inclusão de 30 artigos. **Resultados:** Identificaram-se obstáculos categorizados em condições socioeconômicas, aspectos geográficos, falta de conhecimento, hábitos culturais, logística dos serviços de saúde, variação nos padrões de manifestação da doença e histórico de doenças, configurando barreiras que dificultam o tratamento em tempo adequado e que contribuem para a morbimortalidade associada à doença. **Conclusão:** Os achados reforçam a importância de estratégias integradas de educação em saúde para a população, capacitação profissional, fortalecimento da logística e da infraestrutura dos serviços de saúde. A identificação e a discussão dessas lacunas contribuem para a promoção de políticas públicas que reduzam a morbimortalidade e melhorem a qualidade de vida da população.

Palavras-chave (Fonte DeCS)

Acidente vascular cerebral isquêmico; terapia trombolítica; diagnóstico tardio; barreiras ao acesso aos cuidados de saúde; saúde pública; saúde da população.

Introduction

The ischemic stroke is the most prevalent type, representing approximately 65% of cases in 2021 (1). This condition is the leading cause of functional disability in everyday activities and the second leading cause of death worldwide. It is estimated that, in 2020, strokes were responsible for approximately 6.6 million deaths, according to data from the World Health Organization (WHO) (2, 3).

In light of this scenario, the importance of immediate treatment for ischemic stroke stands out as a means of preventing the onset of serious and irreversible sequelae. Recombinant tissue plasminogen activator (rt-PA), a fibrinolytic agent, is considered the first-line treatment, which requires specialized care from a multidisciplinary team, particularly from nurses, who are responsible for its preparation and administration (4).

The effectiveness of this treatment is time-dependent and requires that the patient receive treatment and medication within 4.5 hours of symptom onset, a period known as the “therapeutic window” (5). However, certain factors can delay the patient’s arrival within this timeframe, thereby compromising the treatment success. Thus, time is an essential factor that can determine the patient’s prognosis (6).

This study therefore proposes a systematic review aimed at identifying, in the literature, the factors associated with delays in thrombolytic therapy for ischemic stroke. It is hoped that this research will contribute to the understanding of this phenomenon and encourage the development of strategies to mitigate this problem.

Materials and Methods

This is a qualitative, exploratory study in the form of a scoping review, which is characterized by examining the extent, reach, and nature of scientific knowledge on a given theme (7). To develop this review, the following steps were followed, based on the methodology proposed by the Joanna Briggs Institute (JBI): Definition of the research question and objectives; definition of eligibility criteria; description of the planned approach for searching, selecting, extracting, and mapping evidence; selection of evidence; extraction of evidence; analysis of the evidence; presentation of the results; and summary of the evidence in relation to the review’s objective (8, 9). The registration protocol for this study is available at the Open Science Framework (OSF) under the title *Fatores relacionados ao atraso da terapia trombolítica do acidente vascular encefálico* (Factors Associated with Delays in Thrombolytic Therapy for Stroke) or via the Digital Object Identifier (DOI) 10.17605/OSF.IO/GEJ8U.

The process of developing the title and research question was based on the “PCC” acronym (P = population; C = concept; C = context), in line with the JBI’s methodological recommendations for scoping reviews.

In this review, the population (P) consisted of patients with ischemic stroke; the concept (C) corresponded to the barriers and factors associated with timely access to thrombolytic therapy; and the context (C) involved the healthcare services and systems within which stroke care is provided. Based on these components, the following guiding question was formulated: What are the barriers and factors associated with timely access to thrombolytic therapy in patients with ischemic stroke across varying contexts of healthcare services and systems?

To establish the identification of the studies, the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) were used to standardize the search for articles indexed in the databases. Thus, the selected DeCS terms were *AVC isquêmico*, *terapia trombolítica*, *tempo para o tratamento*, and *diagnóstico tardio*. For MeSH, the following terms were selected: *ischemic stroke*, *thrombolytic therapy*, *time-to-treatment*, and *delayed diagnosis*, combined using the Boolean operator AND. The study used free-text keywords and synonyms related to the concepts, such as *cerebrovascular accident*, *fibrinolytic therapy*, *treatment delay*, *prehospital delay*, and *door-to-needle time*, to broaden the sensitivity of the search. The following databases were used: PubMed, Scopus, MEDLINE, Embase, and Web of Science.

During the search process, the following were defined as inclusion criteria: Original studies, available in full text, with no language restrictions, published from 2012 onward that addressed the research question. The time frame was selected based on the year in which thrombolytic therapy was established in Brazil, the country of origin of the study (10). Duplicate articles, letters to the editor, reviews, and non-scientific journal editorials were excluded.

Table 1 provides a summary of the search strategies used. The complete search strategies executed in each database, including controlled descriptors, free-text keywords, search fields, Boolean operators, applied filters, and date of execution, are available in the Supplementary Material, in compliance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).

The Rayyan-Intelligent Systematic Review (Rayyan.ai) software was used to ensure the references categorization—included, excluded, or duplicates—and blinding among the reviewers. Additionally, the studies were selected independently by two reviewers during April and May 2025. Following this double-blind screening, 88.5% of the articles were excluded, 2.5% resulted in disagreement between reviewers, and 3% were included in the review by both reviewers. Disagreements that emerged during the blinded process were settled by consensus, without the need for a third reviewer.

Databases	Search Strategies
Embase	(‘ischemic stroke’/exp OR ‘ischemic stroke’) OR (ischemic AND (‘stroke’/exp OR stroke) AND (‘thrombolytic therapy’/exp OR ‘thrombolytic therapy’) OR (thrombolytic AND (‘therapy’/exp OR therapy) AND (‘delayed diagnosis’/exp OR ‘delayed diagnosis’ AND (‘diagnosis’/exp OR diagnosis)
MEDLINE	(ischemic stroke OR cerebrovascular accident) AND (thrombolytic therapy OR fibrinolytic therapy) AND (time to treatment OR treatment delay OR delayed diagnosis)
PubMed	(“Ischemic Stroke” OR “cerebrovascular accident” OR “ischemic stroke”) AND (“Thrombolytic Therapy” OR “fibrinolytic therapy” OR “thrombolytic therapy”) AND (“Time-to-Treatment” OR “treatment delay” OR “delayed diagnosis”)
Scopus	TITLE-ABS-KEY (“ischemic stroke” OR “cerebrovascular accident”) AND TITLE-ABS-KEY (“thrombolytic therapy” OR “fibrinolytic therapy”) AND TITLE-ABS-KEY (“time to treatment” OR “treatment delay” OR “delayed diagnosis”)
Web of Science	(“ischemic stroke” OR “cerebrovascular accident”) AND (“thrombolytic therapy” OR “fibrinolytic therapy”) AND (“time to treatment” OR “treatment delay” OR “delayed diagnosis” OR delay)

Source: Prepared by the authors.

Data analysis was conducted using thematic analysis, following subsequent steps: (i) a cursory review of the included studies; (ii) identification of texts related to factors causing delays in thrombolytic therapy; (iii) coding of the findings; and (iv) grouping into thematic categories. The categories were discussed among the reviewers until consensus was reached, ensuring greater reliability in the interpretation of the data.

Data extraction was performed using a standardized matrix developed by the researchers in Microsoft Excel, containing information related to study identification (title, author, year, and country of publication), methodological characteristics (study type and sample), and main results regarding factors associated with delays in thrombolytic therapy in patients with stroke. Data extraction was conducted independently by previously trained reviewers, with a pilot test of the instrument performed to adjust and standardize the criteria. Any discrepancies identified were discussed among the reviewers and, when necessary, settled by consensus. To ensure the consistency of the collected information, the extracted data were cross-checked, and a final review of the matrix was conducted prior to the results synthesis stage.

The extracted data were synthesized using qualitative thematic analysis, combined with a narrative synthesis of the findings. Initially, the results of the studies were organized and compared, which allowed for the identification of patterns and recurrences, which were then grouped into categories developed based on the evidence.

The factors associated with delays in thrombolytic therapy identified in the studies were recorded individually and organized into preliminary categories based on their characteristics and conceptual similarities. These initial categories were then compared and grouped into broader thematic categories, which represent the main determinants of treatment delay described in the literature.

This process resulted in the final categories related to socioeconomic, cultural, and geographic factors, as well as knowledge gaps, organizational and logistical aspects of healthcare services, clinical manifestations, and patients' preexisting conditions. The categorization was performed independently by the researchers, with any discrepancies being discussed until consensus was reached to ensure the analytical consistency and reliability of the resulting synthesis. The variables extracted from the included studies comprised: Title, author, year of publication, country where the study was conducted, study type, sample characteristics, and main results related to treatment delays.

Since this is a systematic review based exclusively on secondary data available in the literature, this study did not include the direct participation of human subjects; therefore, submission to a research ethics committee was not required.

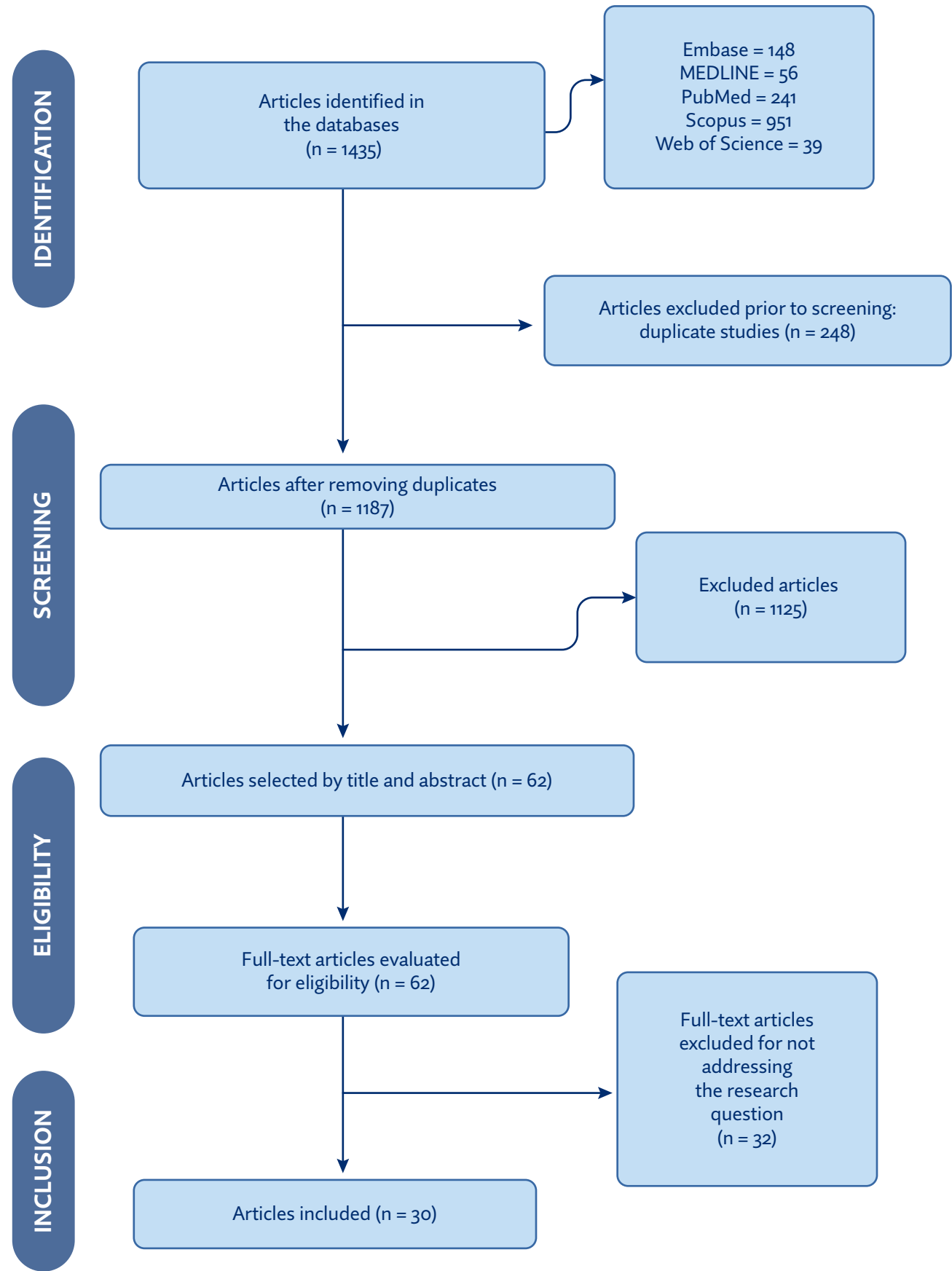
Results

The search identified 1435 articles, of which 248 were removed for being duplicates. Subsequently, the remaining 1187 articles underwent title and abstract screening. At this stage, 1125 articles were excluded for not meeting the established criteria, resulting in 62 articles selected for full-text reading. During this analysis, 32 of these articles were excluded for not directly addressing the proposed research question. Finally, after a rigorous selection process, 30 articles were deemed suitable to comprise the sample, as shown in Figure 1, which illustrates the flowchart with the PRISMA-ScR guidelines.

The studies included in the review were published between 2012 and 2023, with a prevalence of publications in 2016 and 2023, each year comprising a sample of six articles. Regarding country of origin, 19 nationalities were identified, with the United States of America standing out with seven publications. Regarding the study populations, sample sizes varied, ranging from a minimum of 21 patients to a maximum of 27778 patients; longitudinal data analysis was the most common method, used in 16 studies.

The summary of the studies' characteristics is briefly described in Table 2, grouped by title, authors, publication year/country, study type/sample, and results.

Figure 1. PRISMA Flowchart: Search and Selection Process for Studies in the Literature to be Included in the Scoping Review. Crato, Ceará, Brazil, 2025



Source: adapted from Page MJ et al. (11).

Table 2. Summary of the Selected Studies. Crato, Ceará, Brazil, 2025

Title	Authors	Year/ Country	Type of study/sample	Results
Impact Of Emergency Department Transitions of Care on Thrombolytic Use in Acute Ischemic Stroke	Madej-Fermo OP et al. (12)	2012 United States	Observational, longitudinal, retrospective study with 3133 patients	Admissions during shift changes and night shifts.
Barriers To the Use of Intravenous Tissue Plasminogen Activator for In-Hospital Strokes	Bunch ME et al. (13)	2012 United States	Observational, longitudinal, retrospective study with 79 patients	Delay in diagnosis, and failure by the hospital team and the family to recognize the symptoms.
Analysis Of Barriers to the Use of Thrombolytics in Ischemic Stroke in a Private Hospital in Rio De Janeiro, Brazil	Fonseca LHD et al. (14)	2013 Brazil	Observational, retrospective cohort study with 257 patients	Failure to recognize the symptoms and choosing to wait for the symptoms to improve and for the private medical doctor's office to open.
Reasons For Low Thrombolysis Rate in a Norwegian Ischemic Stroke Population	Faiz KW et al. (15)	2014 Norway	A prospective, cross-sectional observational study with 290 patients	Failure to recognize the symptoms of the stroke, choosing to wait for the symptoms to improve, and waiting for the family's medical doctor's office to open.
Eligibility Assessment for Intravenous Thrombolytic Therapy in Acute Ischemic Stroke Patients; Evaluating Barriers for Implementation	Ayromlou H et al. (16)	2014 Iran	Observational, cross-sectional, prospective study with 647 patients	Delays in CT [†] scans and laboratory tests, and financial constraints on treatment.
Poor Recognition of Prompted Treatment Seeking Even with Good Knowledge of Stroke Warning Signs Contribute to Delayed Arrival of Acute Ischemic Stroke Patients in Thailand	Muengtaweepongsa S (17)	2014 Thailand	Observational, cross-sectional, prospective study with 181 patients	Mild symptoms, and failure to recognize the request for treatment.
Hospital Arrival Time and Functional Outcome after Acute Ischaemic Stroke: Results from the PREMIER Study	León-Jiménez C et al. (18)	2014 Mexico	Observational, longitudinal, retrospective study with 1096 patients	Illiteracy, appointment at a public hospital without treatment, and stroke associated with a lacunar <i>ictus</i> .
Time of Presentation of Stroke Patients for Ct Imaging in a Nigerian Tertiary Hospital	Ogbole GI et al. (19)	2015 Nigeria	Observational, longitudinal, retrospective study with 271 patients	Patients' lack of stroke knowledge, delayed neuroimaging results, and a deficient referral and transportation system.
Impact of a Direct-Admission Stroke Pathway on Delays of Admission, Care, And Rates of Intravenous Thrombolysis	Mouthon-Reignier C et al. (20)	2016 France	Prospective longitudinal observational study with 81 patients	Reduced nursing teams and a shortage of medical doctors in the emergency department; shortage of personnel during their shifts; direct transfers of patients with suspected strokes without a medical examination; and overcrowding of hospital beds.
Older Stroke Patients with High Stroke Scores Have Delayed Door-To-Needle Times	Birnbaum LA et al. (21)	2016 *United States	Observational, longitudinal, retrospective study with 652 patients	Delays in decision-making by families when the patient is unable to participate in the decision-making process, and difficulty obtaining information from caregivers regarding the onset of symptoms.

Title	Authors	Year/ Country	Type of study/sample	Results
The Influence of Emergency Department Crowding on the Efficiency of Care for Acute Stroke Patients	Tsai MT et al. (22)	2016 Taiwan	Observational, retrospective cohort study with 1142 patients	Overcrowding in the emergency room and reduced nursing team.
Factors Associated with Delay In Presentation To the Hospital For Young Adults with Ischemic Stroke	Leung LY, Caplan LR (23)	2016 United States	Observational, retrospective cohort study with 141 patients	Diabetes mellitus, single marital status, and unemployed.
Factors Influencing Nonadministration of Thrombolytic Therapy in Early Arrival Strokes in a University Hospital in Hyderabad, India	Pidaparathi L et al. (24)	2016 India	Observational, longitudinal, prospective study with 2593 patients	Delay in referral to a neurologist by the emergency medical team and unaffordable treatment cost.
Delay In Diagnosis of Basilar Artery Stroke	Burns JD et al. (25)	2016 United States	Observational, case-control, retrospective study with 21 patients	Lack of focal signs and symptoms in basilar artery stroke that are indicative of other syndromes, and delayed recognition of the stroke by patients and their families.
Factors Delaying Management of Acute Stroke: An Indian Scenario	Abraham S et al. (26)	2017 India	Observational, longitudinal, retrospective study with 361 patient visits	Victims' lack of stroke knowledge, delays in the patient admission process, long distances between the stroke unit and the CT scan room, and unaffordable treatment costs.
Delays In Door-To-Needle Times and Their Impact on Treatment Time and Outcomes in Get with the Guidelines-Stroke	Kamal N et al. (27)	2017 United States	Observational, longitudinal, retrospective study with 27778 patients	The medical team's inability to determine eligibility, and delays in the diagnostic evaluation for other conditions such as hypoglycemia, hypertension, and seizures.
Status Of Prehospital Delay and Intravenous Thrombolysis in the Management of Acute Ischemic Stroke in Nepal	Nepal G et al. (28)	2019 Nepal	Observational, longitudinal, prospective study with 227 patients	Failure of healthcare professionals to recognize strokes, heavy traffic along the route, distance greater than 20 km, diabetes mellitus, and patients' low income.
Late Hospital Arrival for Thrombolysis After Stroke in Southern Portugal: Who Is at Risk?	Sobral S et al. (29)	2019 Portugal	Observational, case-control, retrospective study with 1247 patients	Lack of resources and stroke knowledge, and difficulties in requesting immediate medical assistance.
Pre-Hospital Delay in Patients with Acute Ischemic Stroke in a Multicenter Stroke Registry: K-PLUS	Nagao Y et al. (30)	2020 Japan	Observational, longitudinal, prospective study with 5102 patients	Debilitating illnesses prior to symptom onset; diabetes mellitus; currently smoking; dementia; and symptom onset between 12:00 a.m. and 6:00 a.m.; symptom onset at home.
Time Of Arrival and In-Hospital Evaluation Processes Among Patients with Acute Ischemic Stroke at Yozgat City Hospital in Turkey: A Retrospective Study	Onder H (31)	2020 Turkey	Observational, longitudinal, retrospective study with 87 patients	Inefficient ambulance use for patient transfers between hospitals and delays in receiving imaging and lab test results.
Delayed Stroke Treatment During COVID-19 Pandemic in China	Gu S et al. (32)	2021 China	Observational, longitudinal, retrospective study with 252 patients	Fear of being infected with SARS-CoV-2, lower level of education, rural residence, mild symptoms due to small-vessel ischemic stroke, and patients transported by means other than an ambulance.

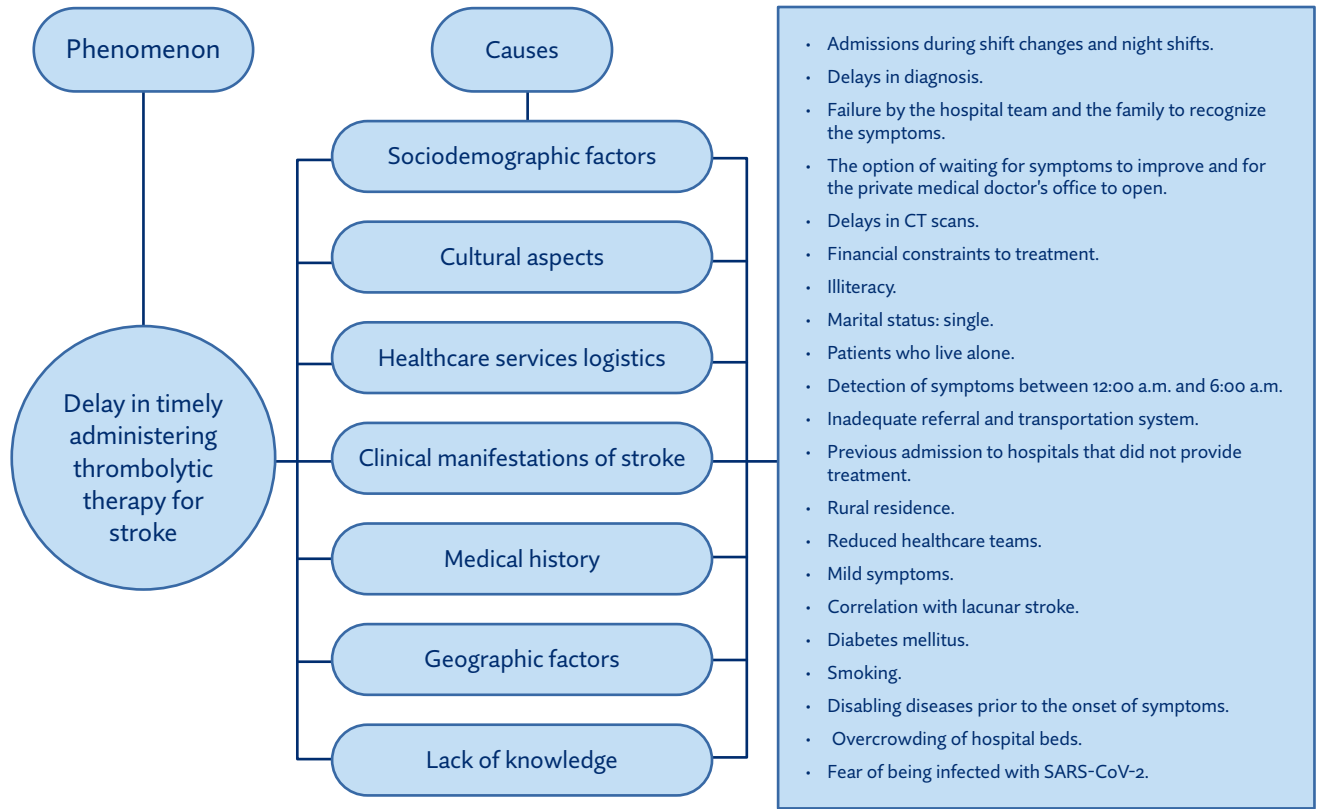
Title	Authors	Year/ Country	Type of study/sample	Results
Pre-Hospital Causes for Delayed Arrival in Acute Ischemic Stroke Before and During The COVID-19 Pandemic: A Study at Two Stroke Centers in Egypt	Aref, HM et al. (33)	2021 Egypt	Observational, cross-sectional, prospective study with 254 patients	Previous admission to hospitals that did not provide treatment, failure to recognize the urgency of a stroke, onset of symptoms during sleep, and fear of SARS-CoV-2 infection.
Pre-Hospital Delay in Acute Ischemic Stroke Care: Current Findings and Future Perspectives in a Tertiary Stroke Center from Romania—A Cross-Sectional Study	Terecoasă EO et al. (34)	2022 Romania	Observational, cross-sectional, prospective study with 770 patients	Transportation to the hospital by personal means and patients who live alone and reside in rural areas.
Delays in the Identification and Assessment of In-Hospital Stroke Patients	Cummings S et al. (35)	2022 India	Observational, retrospective cohort study with 97 patients	Failure of the healthcare team to recognize symptoms during sedation.
Time To Ct Scan Imaging After Symptom Onset Among Ischemic Stroke Patients Presenting to a Quaternary Hospital in Ghana	Duodu F et al. (36)	2023 Ghana	Observational, cross-sectional, prospective study with 114 patients	Late CT scan requests; delays by healthcare professionals in transporting the patient for the exam, financial constraints, unavailability of a CT scanner, and lack of radiologists.
Pre-And In-Hospital Delays in the Use of Thrombolytic Therapy for Patients with Acute Ischemic Stroke in Rural and Urban Egypt	Nasreldein A et al. (37)	2023 Egypt	Observational, retrospective cohort study with 618 patients	Delay in seeking help, initial misdiagnosis, presentation at hospitals not equipped to treat stroke, living in rural areas, and prolonged laboratory testing.
Factors Affecting the Delay of Intravenous Thrombolysis in Hyperacute Ischemic Stroke Patients: A Single Centre Study	Amalia L (38)	2023 Indonesia	Observational, retrospective cohort study with 141 patients	Hypertension, dyslipidemia, low NIHSS score, older patients, and young patients with mild symptoms.
The Effects of the Coronavirus Disease Pandemic on Intravenous Thrombolytic Therapy Among Patients with Acute Ischemic Stroke in Dalian, China	Pan X et al. (39)	2023 China	Observational, longitudinal, retrospective study with 1719 patients	Delays in admission, and epidemiological history assessments and screening of patients requiring prolonged hospitalization during the pandemic.
Reasons Withholding Intravenous Thrombolysis for Acute Ischemic Stroke in an Indonesian Tertiary Center	Situmeang RFV et al. (40)	2023 Indonesia	Observational, longitudinal, retrospective study with 207 patients	Delays in seeking care, lack of knowledge regarding stroke, waiting for spontaneous improvement, and lack of companions.
In-Hospital Emergency Treatment Delay Among Chinese Patients with Acute Ischaemic Stroke: Relation to Hospital Arrivals and Implications for Triage Pathways	Yang H et al. (41)	2023 China	Observational, longitudinal, retrospective study with 1276 patients	Lack of social health insurance; delays in the interpretation of imaging tests; distance between the stroke treatment unit and the CT scan room; and limited availability of services during night shifts.

Note: CT† Computed Tomography; NIHSS‡ National Institutes of Health Stroke Scale.

Source: Prepared by the authors.

To better understand the discussion, the results were grouped into the following categories: Sociodemographic factors, geographic factors, lack of knowledge, cultural aspects, healthcare services logistics, clinical manifestations of ischemic stroke, and history of previous diseases, as shown in Figure 2.

Figure 2. Summary of Factors Related to Delays in Thrombolytic Therapy for Stroke



Source: Prepared by the authors.

Discussion

The studies analyzed show that socioeconomic factors contribute significantly to delays in the administration of thrombolytic therapy. One study highlights that unemployment and low income are conditions found primarily in countries where medical services and access to thrombolytic therapy are not provided free of charge, depriving patients of the necessary treatment (28). Meanwhile, another study identified a higher incidence of stroke in low-income populations compared to higher-income groups, suggesting that difficulties in accessing treatment and gaps in primary prevention measures in these populations explain this finding (42).

This phenomenon reflects the problem of social inequality that permeates health care services, characterized by differences in the care referrals of individuals from varying socioeconomic backgrounds when seeking medical care (43). This reality tends to escalate due to the rising number of chronic disease diagnoses, especially among low-income groups. This is likely due to a lack of

access to healthy lifestyle habits, such as regular physical activity and a balanced diet (44).

Another aspect of socioeconomic factors with significant implications is patients' level of education. Another study found that illiteracy and having less than six years of education influenced victims' decisions to seek medical care, affecting their ability to arrive at the healthcare facility within the therapeutic window. The literature highlights that the higher the level of education, the greater the chances of accessing information related to risk factors for serious diseases (45). This context characterizes functional health literacy, as defined by the WHO, as a social determinant that influences an individual's health. Therefore, poor literacy leads to difficulties in utilizing preventive services and low adherence to recommended treatments (46, 47).

When stroke symptoms appear, it is essential to have a companion present to assist the patient. When this is not possible, there may be significant delays in thrombolytic treatment. One study identified this phenomenon primarily among patients who are single or live alone (23). This condition can affect communication and/or frequent interactions with others regarding their health status (48), whether to detect symptoms or to call emergency services.

This situation tends to worsen in older people. As people age, they generally face physical limitations and debilitating health conditions, which can impair their ability to make quick decisions when the first symptoms appear. This condition contributes to a lack of health care, increased exposure to household accidents, and social isolation, hindering their ability to seek emergency care, as in the case of stroke (49).

Furthermore, it is worth noting that a lack of knowledge among patients, family members, or healthcare professionals may contribute to delays in thrombolytic therapy. Information regarding risk factors, symptoms, management, and treatment of stroke victims remains unknown to a large portion of the population (50). This reality can be explained by the low adherence to educational resources related to stroke that are made available to the public (51). Therefore, to promote a change in the population's risk behavior, it is necessary for people to have information regarding stroke, particularly regarding the identification of early symptoms.

This knowledge deficiency is also found in healthcare professionals, particularly when treatment is discussed, thus highlighting a failure in the dissemination of technical and scientific information regarding stroke. This is alarming and indicates a gap in the training of many healthcare professionals. Corroborating this assertion, a study assessed the level of knowledge among medical students. Of all participants, only 72.9% had moderate knowledge regarding stroke (52). These data highlight potential

weaknesses in higher education in essential areas. Given this, it is essential to promote educational interventions that improve the quality of training for healthcare professionals.

Continuing with the issue of delays in thrombolytic therapy, geographic factors also emerge in the literature as significant obstacles. Living in isolated regions such as rural areas, which are often distant from emergency services, has negatively affected patient management. Generally, ambulance networks are established in urban centers, compromising admission within the first 4.5 hours (26, 53).

Regarding cultural aspects, certain behaviors adopted by the population may impact diagnosis and treatment. Among these behaviors are sleep habits, a preference for appointments with a single healthcare provider, and a reluctance to visit public spaces, as was the case during the COVID-19 pandemic (54). When symptoms arise during sleep, it is not possible to precisely determine when they started, which affects the parameters of the therapeutic window. Furthermore, initially seeking out a specific medical doctor before seeking emergency care can delay treatment, which reflects a hesitation based on the belief that private services offer more effective solutions (55).

During the COVID-19 pandemic, fear of contracting the disease contributed to delayed requests for care in cases where stroke symptoms appeared, as people hoped for spontaneous improvement. Consequently, lockdown measures and the strain on emergency departments hindered access to treatment within the therapeutic window (56, 57).

Another highlighted factor involves aspects related to the logistics of health care services. Personnel shortages and delays in obtaining imaging results, such as from computed tomography (CT) scans, are the main causes of delays in the in-hospital diagnosis of ischemic stroke (58, 59). Furthermore, the distance between the CT scan room and the stroke unit requires patients to be transported to other sectors. A study conducted in Switzerland emphasized that a greater distance between the stroke unit and the CT scan room results in delays in diagnosis and, consequently, in the emergency treatment of ischemic stroke. Furthermore, the reduced number of nursing professionals impairs patient care (60).

Even in high-income countries, recurring problems with the organization of services have been identified, such as gaps in care pathways, delays in testing, and difficulties in the early recognition of symptoms, both by healthcare professionals and patients. Furthermore, studies show that, in countries with lower levels of economic development, challenges related to geographic access and transportation to healthcare services are more significant, constituting an important factor contributing to prehospital delays. Thus, the barriers to timely thrombolysis are multifactorial in nature and cross-cutting across various socio-regional contexts, varying more in intensity and nature than in their presence.

Still on the topic of logistics, the admission of patients to other healthcare facilities before reaching the referral center hinders the implementation of thrombolytic therapy. This process can be time-consuming, especially in remote areas or at small-scale hospitals, where emergency transportation may not be immediately available (61, 62). Therefore, it is essential to educate the population on where to seek help and how to access treatment services.

Other obstacles, such as the varying patterns of disease presentation, have been identified as factors that can lead to delays in treatment. When a stroke presents in a mild form or as a lacunar stroke, nonspecific symptoms such as nausea, dizziness, and general malaise commonly arise, which may lead healthcare professionals to confuse these signs with other syndromic conditions. Furthermore, patients tend not to realize the severity of the situation and do not seek immediate help, waiting for spontaneous improvement (63), which hinders diagnosis and, consequently, the timely administration of treatment.

Regarding medical history, individuals with diabetes mellitus, systemic hypertension, and a history of smoking warrant special attention, as they are at higher risk for developing a stroke. This is particularly true for dizziness and loss of balance, which can delay the decision to seek medical care, since patients may be accustomed to these clinical signs (64, 65).

Furthermore, as highlighted by one of the studies, neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, and some types of dementia can hinder the detection of symptoms (30). It is common for patients to become unable to express or fail to manifest the classic symptoms of a stroke due to physical and cognitive impairment, which also interferes with timely and effective intervention (66, 67).

In light of this scenario, the findings of this review have important implications for nursing practice at varying levels of health care. In community and primary care settings, nurses conduct educational initiatives aimed at the early recognition of stroke signs and symptoms, particularly among vulnerable populations, individuals with low levels of education, and those with chronic diseases.

In the prehospital setting, nurses implement screening and referral protocols, helping to reduce the time between the onset of symptoms and arrival at specialized care facilities, while in the hospital setting, they identify suspected cases early, coordinate care pathways, facilitate communication among multidisciplinary teams, and monitor time-related indicators for thrombolytic therapy. Thus, nursing-led interventions contribute significantly to reducing delays in treatment and expanding access to timely care.

Thus, the role of nursing becomes even more strategic, since many of the identified factors, such as failures in recognizing symptoms, the organization of the care pathway, and intra-hospital response time, are directly related to care practices. By participating in screening, the early identification of stroke, and the timely provision of care, nurses play an important role in improving patients' clinical outcomes.

Collectively, it is clear that there is an urgent need to improve the infrastructure and logistics of healthcare facilities to ensure timely access for patients from varying socioeconomic backgrounds and regions. Meanwhile, educational interventions are essential to improve the technical training of healthcare professionals and students. There is also a need for studies comparing the factors associated with delays in thrombolytic treatment across varying socioeconomic contexts, enabling the implementation of strategies suited to regional specificities and local needs.

This study presents some limitations that should be considered, such as the prevalence of studies conducted in high-income countries, which may limit the applicability of the data to low- and middle-income country contexts, where health systems have different levels of organization and access. Furthermore, as this is a scoping review, the methodological quality of the included studies was not assessed, which may affect the robustness of the synthesized evidence.

Conclusion

The results presented and discussed show that socioeconomic, cultural, and geographic factors; knowledge gaps; the structure of health care services; atypical clinical presentations; and preexisting conditions can significantly influence delays in the time of arrival and treatment of stroke patients.

Therefore, optimizing patient flow in referral hospitals, providing specialized training for medical doctors working in the emergency department, and expanding public awareness and education campaigns on the importance of seeking care at referral facilities can help reduce the time it takes for patients to arrive at the hospital, thereby preserving the therapeutic window for thrombolytic therapy and improving patients' quality of life. In addition, the identified factors may guide future research toward a better understanding and the development of strategies aimed at improving clinical practice related to the early treatment of ischemic stroke.

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